32nd Annual

EVMS Research Day

Virtual Program
Friday, October 16, 2020

32nd Annual EVMS Research Day
October 16, 2020
Timeline of Virtual Events

Connection information and more on the Research Day Website:

https://www.evms.edu/research/research_day/

Oral Presentations

Opening Remarks

12:00-12:10 PM Dr. David Mu, EVMS Research Advisory Committee Co-Chair
Dr. Richard Homan, EVMS President, Provost, and Dean
Dr. William Wasilenko, EVMS Vice Dean for Research
Dr. Eva Forgacs-Lonart, EVMS Research Advisory Committee Co-Chair

Invited Speaker

12:10-1:00 PM Dr. Paul Marik
EVMS Professor of Medicine, EVMS Chief of Pulmonary & Critical Care Medicine
COVID-19: A Clinician's Perspective
Viewers may submit questions using the chat feature

Platform Presentations

Viewers may submit questions using the chat feature – Include Speaker's name first

1:00-1:13 PM Manasa Vallabhaneni, MD 2023 Student
Changes in Liver Macrophage Subtypes Following Sleep Fragmentation in a Mouse Model of NASH
Mentor: Anca Dobrian, PhD

1:13-1:26 PM James Lau & Saivarshith Peddireddy, MD 2022 Students
Anti-Platelet Therapy and Cognitive Function Outcome
Mentor: Hamid Okhravi, MD

1:26-1:39 PM Kendall Howard, MD 2023 Student
In-Vivo Preclinical Model of Glioblastoma Multiforme Induced Seizures
Mentor: Alberto Musto, MD, PhD

1:39-1:52 PM Jinbum Dupont, Medical Masters 2021 Student
BLZ945 Depletion of Perivascular Macrophages in Acute SIV-infected Macaque Brain
Mentor: Woong-Ki Kim, PhD

1:52-2:05 PM Alina Moriarty, Biomedical Sciences PhD 2025 Student
Prolonged Sleep Fragmentation Amplifies Atherosclerosis and Destabilizes Plaques
Mentor: Elena Galkina, PhD

2:05-2:18 PM Tamar Matitashvili, MD, Reproductive Endocrinology and Infertility Fellow
Extracellular Vesicle's miRNA Cargo in Follicular Fluid as Predictor of Oocyte Maturation in Infertile Patients
Mentor: Anca Dobrian, PhD and Laurel Stadtmauer, MD, PhD

Short Break, Switch to Breakout Session Links

2:18-2:30 PM

Continued on page 3

"Live" Poster Question & Answer (Q&A) Virtual Breakout Sessions

2:30-4:30 PM in 20-minute periods (in 6 different concurrent "Room" links)
Over 130 pre-recorded video poster presentations from EVMS students, residents, and fellows are available for viewing prior to Research Day. After watching a presentation, viewers should make a list of any questions about the research and then attend these live virtual sessions to ask their questions of the poster presenters. There will be six different 20-minute Poster Q&A periods occurring in six different BlueJeans virtual meeting spaces concurrently ("Rooms" A-F), for a total of 36 different breakout sessions. Four presenters have been assigned to each session space. Assignments and room links can be viewed on the **Research Day website**.

Watch the Room A Q&A session from Research Day 2020

Watch the Room B Q&A session from Research Day 2020

Watch the Room C Q&A session from Research Day 2020

Watch the Room D Q&A session from Research Day 2020

Watch the Room E Q&A session from Research Day 2020

Watch the Room F Q&A session from Research Day 2020

Short Break; Switch Back to Large Session Link
4:30-4:35 PM

Presentation of Poster Awards and Closing Remarks

4:35-4:45 PM

Awards from the Vice Dean for Research and Vice Dean for Academic Affairs
Dr. Eva Forgacs-Lonart, EVMS Research Advisory Committee Co-Chair

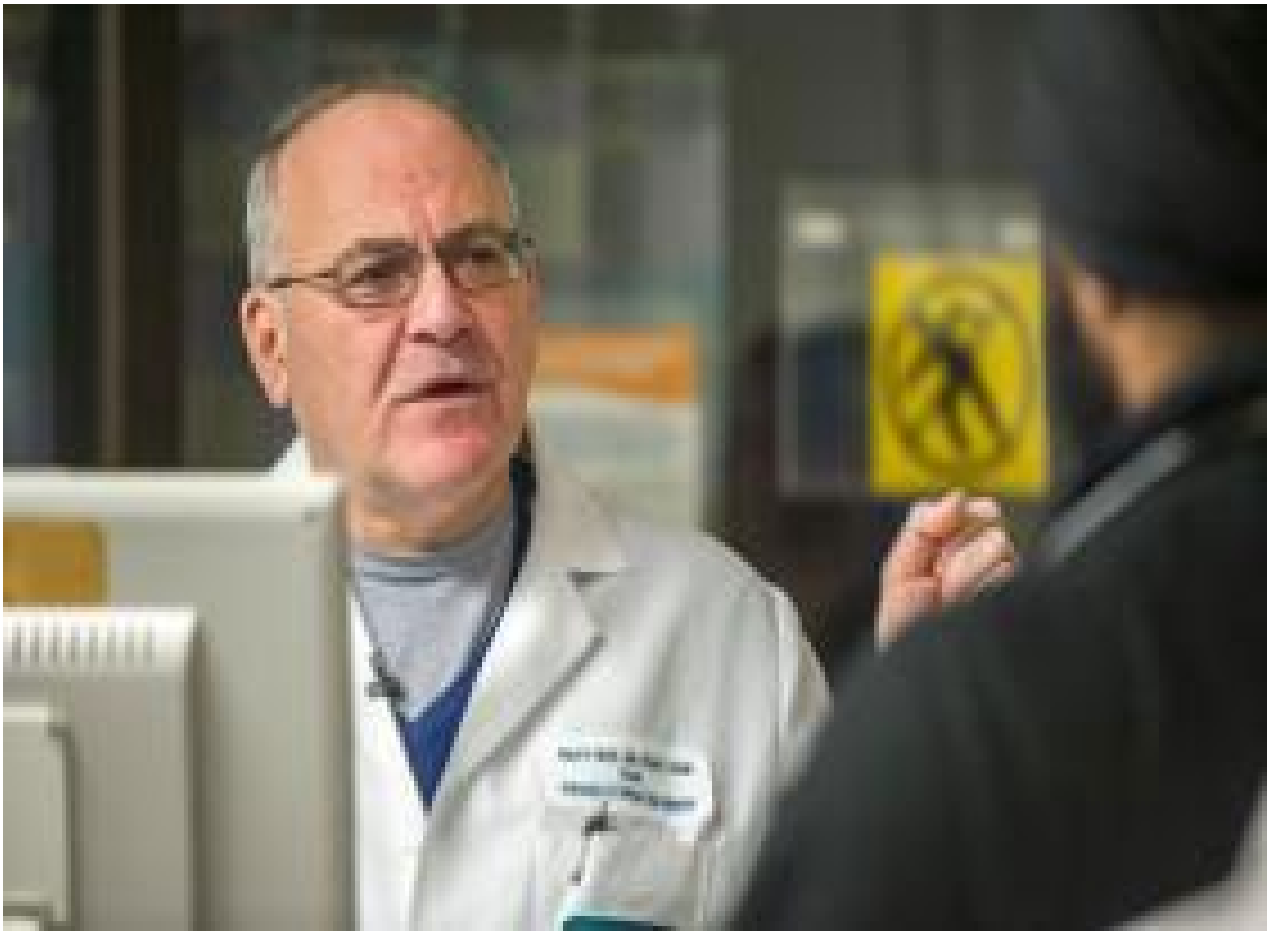
EVMS Medical Master's Program Poster Awards
Dr. Deborah Damon, Director, EVMS Medical Master's Program

EVMS Biomedical Sciences Programs Poster Awards
Dr. Anca Dobrian, Director, EVMS Biomedical Sciences Graduate Programs

EVMS Master of Public Health Program Poster Awards
Dr. Glenn Yap, Assistant Professor, EVMS Master of Public Health Program

2020
KEYNOTE LECTURE

COVID-19: A Clinician's Perspective



Paul Marik, MD, FCCP, FCCM

EVMS Foundation Distinguished
Professor in Internal Medicine
EVMS Chief of Pulmonary
& Critical Care Medicine

POSTER PARTICIPANTS

** Platform Presentation

**** Platform Presentation**

Abstract Title: Using AI and simulation modeling to identify new risk factors for autoimmune pemphigous lesions.

Investigator(s): Waleed Adawi, Candler Clawson, Jamie Geraghty, Nicole Crofton, Justin Zaremba, Tayab Waseem PhD
Department(s): Eastern Virginia Medical School, CAIAC

Abstract

INTRODUCTION:
The initiative CAIAC has created a knowledge acquisition and decision-making platform that generates derivative assets while maintaining privacy and intellectual property. As a proof of principal concept multiple research projects regarding COVID and non-COVID data were launched to generate new insights between health, economic, and social domains. Here, we will show how an integrated data platform with unified data sets can generate new knowledge and insights for disease processes. We will be using the database to determine the most predictive risk and prognostic factors for autoimmune pemphigous lesions, namely bullous pemphigoid (BP) and pemphigous vulgaris (PV), which have among the highest mortality rates of all cutaneous pathologies.

METHODS:
With partnerships across the various multilaterals, CAIAC has unfederated access to over 100 disparate data sources across the globe. The data sources contain information across multiple domains and include data regarding patient demographics, comorbidities, treatments, DEA data, vaccination status, occupation, clinical trial data, genomic sequencing data, state and national policy data, mobility and movement data via apple and google across categories of places and geospatial data via Planet, among other relevant parameters.

RESULTS:
Using ML and computer simulation methods we are looking to find new potential social determinants of health for the development and mortality of BP and PV. The anticipated results can not only help public health officials and policy makers effectively reduce the incidence of pemphigus lesions, but also address how socioeconomic factors contribute to disease onset. We anticipate that lower socioeconomic status will be positively correlated with disease onset and negatively associated with disease resolution. Further, we anticipate that geographic and environmental data fed into the system will identify new risk factors not previously known to be linked to BP and PV.

CONCLUSION:
Using the associations between prognostic variables determined by CAIAC data sourcing, we plan to develop categorical risk factors for patient who develop autoimmune pemphigus lesions. These risk factors can help develop identify at risk patients and ideally lead to policies that will reduce the incidence of disease.

Abstract Title: Stressor Controllability and the Regulation of Fear Memory, Neuroimmune Signaling, and Sleep

Investigator(s): Austin M. Adkins, Laurie L. Wellman, Larry D. Sanford
Department(s): Sleep Research Laboratory; Department of Pathology and Anatomy

Abstract

INTRODUCTION
Stress can induce neuroinflammation, which along with disrupted sleep, are symptoms implicated in a number of fear- and anxiety-based psychiatric disorders. Fear memories associated with stress can persistently resurface and inappropriately produce these symptoms. Our previous studies have demonstrated differential effects of stressor controllability on sleep following stress and fear memory recall using a yoked shuttlebox paradigm based on escapable (ES) and inescapable (IS) footshock. In this study, we determined how fear memories associated with ES and IS impact the neuroinflammatory response and its relationship to sleep.

METHODS
Twenty-seven C57BL/6 mice were implanted with telemetry transmitters for recording sleep, body temperature, and activity, and divided into four groups. On days 1 and 2, ES and IS groups were shock trained (ST) (20 footshocks, 0.5 mA, 5.0 s max. duration, 1 min intervals; the ES mouse could behaviorally terminate the footshock; the IS mouse could not). The mock trained (MT) group was exposed to the shuttlebox on days 1 and 2, but not shocked. On day 7, groups were re-exposed to the shuttlebox without shock (CTX) to assess the effects of fear memory. Animals were video recorded during all three training days to score freezing behavior, a measure of behavioral fear in rodents. The home cage (HC) control group remained in their cage for the entirety of the study. Sleep was recorded following training on days 1, 2, and 7 for all groups. Following CTX, mice were perfused with PBS, their brains extracted, and regions of interest (amygdala [AMY] and hippocampus [HPC]) microdissected and stored in RNAlater at -80°C. RNA was then isolated from these regions and mRNA expression levels of inflammatory gene markers were measured using NanoString inflammatory panels. Fold changes in transcript levels were determined relative to basal levels detected in HC mice.

RESULTS
No differences were found in freezing behavior and body temperature between groups. However, ES produced increases in sleep and IS produced decreases in sleep following ST and CTX. Furthermore, ES animals showed decreased mRNA expression of genes involved in inflammation, cellular damage, and protein aggregation, and increased expression of neuroprotective genes following CTX. IS animals showed increased mRNA expression of genes involved in inflammation, cellular damage, and protein aggregation, and decreased expression of neuroprotective genes following CTX.

CONCLUSION
Sleep regulatory and immune signaling pathways communicate and are influenced by fear and stress systems, though the precise mechanisms mediating their relationship is unclear. Stressor controllability differentially influences fear memory responses in the sleep and neuroimmune systems, even though some major indices of stress and behavioral fear (freezing and temperature) are virtually identical. These differences suggest that changes in sleep and neuroinflammation could serve as indices for better understanding how fear- and anxiety-based psychiatric disorders develop and persist throughout life.

Abstract Title: Isolation, Identification, and antibiotic sensitivity patterns of pathogenic bacteria at Muhimibili National Hospital (MNH) in Tanzania

Investigator(s): Ahmad Al-Husseini

Department(s): Georgetown University Department of Global Health

Abstract

INTRODUCTION: Neonatal deaths represents one of the greatest challenges to Tanzania's health outcomes, as MDG 4 of reducing infant deaths by two-thirds was one of the few goals the country failed to meet by 2015. Neonatal sepsis, bacterial infections present the bloodstream, accounts for 30% of all infant deaths in Tanzania. These infections are either spread via the birth canal or placenta during childbirth from mother to baby, or are nosocomial and a result of the environment. Past studies at Muhimibili National Hospital (MNH) found a sepsis-positivity rate of around 20%, with the most common organisms being Staph Aureus, Coagulase-Negative Staph, Klebsiella and E.Coli.

METHODS: Neonatal blood samples sent to the MNH Central Pathology Microbiology Lab were determined positive or negative for bacterial presence using a Bactex FX40 machine. All positive samples were then cultured on chocolate, blood, and McConkey's Agar media and incubated for 24 hours. Bacterial colonies were then gram-stained to determine if they were gram-positive or gram-negative. Gram positive bacterial identification was done using catalase and coagulase biochemical tests whereas gram negative bacterial identification required API20E biochemical identification strips. Upon identification, bacterial samples were prepared for antibiotic susceptibility testing by being plating on Muller-Hinton agar and antibiotic disk placement. After incubation for 24 hours, zones of inhibition were measured for determination of antibiotic susceptibility. Lastly, patient records were accessed and important clinical factors such as birth weight, gestational age, C-reactive protein levels, apgar score, antibiotic usage, maternal age, gravida, and para were collected for analysis.

RESULTS: Of 156 neonates admitted between September 15 and October 31 presenting with symptoms of sepsis, 103 were confirmed positive for bacterial presence indicating a 66% positivity rate. 17 unique species of bacteria were isolated and identified from neonatal blood samples, including 21 cases of the rare, deadly Pantoea organism. 47% of the neonates positive for sepsis died, compared to a 44% mortality rate in neonates negative for sepsis. AST analysis revealed substantial increases in resistance against Gentamycin, Ceftriaxone, and Amikacin since the previous study at MNH in 2014. Birth weight was determined to be significantly lower in sepsis-positive patients compared to sepsis-negative patients while no maternal factors showed significant differences between the two groups. The average number of antibiotics prescribed to sepsis-positive patients was 3.7, significantly higher than the number of antibiotics prescribed to sepsis-negative patients. Percent resistance was determined to actually be higher in living patients than dying, although the difference was not significant.

CONCLUSION: Improved infection prevention and control measures must be implemented to decrease the prevalence of rare bacterial species in this setting. Isolation of 17 unique bacterial species causing neonatal sepsis is far higher than the 5 species isolated in the previous study at MNH. Disinfection of surfaces and medical equipment, along with restricted access to outside visitors and increased distance between sick patients are some ways that the high rates of infection and mortality can be combated. Clear guidelines for the prescription and administration of powerful antibiotics to these neonates must be implemented to slow the rapid rates of antibiotic resistance.

Abstract Title: Unintended consequences of the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain on Opioid Prescribing Practice and Patient Outcomes – Insights from In-depth Interviews with Health Care Providers in Hampton Roads.

Investigator(s): Sarah Alnaif. BS[1], Tram Phung, BS;[1] Ying Li, MD;[3] Qi Lin, MD;[3] Hongyun Fu, PhD[2]
Department(s): 1) EVMS School of Medicine, 2) EVMS Pediatrics Department, 3) EVMS Department of Internal Medicine, Sentara Healthcare Medical Group

Abstract

Background: In response to the devastating opioid crisis in the United States, the Centers for Disease Control released the *Guideline for Prescribing Opioids for Chronic Pain* in 2016, with subsequent legislations being enacted to regulate the use of opioid prescription at the State level. Concerns were raised that the pressure of the 2016 Guideline may have led to unintended reduction in opioid prescriptions use in palliative care and compromised patients' wellbeing. However, few empirical research has been conducted to inform our understanding on this issue.

Methods: In Summer 2020, we conducted in-depth interviews with a convenience sample of health care providers (N=14) to understand their experiences with and attitudes towards the 2016 CDC Guideline and opioid prescribing practices. Respondents were recruited through snowball sampling method and peer-referral networks in palliative and hospice care and primary care settings in Hampton Roads. Online interviews were conducted (30-60 minutes each), following a semi-structured interview guide. Interviews were transcribed and data were coded into themes, guided by the grounded theory.

Results: Overall, health care providers voiced that the 2016 Guideline has been over-interpreted, causing barriers to and stigma associated with the use of opioid prescription for palliative care at three levels: 1) At the policy level: reduced drug production and supply, more stringent monitoring of opioid prescribing and insurance reimbursement policy; 2) At the health care provider level: concerns of being the "top prescriber on the list", extra precautions and unwillingness to prescribe opioid drugs, gaps in service referrals and care transition; 3) At the patient level: misunderstanding about certain opioid drugs, concerns over drug dependence and addiction, cautious about initiating opioid prescription, gaps in access to opioid prescription for needy patients, particularly during care transition. Primary care physicians talked about the extra precautions that had to be taken as well as limitations on the number and types of medications, while palliative care providers raised more concerned over stigma associated with opioid drugs and increasing gaps during care transition.

Conclusion: Findings indicated that 2016 CDC Guideline has overall increased precautions about opioid prescription use in health care settings; however, the pendulum has swung from over-prescribing to under-prescribing of opioid medication, including in palliative care settings.

Abstract Title: Effects of Sleep Fragmentation on metabolic phenotype in two animal models of diabetes and NASH

Investigator(s): Sezgi Arpag-Mcintosh MSc, Tyree Hamilton, Ravin Fisher, Anca Dobrian PhD
Department(s): Physiological Sciences

Abstract

INTRODUCTION Sleep dysregulation is associated with increased stress and metabolic abnormalities in humans. Reduced sleep and sleep apnea is known to exacerbate various cardio-metabolic diseases such as diabetes and atherosclerosis. However, the underlying mechanisms are incompletely understood. The overarching goal of our project is to establish mechanisms by which sleep deprivation impacts on liver disease and type2 diabetes. Sleep fragmentation (SF) in rodents is an experimental intervention that mimics reduced sleep and possibly sleep apnea in humans. We used this paradigm to address the effects of SF in two different preclinical rodent models: DIAMOND (Diet Induced Animal Model of NASH Disease) mouse, that gradually develops steatohepatitis on high fat and sugar (western) diet; and, db/db mice that develop accelerated insulin resistance, obesity and type 2 diabetes due to lack of the leptin receptor. To test our mechanistic hypothesis we needed to establish the effects of SF on metabolic fitness, longitudinally, in both models. In this poster we will present the effect of SF on survival, body weight and circulating insulin and glucose, as surrogate markers for metabolic dysregulation.

METHODS SF was applied in a special habitat chamber for every two minutes, 6 hours/day for two weeks. We used age and gender matching controls without any sleep interruption. Body weight was measured daily during the SF period. Terminal plasma was used to determine insulin and glucose using ELISA and a colorimetric assay, respectively. We used 3 cohorts of DIAMOND male mice 46 wks, 33wks and 24wks of age that were randomly assigned to SF protocol or used as controls (n=5-6/group). These time points were selected based on documented changes in liver disease stages in this model (from fatty liver to steatohepatitis with extensive fibrosis). We used db/db male mice at 8 weeks of age that were randomly assigned to SF or control groups (n=16-17). This is the time point when the mice become severely hyperglycemic and hyperinsulinemic, corresponding to the pre-diabetes stage. Data was analyzed using t-test to establish differences between SF and control groups at each time point. Kaplan-Mayer curves were used to represent survival in SF and control groups. The null hypothesis was rejected at a p-value<0.05.

RESULTS DIAMOND Mice: We observed 56% survival in the SF group compared to 94% in controls in overall age groups. Survival rate for each age group in SF was; 43% at 46wks, 63% at 33wks and 71% at 24wks. Both control groups of 33 and 24 wks of age survived at 100%, 46wks controls survived at 86%. Significant weight loss was found in the 33wks and 24wks old mice mice during the fragment period compared to controls. There was no significant weight change between the 46wks SF and controls. There was significant increase in plasma glucose levels in 33wks SF group compared to controls but not in the other two age groups. Insulin levels remained unaffected by SF in all age groups.

Db/db mice: Only 68% of the db/db mice survived after SF. Controls survived at 100%. Weight loss was very significant between the SF and control groups (p=0.000002). Plasma glucose was also significantly lower in the SF group vs. controls (p=0.01). Insulin levels remained unchanged by SF compared to the control group.

CONCLUSION This data showed the impact of SF on survival, body weight and plasma glucose and insulin in the two mouse models. This data shows that in DIAMOND mice despite weight loss, glucose sensitivity is impacted by SF protocol. On the contrary, in the db/db model, weight loss results in a reduction in circulating glucose. Understanding these changes will help evaluate the confounders on data obtained in future studies. Also, this study clearly shows that SF has a major impact on survival that is age-related in DIAMOND mice. Extensive characterization of liver inflammation and fibrosis and pancreatic islets morphology are presented in other posters from our group. Using this experimental paradigm of SF in these two pre-clinical models we can further test interventions to ameliorate the pathogenic mechanisms of SF in type 2 diabetes and NASH.

Abstract Title: Preparing Surgical International Medical Educators (IMEs) for Immersion in Malawi

Investigators: Karma Barot, Surya Gourneni, Kathleen Casey, M.D., Alexandra Leader, M.D., M.P.H., Leslie Toledo, M.S
Department: EVMS Office of Research, Eastern Virginia Medical School

Abstract

INTRODUCTION: Malawi, a landlocked country in southeastern Africa, has realized improved health outcomes over the past two decades. However, there is still a large health crisis in Malawi due to dual pressure from communicable and non-communicable diseases, compounded by extreme poverty. There is a severe dearth of health professionals, with only 600 physicians for a population of 19.2 million. The ratio worsens when accounting for surgeons, who number around 50. Physicians for Peace (PFP) is a nonprofit organization that sponsors physicians, surgeons, and other health professionals to help educate and empower local healthcare providers in under-resourced communities around the world, including Malawi. In Malawi, PFP has specifically mobilized volunteer surgeons, called International Medical Educators (IMEs), to provide hands-on surgical training, didactic training, and surgical mentorship at the Queen Elizabeth Central Hospital (QECH) and Mercy James Center for Pediatric Surgery and Intensive Care for periods of three months or more. The goal of this project is to improve the on-boarding process of IMEs for Malawi immersion through the creation of an informational guidebook. The guidebook will equip IMEs with a comprehensive resource to facilitate IMEs' work in Malawi and enhance the impact of their educational and clinical contributions.

METHODS: The authors developed a foundational understanding of Malawi healthcare and health statistics through international health reports and scientific articles. The authors then reviewed historical output reports and testimonials of previous IMEs to understand the scope of the work they did and the issues they addressed, as well as PFP's impact on clinical and education metrics at QECH. The authors also gathered information relating to the clinical setting at QECH as well as the cultural climate and lifestyle in Malawi. The authors then created a survey to collect qualitative data on the experiences of recent IMEs. A semi-structured interview format was used to query both recent IMEs and the primary clinical point of contact at QECH. Future surveys will be sent to compare experiences between IMEs that traveled before and after the changes of the on-boarding process.

RESULTS: Correlating the results of the IME interviews and historical reports with Malawi health statistics, three thematic priorities emerge for surgical care in Malawi: supplies, staffing, and access to healthcare. Based on IME interviews and output reports provided, 100% of the IMEs have reported a lack of resources (i.e. sutures, cauterizing utilities, etc.) during their time in Malawi. 100% of the IMEs have also stated that QECH is understaffed from surgeons to nurses to anesthesia clinicians. A qualitative note from two IMEs state that access (i.e. transportation) is a major issue in follow-up care with patients. 100% of the IMEs report that a comprehensive guide would help prepare future IMEs for their time in Malawi. The project is currently ongoing with survey collection of experiences of IMEs that traveled before the on-boarding process.

CONCLUSION: Surgical care in Malawi is severely under-resourced across most, if not all, standard metrics. Physicians for Peace is a nonprofit organization dedicated to improving access to safe, timely, and quality care in Malawi and impacts this through collaborating with community's healthcare network and supporting local education of the surgical team with provision of long-term volunteer International Medical Educators (IMEs). Opportunities have been identified to improve the on-boarding and pre-travel preparation of IMEs to ease their assimilation in the country and improve educational and health impacts. We are contributing to this opportunity with the creation of a Guidebook for Malawi-designated IMEs.

Abstract Title: An Investigation of Sun-Protective Clothing Behaviors and Knowledge in Virginia Beach, VA

Investigator(s): Erin Bartholomew, BA, Sekar Novika, MS, Edward Prodanovic, MD; Joshua Edwards MPH
Department(s): Dermatology; HADSI

Abstract

Background: There is currently little data published on the preference of using sun-protective clothing versus traditional sunscreen.

Objective: To assess differences in sun protective behavior among beachgoers in the age groups 18-29, 30-49, and 50+ years old regarding wearing sun-protective clothing.

Methods Anonymous data was collected at Virginia Beach, Virginia. Beachgoers 18-years and older completed a 15-question survey that collected patient demographics and sun protective behavior data. A chi-square test was performed to determine differences between age groups and gender.

Results: Out of 101 survey participants, the 18-29 age group had the highest proportion of participants wearing sun-protective clothing and demonstrated better knowledge about sun protection. However, the 50+ age group most adhered to sun protective behaviors such as seeking shade and wearing sunscreen.

Limitations: Some surveys were not completed in full, and thus the data extracted and analyzed was solely based on the questions that were completed. This study had a small sample size and an uneven distribution of participants among the three age groups.

Conclusions: There is a need for additional education regarding sun-protective clothing and sun-protective behaviors for beachgoers. In addition, perception of skin cancer risk and incentive to use sun protective clothing should be considered in future research.

Abstract Title: A Novel Immunization Catch-Up Clinic during COVID-19 in Hispanic Clínica Comunitaria Esperanza Pediátrica Patients

Investigator(s): E. Beverly MS, G. Enciso MS, A. Gibson MD
Department(s): HOPES Free Clinic and Clínica Esperanza

Abstract

INTRODUCTION

Clínica Comunitaria Esperanza Pediátrica (CCE-P) is a bilingual, student-run free clinic (SRFC) serving uninsured Hispanic residents of Hampton Roads, Virginia. CCE-P operates in partnership with the Eastern Virginia Medical School HOPES free clinic, which serves English-speaking patients in the region. CCE-P also partners with the local Virginia Department of Health (VDH) to provide clinic space and immunizations for the pediatric patients. (1) The recent COVID-19 pandemic has prompted a transition from in-person well child visits to telehealth appointments, resulting in major disruptions to the pediatric immunization schedules. This potentially leaves pediatric patients at risk for vaccine-preventable diseases (2,3). One unique challenge that CCE-P faces is incomplete vaccine records in the Electronic Health Record (EHR). The reasons for this are varied; for example, a majority of CCE-P patients have immigrated from different regions, and their immunization histories are disparate (4). To address the recent decline in routine vaccinations amidst COVID-19, and due to the incomplete immunization records of CCE-P patients, leaders of the VDH and CCE-P organized a Pediatric Immunization Catch-Up Clinic to take place in July 2020.

METHODS: CCE-P student leaders used the EHR search criteria "under age 18" and those who had a "signed encounter" between July 2019 and July 2020 to identify 63 pediatric patients eligible for the program.

Stage 1- Acquiring Immunization Records: Pediatric immunization records were requested by the VDH to determine which patients lacked vaccinations. In order to acquire records for the targeted patients, CCE-P leaders assembled a team of 10 medical student volunteers, who were each responsible for contacting a subset of patients to obtain their vaccination records. Students followed the protocols written by project leaders in the Novel Pediatric Immunization Catch-Up Clinic Guide (see presentation link) to ensure uniformity in record collection. All acquired records were faxed to the VDH. A list of patients identified by the VDH as being behind on routine vaccinations was sent to the authors for further scheduling.

Stage 2 - Scheduling CCE-P: Leadership scheduled patients using 20-minute appointment intervals. Reminder texts were sent the morning of the Immunization Catch-Up Clinic.

Stage 3 - Vaccination Clinic: Patients were screened for COVID-19 upon arrival at the clinic. They were escorted to the nursing staff for a final review of immunization records and immunization administration.

RESULTS: A total of 10 immunizations were administered to four CCE-P patients between the ages of 2 years and 16 years.

CONCLUSION: In accordance with COVID-19 precautions and the availability of VDH nursing staff, 6 patients identified as behind on immunizations were invited to participate in the Pediatric Immunization Catch-Up Clinic. Of these, four patients completed their immunization catch ups that evening. This novel protocol and approach lays the framework for future immunization catch up endeavors with the Hispanic pediatric patient population cared for by the CCE-P. The process also demonstrates the need for future vaccination partnership efforts between CCE-P and the VDH.

Abstract Title: Recurrent Inflammatory Myofibroblastic Tumor of the Maxillary Sinus successfully treated with COX-2 Inhibitor

Investigator(s): Suhas Bharadwaj MS, Dr. Matthew J. Lelegren MD, Dr. Marc L. Silverberg MD and Dr. Kent Lam MD

Department(s):
EVMS Otolaryngology, Sentara Pathology

Abstract

INTRODUCTION: Inflammatory Myofibroblastic Tumor (IMT) has many noted idiosyncrasies in therapeutics, oncologic behavior and immunohistopathology in the literature. IMT lesions are composed of variable cellular components including myofibroblasts, inflammatory cells and fibroblasts. While IMT lesions can occur in any area, lesions in the paranasal sinuses, pterygopalatine fossa and paranasal sinuses, have demonstrated a penchant for increased neoplastic potential. The literature regarding IMT demonstrates variable responses to aggressive pharmacotherapeutic regimens and surgical resection. We present the first documented case of recurrent IMT in the maxillary sinus treated using salvage cyclooxyngease-2 inhibitor therapy.

CLINICAL FINDINGS: A 35-year old otherwise healthy male was referred for a two week history of right nasal congestion and epistaxis. Computed Tomgraphy (CT) revealed soft tissue sinonasal mass extending into R maxillary sinus extending into the nasopharynx posteriorly without bony destruction as well as complete opacification of R paranasal sinuses. He was then taken for endoscopic resection at which time a large obstructive well-mucosalized mass was found in the nasal vestibule and maxillary sinus extending into the posterior nasopharynx. Final Pathology showed ulcerated low-grade spindle cell proliferation consistent with inflammatory myofibroblast tumor (IMT). Immunohistochemistry showcased Positive: Vimentin, Smooth Muscle Actin (SMA) and Negative: ALk-1, S100, ERG, CD34, D2-40 and MIC2. Six weeks after his first resection the patient returned with right sided nasal pain and epistaxis. On nasal endoscopy, the lesion had increased in size and a repeat CT revealed recurrent soft tissue mass infiltrating the R paranasal sinuses with complete opacification of the right paranasal sinuses. He subsequently underwent revision endoscopic sinus surgery with findings of a well vascularized mass in the nasal vestibule extending to the posterior nasopharynx. The final pathology showed recurrent low-grade IMT with similar immunohistochemistry**.** Postoperatively, he was placed on aggressive oral corticosteroid therapy, diclofenac and budesonide rinses. For four months, the patient continued to improve clinically before returning to our clinic with recurrent epistaxis. Patient subsequently underwent a third endoscopic sinus surgery for definitive resection, and his case was presented at our multidisciplinary head and neck tumor board conference. Due to the recurrent nature, a pathological consultation with an outside institution was performed. The outside pathologist reported immunohistochemistry showcasing negative ALK-1 and HPV 16-18 and findings consistent with IMT. Notably, the patient was diagnosed with Diabetes Mellitus type II just prior to his third resection, which complicated his options for post-op anti-inflammatory therapy with aggressive long term oral steroid therapy. The patient was subsequently switched from diclofenac and oral steroid maintenance therapy to Celebrex. He has remained asymptomatic without disease recurrence to date.

CONCLUSION: COX-2 inhibitor therapy may provide an alternative adjuvant or monotherapy modality for IMT of the paranasal sinus. Our patient had recurrent disease after his first resection with post-operative long term corticosteroid therapy. Subsequently had another recurrence after endoscopic resection and aggressive corticosteroid, diclofenac and budesonide therapy. He eventually achieved enduring remission after his third recurrence after undergoing a third resection and post-op celecoxib therapy. Our case also demonstrates celecoxib treatment for ALK-negative IMT's where selective ALK-1 inhibition therapy is not indicated. Given the remarkable results, a trial of celecoxib should be considered in any patient with recurrent IMT.

Abstract Title: Preoperative Analysis of Access Vessel Anatomy to Predict Adjunctive Procedures and Access Related Complications in TEVAR

Investigator(s): Suhas R. Bharadwaj MSc, Christopher Murter MD, Tomaz Mesar MD, Sami Assi MSH, David J. Dexter, MD, Animesh Rathore MD, Jean M. Panneton MD
Department(s): EVMS & Sentara Vascular Specialists

Abstract

Introduction
Thoracic endovascular aortic repair (TEVAR) in patients with suboptimal iliofemoral anatomy may require planned or emergent adjunct procedures. The goal of this study is to identify which anatomic factors can predict the need for these adjunct procedures and post-op access site complications.

Methods
We reviewed all TEVARs for standard indications performed in a single healthcare system between September 2012 and March 2017. Elective adjuncts were defined as any procedure used to facilitate device delivery in the iliac or femoral artery. Emergent adjuncts were defined as any procedure performed intraoperatively to repair an injury in the iliac or femoral artery. Preoperative CT scans were analyzed using centerline measurements using TerraRecon. Iliac diameter and calcification were graded on a scale from 0 to 3 to develop an iliac morphology score (IMS: scale of 0-6).

Results
A total of 189 patients with adequate preoperative imaging underwent TEVAR during the study period. 121 (64%) of the patients were male with a mean age of 64.5. 137 patients (72.5%) had percutaneous access. Average device outer diameter was 7.8 mm. 47 patients (24.9%) required 36 open adjuncts or conduits and 11 endovascular adjuncts. Of the 47 adjunct procedures, 20 (42.5%) were emergent and 27 (57.5%) were elective. Access artery calcifications and diameter were scored from 0-3 to create our IMS. Patients were divided into high (IMS≥3, n=41) and low (IMS < 3, n=148) risk groups. High risk patients had higher rates of elective adjuncts (31.7% vs 11.5% p=.001), emergent adjuncts (29.2% vs. 5.4% p=.001) and post-op access site complications requiring intervention (24.4% vs. 7.4% p=.002).
Adjunct procedures led to more access site complications (28% vs 5.6% p=.001), however subgroup analysis showed endovascular adjuncts (14.3% vs 10% p=.109) and conduit use (11.1% vs 4.6% ;p=.664) did not. Overall, adjunct usage did not lead to increased readmission rates (p.=16) or 30-day mortality (p=.76).

Conclusion
We created a scoring system that accurately predicts both elective and emergent adjunct usage and post-op access site complications requiring intervention. Adjunctive procedures were associated with increased morbidity but not increased mortality or hospital readmissions. Using iliac morphology score to plan deployment of endovascular adjuncts or conduits could limit access site complications and emergent adjunct deployment.

Abstract Title: "Protective effect of Ginkgolic acid against Herpes simplex virus type 1 (HSV-1) zosteriform infection in a mouse model"

Investigator(s): Maimoona Bhutta & Ronen Borenstein
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION
Herpes simplex virus type 1 (HSV-1) is a prevalent human pathogen with an estimated global prevalence of 66% (3.8 billion people). HSV-1 causes a lifelong latent infection, and it is primarily transmitted by skin-to-skin contact, entering through skin or mucosal surfaces. Common classes of antiviral drugs used to treat HSV infection are nucleoside analogues, such as acyclovir (ACV). However, emergence of ACV-resistant HSV (ACV^R-HSV) isolates have been reported in immunocompromised individuals. The emergence of resistant viral strains creates a genuine need to find and develop new anti-HSV agents. Recently, our lab discovered that Ginkgolic acid (GA), alkylphenol constituent of the leaves of Ginkgo biloba, has potent ***in-vitro*** antiviral activity against enveloped viruses with no toxicity in the active range. It is important to assess the application of a proposed antiviral drug on cutaneous infections. We examined the efficacy of GA, formulated in polyethylene glycol (PEG), in protecting against the early stage of cutaneous HSV-1 infection using an epidermal scarification-zosteriform model in female BALB/cJ mice.

METHODS
Female BALB/cJ mice were inoculated with 5×10^4 PFU of GFP-HSV-1 strain 17+. The inoculation sites on the mice were treated twice daily with DMSO (vehicle-control) formulated in PEG buffer, 10mM GA in PEG buffer, or 10mM ACV in PEG buffer (treatment-control for the standard of care), and continued for 14 days. Disease at the inoculation site was scored by the appearance of vesicles and lesions.

RESULTS
Our preliminary results indicated that GA-treated animals showed an 80% rate of survivability post-infection, compared to a 20% rate of survival in vehicle-treated control animals across 14 days ($p<0.05$, Log-rank (Mantel-Cox) test). GA-treated animals demonstrated a significant reduction in the appearance of vesicles and infected lesions starting from days 3 through 8, compared to DMSO-treated animals ($p<0.001$ and $p<0.05$, Independent t-tests). GA-treated BALB/cJ mice also demonstrated faster signs of healing than DMSO-treated animals.

CONCLUSION
In conclusion, we demonstrated potent inhibition of HSV infection and faster healing following treatment with GA, due to its' virucidal and fusion inhibition activity and ability in inhibiting the cell-to-cell spread of infection, relative to vehicle-treated DMSO controls. Experiments to test the protective effect of GA against ACV^R-HSV infections are ongoing.

Abstract Title: Mental health and professional concerns of medical students and residents during the 2019 novel coronavirus disease pandemic

Investigators: Sarah E. Birk, MPH[1]; Emily K. Ayuso, MS[1]; Nelly Amini, MS[1]; David R. Spiegel, MD[2]
Department: EVMS School of Medicine[1], EVMS Department of Psychiatry and Behavioral Sciences[2]

Abstract

INTRODUCTION: Evaluating the mental health impacts of the COVID-19 pandemic on current residents and medical students is critical to providing support to the next generation of medical doctors. At baseline, residents and medical students have documented increased levels of depression, anxiety, and OCD-like behaviors. Quantifying the impacts of COVID-19 can help promote institutional and societal awareness and provide a roadmap to building successful mental health initiatives.

METHODS: A cross-sectional survey was conducted of medical students and residents at a Virginia medical institution. Mental health disturbance level was estimated using PHQ-8, OCI-6 (washing and checking subtype), and GAD-7. Residents and medical students were grouped into three clusters using their scores from each with Euclidean distancing and k-means.

RESULTS: Among 144 medical students and residents, 52% had subthreshold mental health disturbances, 35% had mild to moderate mental health disturbances, and 13% had moderately severe to severe mental health disturbances (Table 1). Mean PHQ-8 and GAD-7 scores were significantly higher for medical students (PHQ-8: 6.00; GAD-7: 6.46) versus residents (PHQ-8: 4.11; GAD-7: 3.70), $p = 0.04$ and $p = 0.002$, respectively. There was no significant difference in mean OCI-6 score in medical students (4.22) versus residents (3.26), $p = 0.17$.

Residents and medical students in cluster 3 (moderately severe to severe mental health disturbances) were more likely to state that COVID-19 had a negative impact on mental health versus cluster 2 and 1 (72% vs. 69% vs. 32%, $p < 0.001$), and 50% reported that they had not been diagnosed with a mental health disorder before COVID-19. However, there was no significant difference in cluster and accessing mental health services since the start of the COVID-19 pandemic ($p = 0.10$). Despite moderately severe to severe mental health distress, 83% of those in cluster 3 had not accessed any mental health services since the start of the pandemic. In addition, those in cluster 2 and 3 were more likely to believe their institution was not providing adequate mental health resources (68% and 66%, respectively) versus cluster 1 (41%), $p = 0.009$.

Medical students in cluster 3 were more likely to worry about the effects of COVID-19 on their education, career, and their likelihood to match into their desired specialty ($p < .01$). Students in cluster 3 were also more likely to consider a different specialty due to COVID-19 ($p = 0.02$), and were more likely to desire a specialty with lower perceived stress levels ($p=0.03$).

Residents who were working on a high-risk unit were more likely to have spent time isolated from family (82% vs. 42%, $p = 0.02$), but overall, there was no significant difference in mental health distress levels and perceived adequacy of PPE, direct contact with COVID-19 patients, or working in a high-risk unit. Elevated mental health distress in residents did not correlate with worries of the impact of COVID-19 on their career or education. There was also no significant difference in cluster and year in school, year in residency, gender, age, or whether the participants were on clinical rotations or had a close contact infected with COVID-19.

CONCLUSION: The COVID-19 pandemic has introduced new stressors for both medical students and residents. Most students and residents who met criteria for moderately severe to severe mental distress have not sought mental health services, and the majority of participants who had elevated levels of distress did not believe their institution was providing adequate mental health resources. The mismatch between the significant mental distress and utilization of mental health services clearly indicates that many students and residents are having to manage these additional stressors independently.

Abstract Title: Pericyte subsets are linked with altered amyloid beta distribution in the Alzheimer's brain

Investigator(s): Diana Bohannon, Danielle Long, Woong-Ki Kim
Department(s): Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION: Over the past several years, the peripheral blood or cerebral spinal fluid (CSF) ratio of amyloid beta (Aβ) 42 to 40 (Aβ 42:40) has been used as a clinical diagnostic or prognostic marker of Alzheimer's disease (AD). Patients who display a low Aβ 42:40 ratio in the blood or CSF are at increased risk of developing high cerebral amyloid burden, increased rates of cognitive decline, and developing AD; but the underlying mechanism that drives this phenomenon is yet unknown. Blood-brain barrier (BBB) pericytes have recently been indicated as one of the primary cells capable of inducing Aβ efflux from the brain parenchyma to the peripheral blood. Our recent findings suggest that a subtype of pericyte which is increasingly prevalent during AD and may contribute to changes in Aβ efflux and parenchymal population densities.

METHODS: Formalin fixed paraffin embedded hippocampus and prefrontal cortex (BA10) archival brain sections from 8 AD patients (8 BA10, 8 hippocampus) and 6 age matched controls (AA, 3 BA10, 4 hippocampus) were sectioned for immunofluorescent (IF) and immunohistochemistry (IHC) staining, imaging, and analysis. Antibodies against Aβ 1-42, Aβ 1-40, glut-1, PDGFRB, and SMA were used to visualize the relationship between Aβ and pericyte sub-populations at the BBB microvasculature. IF staining was imaged on a Zeiss Azio Observer with AxioVision or a Zeiss 880 laser scanning confocal microscope with ZEN black and analyzed using ImageJ. Aβ40 and Aβ42 IHC slides were digitized at 20X with a NanoZoomer and quantified via QuPath 0.2.2 using a Random Tree classifier at 0.88um/pixel read frame for the section of entire tissue. The pixel classifier was trained by selecting 25 dense cores from dense core plaques labeled "dense aggregates", 25 diffuse amyloid plaques labeled "diffuse aggregates", and 25 amyloid negative areas labeled "negative control" with a digital like-pixel selection wand. All graphing statistics were performed using GraphPad Prism.

RESULTS: Despite having proportional levels of cerebral Aβ40 and Aβ42, patients displayed a varied distribution of Aβ between dense and diffuse aggregations of these Aβ populations. Patients with a higher percentage of type 2 pericytes (%PC2) had a lower percentage of dense Aβ42 and a higher percentage of dense Aβ40, which correlated with a low degree of BBB breakdown and low pericyte loss. In contrast, patients with low %PC2 displayed a high degree of dense Aβ42 aggregations and a lower percentage of dense Aβ40, which correlated with a high degree of BBB breakdown and high pericyte loss.

CONCLUSION: As pericytes are known to actively transport Aβ from the brain parenchyma into the bloodstream, our data suggests that differences in Aβ efflux between pericyte subsets could contribute to the clinical correlation seen between AD and Aβ 42:40 ratios. Patients with high %PC2 would likely demonstrate a higher Aβ 42:40 ratio as more Aβ42 is effluxed into the blood and Aβ40 forms more dense aggregates in the brain; this would correlate to an improved prognosis for these patients, which is supported by our low BBB breakdown and pericyte loss data. On the contrary, patents with low %PC2 would likely demonstrate a lower Aβ 42:40 ratio with more Aβ42 forming dense aggregates and more Aβ40 effluxing into the bloodstream; correlating to a poorer disease prognosis as is supported by increased BBB breakdown and increased pericyte loss. Ultimately, further investigation of Aβ trafficking in pericyte subsets in an active *in vitro* or *in vivo* model is required to validate these findings, but our initial results suggest that alterations in Aβ distribution may be associated with the ratio of pericyte subsets in the brains of AD patients.

Abstract Title: Commonly Seen Scooter-related Injuries at Imaging for a Level 1 Trauma Center

Investigators: Richard Bonney, DO, Sarah Shaves, MD, Ryan Harris, M1
Departments: EVMS Radiology, EVMS Medical School

Abstract

INTRODUCTION: Electric scooters are widely available in urban and suburban neighborhoods in our area. In fact their use is banned on sidewalks, and streets have been marked with symbols signifying that scooters are to share the road with cars and truck. Noting a large number of significant scooter-related injuries at our level I trauma center, we will retrospectively identify cases of scooter injuries requiring imaging and presenting to the radiology department.

MATERIALS AND METHODS: Using the Nuance mPower search tool in the Powerscribe dictation platform used at our institution, we searched for patients with a clinical indication of scooter injury for whom imaging was obtained over the past 12 months. A review of Epic notes from the ED visit was also performed to identify the percent of injuries requiring operative intervention and percent of patients requiring hospitalization. Classification of scooter-related injuries were also classified by age, sex, organ system and classify patterns of injuries.

RESULTS: The majority of injuries in the analysis were musculoskeletal injuries of the extremities with neurological and genitourinary injuries being the least common. Males were more likely to be involved in injuries at 60%. Thirty-Eight percent of patients required hospitalization for injuries and 38% also required some sort of operative intervention.

CONCLUSION: The majority of scooter-related injuries were musculoskeletal injuries with a significant resulting in operative management and hospitalization.

Abstract Title: Sex differences in the molecular cause of perioral skin wrinkling.
Investigators: Brown ID, Dillen, C, Ly BC, Shyam N, Kang S, Chien AL.
Departments: Department of Dermatology, Johns Hopkins University, Baltimore, MD, USA.

Abstract
Wrinkling is the hallmark of skin aging. We have previously reported that perioral wrinkling is more severe in females; however the molecular basis for this is unknown. We enrolled 12 subjects (n=6 male/female) age 54-86 with Griffith's photoaging grade between 4 and 8 (0=none, 8=severe) and took biopsies from both the perioral and periocular region. Using qPCR, we assessed RNA expression of collagen I, collagen III, cysteine-rich angiogenic inducer 61 (CYR61), and insulin like growth factor 1 (IGF-1). CYR61 causes dermal fibroblast senescence in response to photodamage, leading to the decreased collagen production linked to skin wrinkling. IGF-1 is produced by dermal fibroblasts and plays a role in regulating the hair cycle and promoting oxidative stress. While there was no difference between females' and males' Griffith's grade (6.67 and 5.67 respectively, p=0.096) or periocular wrinkling grade (3.2 and 2.6 respectively, p=0.421), females had a significantly more severe perioral wrinkling grade when compared with males (6.2 and 2.8 respectively, p=0.035). Consistent with the increase in severity in perioral wrinkling, females also expressed significantly more CYR61 (p=0.018) than males, however, they also expressed more collagen III (p=0.016). In this location, there was no significant difference in collagen I (p=0.115) or IGF-1 (p=0.124) expression between males and females, although females trended towards higher expression of both, with the latter marker's role in oxidative stress potentially contributing to the increased perioral wrinkling in females. In the periocular region, there were no significant differences between males and females in the expression of all four markers. While both sexes had similar overall photoaging and gene expression in the periocular region, the perioral region expressed significant molecular differences between the sexes, which may contribute to the greater perioral skin wrinkling seen clinically in females. It also highlights the complex process of skin aging and the influence of specific anatomic milieu in this process.

Abstract Title: Imaging Flow Cytometry as a method to explore extracellular vesicle internalization and cellular fate

Investigator(s): Michael Brown, Allison Mathiesen, M.S., Tyree Hamilton, Nigeste Carter, Anca Dobrian, PhD.
Department(s): Department of Physiological Sciences, Eastern Virginia Medical School

Abstract

INTRODUCTION: Extracellular vesicles (EV) are small membrane-bound entities carrying a versatile cargo that includes proteins, nucleic acids, lipids and metabolites. Based on their biogenesis, EVs fall into two major categories: microvesicles that range between 200 and 1000nm in diameter and exosomes (also known as sEV) with a diameter between 40-200nm. There has been increase evidence and appreciation of the importance of EVs in cell signaling and disease pathologies, including cancer. This fueled investigation for potential uses of EVs as biomarkers as well as an approach for drug delivery due their ability to be taken up and deliver cargo into a recipient cell. However, due to the heterogeneity of EVs as well as the different phenotypic features of recipient cells, the EV uptake can be highly variable and selective. Studies from our lab and others show that, in vitro, not all the cells in a given cell population take up vesicles with similar kinetics and avidity. Therefore, understanding the uptake of EVs by cells in different physiologic states (eg, quiescent vs. proliferative) as well as the intracellular fate of EVs is key for the experimental design of studies that employ EV-cell interactions. We used the interaction of EVs from various endothelial cells with PC3ML prostate cancer cells as a proof of concept approach to test the applicability of imaging flow cytometry to address our research question.

METHODS: EVs were isolated from a 3-day culture media of human adipose tissue endothelial cells (HAMVEC). The isolation protocol was aimed at obtaining the exosomal fraction of vesicles. For this purpose, culture media was centrifuged at 500 x g and the pellet was discarded before proceeding with a 10,000 x g, spin for 40 min and 2x 90min spins at 100,000 x g. The pellet containing the EVs was re-suspended and the concentration and size distribution of EVs was determined using the nano-tracker imager NanoSight 300. EVs were fluorescently labeled using the lipophilic dye DiD, at a dilution of 1:200. Excess unbound dye was removed by overnight dialysis, at 4C using purified water. EV concentration was based on previous experiments and was set at a saturation uptake value of 2-3x10^{10} EVs per 1.0x10^{6} cells. EV uptake and co-localization with lysosomal compartment were done in a time-dependent manner by incubating EVs with PC3ML cells for 30min, 1 hour, 2 hour and 4 hours. Following these incubations, cells were stained with LysoTracker Green DND-26 at 65nM for 5 min without fixation. In a separate experiment, EVs were incubated with cells overnight and nuclei were stained with either DAPI or Hoechst. Data was collected using an Amnis® ImageStream®XMk II. For all experiments ~10,000 cells were collected and single stained cells without brightfield turned on were used to perform compensation within IDEAS 6.2 software. Using the appropriate wizards within the IDEAS 6.2 internalization and co-localization were quantified and exported along with fluorescence values into Prism software for correlation analysis.

RESULTS: Preliminary analysis of cells incubated with DiD stained EVs overnight showed a negative correlation between nuclear stain fluorescence and the internalization of EVs, using two different nuclear dyes (DAPI $r = -.067$ $p < 0.0001$ and Hoechst $r = -.119$, $p < 0.0001$) This result was independently confirmed for DAPI nuclear staining using fluorescence microscopy ($r = -.1352$ $p = 0.0004$). The negative correlation between nuclear staining and internalization may be cell cycle-dependent. The percentages of cells that were positive for EV internalization at different incubation times were: 1.01%, at 30 min; 17.9%, at 1 hr; 13.2% at 2hrs and 35.08% at 4hrs. Next, we analyzed the intracellular fate of the internalized EVs. We determined the co-localization of the EVs with the lysosomal compartment. Out of the total cell population that internalized EVs at each time point, the following percentages of cells displayed a detectable signal for co-localization: 49% at 30min; 52.8% at 1hr; 31.25% at 2hrs; and, 40.7% at 4hrs. Notably, the number of co-localization events/cell was very low for all of the cells analyzed at different time points, suggesting that the majority of the internalized EVs escape lysosomal degradation after up to 4 hours of incubation with recipient cells.

CONCLUSION: These proof-of-concept experiments showed that imaging flow cytometry is a promising tool to quantify selective uptake and cellular fate of EVs. Understanding the kinetics of uptake and cellular fate of EVs is key for an informed experimental design aimed to study molecular and functional effects of EVs. These results can be complemented with live cell imaging using super-resolution microscopy (please see poster by Hamilton, T et al). Future studies will include, amongst others, cell sorting based on EV uptake and correlation between EV uptake and cell cycle.

Abstract Title: Androgen Receptors Dynamically are Expressed in the Ovulatory Follicle of Non-Human Primates

Investigator(s): Danielle Bryner; Diane M. Duffy, Ph.D.
Department(s): Physiological Sciences

Abstract

INTRODUCTION: Androgens and androgen receptors, while typically associated with men, are actually crucial to the female reproductive system. Preliminary data generated in our lab supports the concept that intrafollicular androgens are required for oocyte maturation and fertilization in primates. Additionally, recent work in rodents and bovine suggests that androgens may be needed for the final stages of healthy oocyte maturation in preparation for fertilization. Androgens act via specific receptors. Classical androgen receptors (AR) are active in the cell nucleus. Recently, a new androgen receptors was identified, SLC39A9 (ZIP9), which is associated with the plasma membrane. This study aims to determine if one or both of these androgen receptors are dynamically expressed in the follicle throughout the ovulatory period.

METHODS: A controlled ovarian stimulation model developed for the collection of multiple oocytes for in vitro fertilization was used to obtain granulosa cells and whole ovaries from adult female cynomolgus macaques (Macaca fascicularis) at Eastern Virginia Medical School (EVMS). Beginning within 3 days of initiation of menstruation, FSH was administered for 6–8 days, followed by daily administration of 90 IU FSH plus 60 IU LH for 2 days to stimulate the growth of multiple preovulatory follicles. Macaque ovaries were obtained after ovarian stimulation but in the absence of hCG (0 hour hCG) as well as 12, 24, and 36 hours (h) after hCG, as these time points span the ovulatory period. Ovarian tissue was fixed in 10% formalin for paraffin sections. Immunohistochemistry was performed using an AR primary antibody with basic antigen retrieval. Total RNA was obtained from granulosa cells using Trizol reagent, treated with DNase and reverse transcribed. Determination of granulosa cell levels of AR and BACT mRNAs was conducted by qPCR using a Roche LightCycler (Roche Diagnostics, Indianapolis, IN). Similarly, immunohistochemistry and qPCR will be used to study expression of SLC39A9.

RESULTS: Immunostaining showed the presence of ARs in the nuclei of granulosa cells in periovulatory follicles throughout the ovulatory period, with highest levels in granulosa cells of 0 h ovaries. Androgen receptors were also detected in granulosa cells in 12 h, 24 h and 36 h ovaries. Additionally, evidence of ARs was seen in stromal cells, presumed to be thecal cells. Quantification of AR and SLC39A9 mRNA in follicular granulosa cells is underway.

CONCLUSION: This study demonstrates that androgen receptors are present in the periovulatory follicle, with highest levels detected before hCG administration. In this study, we will identify the cells of the ovulatory follicle which express nuclear and membrane androgen receptors to determine what cells may be affected by androgens. This information will allow for future, hypothesis-driven investigations of cell signaling pathways used by androgens to ultimately influence oocyte maturation and fertilization. Studies pertaining to androgen receptors may suggest treatments for Polycystic Ovarian Syndrome (PCOS) or other types of female infertility.

Abstract Title: Assessing the Impact of the CMS National Partnership on Antipsychotic Medication Use, Mortality, and Cardiovascular Events: Differences between Racial and Ethnic Groups among Nursing Home Residents

Investigator(s): Adrianna Carrasco, MS3, Hamid R. Okhravi, MD, Brynn Sheehan, PhD, Melissa P. Hunter, PsyD
Department(s): Geriatrics, Healthcare Analytics Institute, Psychology

Abstract

INTRODUCTION
The Food and Drug Administration (FDA) has issued a black box warning of increased mortality, cardiovascular events and cerebrovascular accidents with the off-label use of antipsychotics. In 2011, 24% of nursing home (NH) residents received antipsychotic medications to control behavioral and psychological symptoms of dementia (BPSD). In early 2012, the Centers for Medicare & Medicaid Services (CMS) launched the National Partnership (NP) to improve dementia care in nursing homes by reducing the rate of antipsychotic prescriptions. As a direct result of this initiative, the use of antipsychotics in NHs has decreased 34% in 2017. Emerging studies have shown differences in both the incidence of BPSD and the use of FDA-approved medications among different ethnic groups. However, it remains unknown how the NP has influenced the mortality rate and incidence of cardiovascular events in NH patients with dementia or their hospital admissions. Further, it remains unknown whether and how this partnership has affected racial and minority groups, whom experience BPSD at a disproportionate rate. Our objective is to compare the prevalence of BPSD, antipsychotic medication use and related outcomes such as, mortality, cardiovascular events and hospital admission rates, among ethno-racial groups in local, statewide, and nationwide NH residents with dementia before and after the implementation of the NP.

METHODS
We will analyze Medicare data on a random sample of approximately one million NH residents from the second quarter of 2011 through the last quarter of 2016. This period will include one-year data prior to the NP, to serve as baseline measures, and 4 years post-partnership data. A descriptive summary of data will be presented as mean ± SE or frequency (percentage). Baseline categorical variables and rates will be compared using Chi-square or Fisher's exact test. These tests will be performed to compare the outcomes such as the rate of myocardial infarction and death between racial groups.

RESULTS
We expect to find a discrepancy in the incidence of BPSDs, antipsychotic medication use and reduction, mortality and cardiovascular events across ethnic and racial NH residents both before and after the partnership implementation.

CONCLUSION
Our findings will enhance our current understanding of the social and demographic factors that contribute to the differences of dementia and related health care outcomes among U.S. NH residents with dementia, whom are increasingly socially and ethnically diverse. Most importantly, the results of this study will identify the association between the partnership and disparities among different ethno-racial groups in NHs. Although this initiative was created to equally reduce a health disparity in U.S. NHs nationwide, it may have failed to do so by not appropriately addressing racial, socioeconomic, and ethnic disparities. Furthermore, it may have positively affected one group over another and/or unintentionally increased the rate of undesired replacement medications (e.g., mood stabilizers). These findings will highlight the need for interventional programs and promote further investigation into these discrepancies.

Abstract Title: An Atypical Case of VV1 Creutzfelt-Jakob Disease Subtype

Investigator(s): Adrianna Carrasco MS3, Hamid R. Okhravi, MD
Department(s): Geriatrics

Abstract

INTRODUCTION
Creutzfeldt-Jakob disease (CJD) is rare form of rapidly progressive dementia due to the presence of abhorrent prion protein and affects 1-1.5 cases per million per year. An estimated 85% of these cases are sporadic, and the remaining 5-15% develop CJD from inherited mutations of the prion gene. Sporadic CJD (sCJD) is further subdivided into six subtypes based on genetic polymorphisms, with the VV1 subtype occurring at a rate of 1 case per one-hundredth million population per year. These subtypes have been shown to correlate with age of onset, clinical course, disease features and duration. Early manifestations of CJD may present with neuropsychiatric disturbances prior to illness onset. Clinical characteristics of the VV1 subtype has been reported to show, early age of onset (39 years), disease duration of 15 months, elevated 14-3-3 and total tau in the CSF, absent PSWCs on electroencephalography (EEG), and magnetic resonance imaging (MRI) hyperintensities in the cerebral cortex with usual negative signal in the basal ganglia or thalamus.

CLINICAL FINDINGS
We present an atypical case of the rarest VV1 sCJD subtype. Contrary to current data on VV1, our patient presented with an unusual age at onset (63 years), longer disease duration (20 months), and positive signal in the basal ganglia on MRI. The real-time quaking-induced conversion (RT-QuIC) was negative. Presenting clinical symptoms included paranoid thoughts and agitation, progressing with rapid memory decline, prosopagnosia, and later development of myoclonus and mutism. Other findings showed positive antithyroid peroxidase antibodies (anti-TPO), absent PSWCs on EEG, positive 14-3-3 and elevated tau on CSF. High dose steroid therapy treatment was administered based on positive anti-TPO findings, which failed to illicit any improvement and the patient continued to decline.

CONCLUSION
Only a handful of confirmed VV1 cases, including our patient, have been reported to have a negative result on RT-QuIC. This may indicate a unique characteristic to VV1 and aid in the diagnostic work up in suspected sCJD cases with this finding. However, given the rarity of our patient's subtype, and the relatively novel RT-QuIC, current data is based on a small number of cases and larger cohorts of confirmed VV1 cases with RT-QuIC testing need to be reported. It is important to consider CJD and the rare VV1 subtype in suspected CJD cases with unusual clinical manifestations such as negative RT-QuIC, and a prolonged disease course. Early subtype detection may aid in potential future treatments and advance care planning.

Abstract Title: Modulation of endothelial cell angiogenic potential via extracellular vesicles

Investigator(s): Nigeste Carter, Allison Mathiesen, Bronson Haynes, Anca Dobrian
Department(s): Department of Physiological Sciences

Abstract

Introduction: It has previously been shown by our lab that endothelial cells from obese adipose tissue secrete extracellular vesicles (EVs) that may promote inflammation, and thus contribute to the development of obesity comorbidities such as cardiovascular disease. EVs from vascular beds exposed to local inflammatory mediators (such as in adipose tissue) can propagate molecular signatures known to produce endothelial dysfunction to distant vascular beds such as the coronary circulation. In addition, cells may be impacted by EVs in a paracrine or autocrine manner. Published data from our lab showed that EC in inflamed adipose tissue produce EVs that have a potent angiostatic effects in ECs from the same tissues that were not exposed to a pro-inflammatory environment. Whether this effect is specific to EVs from adipose tissue endothelium or is a more general feature of the endothelial EVs exposed to pro-inflammatory cues is currently unclear. In this study, we focused on the interaction between EVs produced by human coronary artery endothelial cells (HCAECs) and human adipose tissue endothelial cells (HAMVECs) exposed to pro-inflammatory mediators in vitro, and naïve HCAEC. We investigated the effect of EVs on the angiogenic potential of recipient HCAECs. Coronary circulation is critical for recovery of the ischemic myocardium and effective angiogenesis is key to support an adequate repair response.

Methods: To mimic the pro-inflammatory environment in vivo, HCAECs and HAMVECs were treated for 6 days with a combination of TNFα, interferon γ, and TGFβ (5nM each). These pro-inflammatory cytokines (PIC) were reportedly increased in circulation in chronic inflammation related to obesity and, at comparable levels with the ones used in vitro. EVs were isolated from culture media of PIC-treated cells (EV-PIC) or from media of untreated control cells (EV-C) using differential ultracentrifugation. EV concentration and size distribution were determined by nanoparticle tracking analysis using the NanoSight 300 instrument. To determine the uptake of EVs by the cells, we labeled the former using the lipophilic dye DiO and counted the number of cells that showed a positive fluorescent signal using fluorescent microscopy. Cellular nuclei were stained using DAPI. Data was expressed as % cells that were positive for EV fluorescence to total cells/microscopic field. For angiogenic potential measurement cells were treated with EVs overnight and then seeded on a matrigel gel for evaluation of tube formation. Different angiogenic parameters, such a mesh formation, tube lengths and number of nodes were measured using an ImageJ software plug-in. Statistical analysis to determine differences between treatment and control conditions was done using Kruskal-Wallis non-parametric test. The null hypothesis was rejected for a p-value of<0.05.

Results: Both untreated and PIC treated HCAECs released $\approx$4.0-fold more EV/cell compared to untreated and PIC treated HAMVECs, but there was no significant difference in average size or in size distribution of the EVs regardless of cell origin or treatment. Following 24-hour incubation with EVs, HCAECs were able to uptake both HAMVEC and HCAEC generated EVs. Cells treated with EVs isolated from both HAMVECs and HCAECs showed reduced in vitro angiogenic responses compared to untreated control cells. The angiostatic effect of EVs was reflected in reduction of several parameters including node, branch, and mesh formation, compared to the control cells (p-value=0.096, 0.0018, and 0.047, respectively). While all EV treatments were angiostatic, the magnitude of the effects was different for different EV preparations.

Conclusion: This experiment showed that the angiostatic potential of EVs is not unique for adipose tissue endothelial cells. HCAEC derived vesicles were also angiostatic via an autocrine mechanism. This effect was even more potent compared to EV-PIC isolated from HAMVEC cells. This effect may be physiologically meaningful in post-ischemic myocardial events when there is potential for increased access of EV to the coronary endothelium due to local tissue damage. Importantly, EVs may prevent a robust angiogenic response needed for tissue re-vascularization. In current studies we examine the EVs cargo to identify key miRNA and proteins that could be responsible for the angiostatic effects.

Abstract Title: Nursing Home Stakeholder Perspectives on the Use of Pharmacogenetics in Medical Care

Investigator(s): Madison Cauble, BA[1]; Andrew Wise, BS[2]; Andy H. Szeto, PharmD[3]; Dan Crona, PharmD, PhD[3]; Tim Wiltshire, PharmD, PhD[3]; Sheel Patel, PharmD[3]; C. Adrian Austin, MD, MSCR[4]; Kimberly Ward, BA[5]; Christine E. Kistler, MD, MASc[4,5]

Department(s): Eastern Virginia Medical School, Norfolk, VA[1], School of Medicine, University of Georgia, Augusta, GA[2], Eshelman School of Pharmacy, UNC-CH[3], School of Medicine, UNC-CH[4], Cecil G. Sheps Center for Health Services Research, UNC-CH[5]

Abstract

Introduction: Pharmacogenetics (PGx), the study of how genetics affects medication response, may improve prescribing in nursing home (NH) residents. This study aimed to assess attitudes towards PGx to help determine the feasibility of using PGx to improve prescribing in NHs**.**

Methods: We conducted a one-time survey of NH residents, legally authorized representatives (LARs), and nurses about PGx, including their personal experience with PGx, medication adverse events, and attitudes towards PGx using 5-point Likert scales (strongly agree to strongly disagree). Participants were volunteers from a large single nursing home in central North Carolina. If a NH resident had cognitive impairment at time of consent, their LAR was invited.

Results: We enrolled 32 subjects (7 NH residents, 14 LARs, and 11 nurses). The mean NH resident age was 80.3 years±10.2, 4 were female. Mean LAR age was 60.9±9.8 years, 9 were male, and 13 (93%) had completed some college. Mean nurse age was 45.7±12.7 years, and 10 were female. Most subjects (n=23) reported a prior adverse event from a medication. One subject had genetic testing done in a medical setting, and 5 “knew someone” who had. Four subjects had undergone personal genotyping. All residents, 11 LARs, and 2 nurses agreed with the statement “I would want my medication to be selected based on the results of PGx testing.” All NH subjects, 13 LARs, and 2 nurses agreed with the statement “PGx may improve my current medication treatment.” All participants agreed or were neutral towards the statement “PGx is useful in managing drug therapy.” Almost half of the nurses could not explain the rationale for PGx in clinical care (n=4) or discuss the risks (n=4) and benefits (n=5) with patients.

Conclusion: While personal experience with PGx was low, NH residents and LARs consistently held positive attitudes towards PGx. NH nurses had more concerns, but still thought that PGx might be useful. These findings highlight the need for more nursing education about PGx prior to using PGx in NHs.

Abstract Title: Utilization of Ambulatory Surgery Center and Acute Management Pathway to Improve Stone Treatment Time

Investigator(s): Andrew Wang, Johanna Cecelic, Helen Kim, Carol McCammon, Jack Lambert, John Malcolm, Michael Fabrizio
Department(s): EVMS

Abstract

INTRODUCTION: Patients with acute renal stone disease often have lengthy wait times from emergency department (ED) to urologist to definitive treatment. Along with this increased wait time comes return ED visits due to pain, which become costly and inconvenient. This prompted our team to create a protocol, called Acute Rapid Stone Treatment Pathway or AiRSTRiP, to be used in conjunction with an ambulatory surgery center (ASC) in effort to use a systematic approach to decrease this wait time and lessen the burden associated with renal stone disease.

METHODS: We reviewed our database of patients who presented to the ED with renal colic due to a unilateral stone and subsequently underwent lithotripsy or endoscopic procedures after we gained access to an ASC. Data was collected during an 8-month period from July 2016 to February 2017 using CPT codes. Halfway through the study, we introduced the AiRSTRiP protocol into our large urology group practice. Pre and post-pathway data were compared using Student t-test to assess AiRSTRiP's ability to decrease wait time from ED to office follow-up and ED to stone treatment.

RESULTS: Out of 2075 procedures performed on 1485 patients, 228 patients qualified for our study, including 79 in our pre-pathway cohort and 149 in our post-pathway cohort. The average stone sizes for each cohort were 7.2 and 7.0 mm, respectively. Utilization of the ASC increased from 31.5% to 48% following implementation of the pathway. Wait times from initial ED visits to office follow-up were notably reduced from 6.4 to 4.3 days ($p = 0.032$), while ED to treatment time decreased significantly from 22.4 to 14.2 days ($p = 0.0018$).

CONCLUSION: We have demonstrated for the first time that implementation of a stone management pathway, in combination with access to an ASC, can significantly reduce wait time for follow-up and definitive treatment for stone disease.

Abstract Title: REM Sleep as a Mediator of Fear-Based Memory

Investigators: Anjali C. Chacko, Austin M. Adkins, Brook L. Sweeten, Larry D. Sanford and Laurie L. Wellman
Departments: EVMS Sleep Research Laboratory, Pathology and Anatomy

Abstract

INTRODUCTION
Post-traumatic stress disorder (PTSD) is a stress and trauma-related psychiatric disorder characterized by hypervigilance, sleep disturbances, and flashbacks caused by the persistent recall of fear memories. Though it is still unknown why certain individuals develop PTSD over others following a traumatic event, previous studies in our lab have shown that individual differences in post-stress rapid eye movement (REM) sleep may be implicated in the development of PTSD. Research suggests a link between REM theta wave signaling with proper emotional processing memory consolidation. Therefore, REM and REM-related theta wave activity, may be useful to elucidate the etiology of PTSD and other fear-based disorders.

METHODS
Twenty-four outbred Wistar rats were surgically implanted with electrodes to record the electroencephalogram (EEG) and electromyogram (EMGs), and intraperitoneal data loggers to record body temperature. After recovery, baseline measurements were recorded. The rats were then exposed to a shock chamber for shock training (ST) consisting of a 5-min pre-shock period, then a 20-min footshock period (once per minute, 0.8mA, 0.5s max duration), followed by a 5-min post-shock period. They were returned to their home cage for sleep recording following ST and divided into groups based on their REM responses. Those having >50% REM compared to their baseline were considered resilient (Res) (n=15) and those with <50% REM compared to their baseline considered as vulnerable (Vul) (n=9). To assess the effects of fear memory on REM, the rats were then subdivided into two groups (n=12 each) and contextually re-exposed to the shock chamber without footshock (CTX) either 24 or 48 hours following ST. One week following CTX, they were re-exposed to the shock chamber without shock again for assessment of extinction learning (EXT). Each session was video-taped for recording of freezing, a measure of behavioral fear in rodents. Sleep was recorded following each experimental session for 20 hours.

RESULTS
There were no significant differences in freezing behavior or body temperature between groups or across days. However, REM differed between groups, where resilient animals showed increased REM and Vul animals showed decreased REM following ST. Interestingly, there were no differences in REM between groups following CTX, but Vul animals showed decreased REM following EXT compared to Res animals. Res animals exhibited more REM episodes compared to Vul animals following ST, but Res and Vul had similar number of episodes of REM during CTX. During EXT, however, Res animals had more episodes of REM than the Vul group. The durations of REM episodes was similar for both groups, although Vul had a significantly longer duration of sleep than Res after the 8 day EXT. EEG spectra showed an increase in theta during REM after ST and EXT for Res animals, but not for Vul animals.

CONCLUSION
Individual differences in REM following a traumatic event may moderate the relationship between adaptive and maladaptive emotional processing and fear memory. A decrease in REM and REM-related theta activity may result in a lack of appropriate emotional processing and thus be predictive for the development of PTSD. Further study focusing on the role of REM-related theta activity may provide insight into the mechanism underlying the role of REM in processing fear memory and its role in PTSD.

Abstract Title: A Demographic Overview of the HOPES Student-run Free Clinic

Investigator(s): Charlotte Chambers, Rebecca Clawson, Saritha Attanagoda, Tamanna Sahni, Catherine Eccleston, Mackenzie Hunt, Marc Nepomuceno
Department(s): School of Medicine, HOPES Clinic

Abstract

INTRODUCTION: The HOPES clinic has been treating the uninsured community of the Norfolk, VA area since 2011. Monitoring of the demographics of this population allows the clinic to predict what medical specialties, medications, and other resources should be provided by the clinic in order to best serve the needs of the population at hand. Additionally, the recent Virginia Medicaid expansion that began in January 2019 also created the potential for rapidly changing demographics within the HOPES clinic, as many patients experienced a change in insurance status. By monitoring the changing demographics within the HOPES clinic, the Metric, Evaluations, and Quality (MEQ) team will be more equipped to guide how HOPES can efficiently and effectively alter the resources that they need for their current patient population, as well as identify populations HOPES can better serve in the future.

METHODS: Using the PracticeFusion EMR "reports" function, the MEQ team created patient counts categorized by individual or combined demographic variables and separated into both month and year of clinic operation. The demographic variables collected included age, sex, diagnosis, medications, ethnicity, and primary language spoken. Diagnoses were determined using the available ICD-10-CM codes and patients who satisfied more than one collected diagnosis were included in all relevant diagnosis groups. Once collected, the variables were compared by month and/or year to observe changes over time. Excel was used for data analysis.

RESULTS: The majority of encounters at HOPES are for female patients and have been for the duration of the HOPES clinic. The proportion of female patients has decreased over the years from a peak of 82% of patients in 2014-2015 to 65% of patients in 2019-2020. The age group which has utilized HOPES the most is the 50-60 age group. However, the most recent two years saw an increase in younger patients. There was a dramatic increase in Spanish-speaking patients at HOPES after the 2016-2017 year, from 1% of HOPES patients to 57% of patients currently. The diagnoses HOPES most commonly sees are those for chronic conditions such as hypertension and diabetes, which were the top two diagnoses throughout HOPES' history. Anti-hypertensive medications were the most commonly prescribed medications at HOPES. We found that for the majority of HOPES patients, patient race and/or ethnicity was not recorded in the EMR.

CONCLUSION: Based on the trends in patient demographics, the HOPES clinic population is largely female. HOPES should continue to invest in resources related to women's health, including but not limited to supplies for well-woman exams, pap tests, and feminine hygiene products. There is also high utilization of the HOPES clinic by patients in the 40-60 age group. At this age, many patients develop chronic diseases such as hypertension and diabetes, and begin health screenings such as mammograms and colonoscopies. Health maintenance for this population should be a priority via both in-clinic interventions such as checking HbA1c, lipids, and blood pressure, as well as forming and maintaining partnerships with organizations outside of HOPES that provide cancer screenings to uninsured patients in Hampton Roads. The most dramatic demographics change in the HOPES clinic is the increase in Spanish-speaking patients which now make up the majority of all patients at HOPES. Expanding the HOPES Esperanza clinic and increasing the number of interpreters available to HOPES would help better meet the needs of this growing clinic population. Moving forward, the MEQ team would like to improve the consistency of recording patient race and ethnicity in the HOPES EMR in order to help the clinic identify which uninsured populations in the area it is and is not reaching, and determine whether the diversity of clinic patients is representative of Norfolk's uninsured population. We plan to utilize research tools such as RedCap to better analyze relationships between multiple demographic variables and perform a more detailed investigation of the changing clinic demographics. Furthermore, we would like to explore how the ongoing COVID-19 pandemic has affected the demographics of the HOPES and determine how HOPES is reaching its patient population during this time.

Abstract Title: Reminder Texting Provides More Effective Communication Between Patients and HOPES Free Clinic Without Impacting Patient Care

Investigator(s): Ted Chen, Steven Liu, Eunice Wu
Department(s): EVMS HOPES free clinic

Abstract

INTRODUCTION: Patient no-shows and miscommunications create significant problems for the function and logistics of HOPES Free Clinic.

Communication between patients and HOPES is the responsibility of the Continuity Coordinators (ConCoord) Team. In the past, ConCoord volunteers would make phone calls to each patient on the week of their appointments as a way to not only remind of their upcoming appointment, but also to provide an avenue for patients to cancel. However, this approach has several issues. First, due to the daily schedule of our student volunteers, most phone calls by necessity are made during hours where many of our patients are unlikely to answer. Also, given the recent rise in the number of robocalls in the US, patients can be less likely to answer calls from unknown numbers. Further, we have found that making reminder calls is the most time consuming non-clinic assignment for our student volunteers. These factors combined make reminder phone calls non-ideal.

Instead of phone calls, text message reminders provide several key advantages. Texts, contrasting with calls, are asynchronous in nature, meaning that texts sent during working hours will reach their recipients regardless of their ability to answer at the moment. Additionally, reminder texts can be made by utilizing a template and an automation script, making the process much less time intensive for our student volunteers.

METHODS: ConCoord officially switched to reminder texts in September 2019, and data was collected on effectiveness of patient communication both before and after the switch via chart review in Practice Fusion, the HOPES clinic EMR of choice. Specifically, data was gathered on clinic date, clinic type (ie Primary Care, Specialty, etc.), appointment type (new or followup), longevity of patient's history at HOPES, patient age, patient gender, and whether the patient was able to be reached prior to clinic date in order to confirm the appointment. This data was then correlated with the show, cancel, or no show status of the patient.

RESULTS: Since switching to texting, we have found that patients no-show rates have significantly decreased from 26% to 17% (one-tailed p-value < 0.01), while appointment cancellation rates have increased correspondingly, from 17% to 26% (one-tailed p-value < 0.01), without decreasing the overall proportion of patients coming to their scheduled appointments (42% to 43%, two-tailed p-value $= 0.91$). Spanish-speaking ConCoord, having made a similar switch in June 2019, saw similar findings (Trainor et al, 2019 EVMS Research Day).

We postulate that the change in no-show rate and corresponding change in cancellation rate are due to the fact that reminder texts, due to their asynchronous nature, are able to effectively reach a wider range of patients (who otherwise are unable to answer phone calls). By providing an effective means of communication, those patients who could not attend their appointments are more likely to communicate with HOPES clinic and cancel their appointment, leading to potentially reassignment of their appointment slot, as well as more efficient use of clinic resources

CONCLUSION: While our current data show reminder texting provides more effective communication between patients and HOPES Free Clinic, the data was collected only during the pre-COVID era. It will be important to continue collecting data in the current COVID era and beyond to ensure any changes in patient demographics, world events, etc. do not significantly impact patient-clinic communication in the future. Additionally, more data needs to be collected from our student volunteers to quantify the effects of switching from reminder phone calls to reminder texts.

Abstract Title: State of the art understanding of EVs as mediators linking sleep dysregulation and metabolic dysfunction

Investigators: Vaisali Chilamkurthy, Manasa Vallabhaneni, Ravin Fisher, Sezgi Arpag-McIntosh, Larry Sanford, Anca Dobrian
Department: EVMS Department of Physiology

Abstract

Introduction: Sleep deprivation has become increasingly prevalent with many Americans reporting less than 7 hours of sleep per night. Further, there is growing evidence that underscores a link between sleep dysregulation and metabolic dysfunction. Sleep loss and altered sleep patterns disrupt metabolic homeostasis and precipitate the onset of obesity, diabetes, NASH, and other disorders. One way that sleep deprivation affects the body is through changes in cellular makeup; this is most notably seen through circulating extracellular vesicles (EV). Extracellular vesicles are novel carriers of cell-specific cargo that aid in inter-organ communication. They transport various cellular material such as lipids, proteins, and miRNA. The biological activation of EV cargo has been shown to induce effects in immune response, oncogenesis, and cellular dysregulation. EV are a relatively recent paradigm that have helped shape our understanding of the metabolic state of a cell in physiologic and pathologic conditions. Remarkably EVs can cross the blood-brain barrier and therefore mediate exchange of miRNA, proteins or metabolites between brain and peripheral organs. The goal of this review is to present a current understanding of the role of EV in sleep and metabolism and assemble epidemiologic evidence of EV as potential mediators between the two.

Methods: This review was structured into distinct chapters. The main chapters are 1. Physiologic and pathologic sleep, 2. Metabolic dysfunction associated with sleep disorders, 3. Mechanisms leading to metabolic dysfunctions in sleep disorders, 4. Background on extracellular vesicles, 5. Extracellular vesicles and metabolic diseases, 6. Extracellular vesicles and metabolic diseases 7. Can EV mediate effects of sleep dysregulation on metabolic dysfunction? A comprehensive search was done using PubMed and some of the keywords used were extracellular vesicles, exosomes, NASH, obesity, type 2 diabetes, sleep apnea and sleep deprivation. The search was distilled down to 105 references that report key findings relevant to each of the chapters.

Results and Conclusions: There are 4 papers that show a link between sleep and metabolism via EVs. Chronic sleep fragmentation causes changes in EV cargo leading to alterations in clock gene expression, reduced peripheral insulin sensitivity and increases in tissue adiposity among other changes. There is abundant and growing evidence of epidemiologic links between sleep, EV and metabolic disorders. However, there still remains uncertainty surrounding the contribution of brain-derived EV to the plasma pool and the mechanism of uptake of EV by targeted organs. Further studies on the interplay between sleep, EV and metabolism are necessary and hold potential for informing therapeutic interventions.

Abstract Title: Identification and Characterization of Clinical *Staphylococcus aureus* Isolates

Investigator(s): Caitlin Clark; Katelyn Cranmer, MS; Julia A. Sharp, PhD
Department(s): Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION
Staphylococcus aureus is a major and persistent human pathogen responsible for a variety of hospital- and community-associated infections. Highly adaptable, *S. aureus* has developed resistance against several classes of antibiotics, including methicillin. The rise of methicillin-resistant *S. aureus* (MRSA) in the community necessitates genotypic and phenotypic characterization of community-associated MRSA (CA-MRSA) strains to understand their distribution and identify conserved features that may be used to combat infections.

METHODS
To characterize genomic profiles of community-associated *S. aureus* strains, *S. aureus* clinical isolates were examined for sequence type and staphylococcal cassette chromosome mec (SCCmec) type, a mobile genetic element that contains the methicillin-resistance gene (*mecA*). Briefly, isolates were grown overnight and genomic DNA (gDNA) was extracted using heat. gDNA was subjected to Multilocus Sequence Typing (MLST) using PCR and Sanger sequencing methods, and SCCmec typing using multiplex PCR. Contiguous sequences (contigs) were created with GeneStudio, then queried using the "*Staphylococcus aureus* isolates database" to identify alleles and subtype isolates.

RESULTS
SCCmec typing found all MRSA isolates to be positive for the *mecA* resistance gene, as expected, while methicillin sensitive lab strains were negative; several SCCmec types were identified among the isolates. Analysis via MLST of 7 housekeeping genes successfully identified isolates by sequence type.

CONCLUSION
Our data shows evidence of sequence- and SCCmec- type variation among the local community from clinical isolates that can be further characterized phenotypically for similarities and differences. An understanding of the types of local community *S. aureus* strains can provide insight clinically to more efficiently treat CA-MRSA infections when they arise.

Abstract Title: Using Artificial Intelligence to Create a Live Literature Review of COVID-19 Associated Pernio-like Lesions

Investigator(s): Candler Clawson, MS3; Waleed Adawi, MS1, Mika Tabata, MD, Justin Ko, MD, Tayab Waseem, PhD

Department(s): EVMS, Massachusetts General, Stanford Medical, Wagner Macula and Retina Center

Abstract

INTRODUCTION: With the rapidly evolving pace of publishing COVID-19 literature, it is more crucial than ever that medical and scientific professionals are able to rapidly evaluate and stay up-to-date on relevant studies and publications. One topic of relevance, is a question of the relationship between findings of acro-ischemic lesions of their toes and fingers in children and adults with SARS-CoV-2. In order for clinicians to know how to best evaluate and treat these patients clinically, they must be able to stay up to date on the literature and evolving evidence surrounding this question.

METHODS: Using the CORD-19 dataset, AI extracted relevant parameters from manuscripts that discussed acro-ischemic lesions and COVID-19. These included the publication date, manuscript title, journal, study type, sample size, study population demographics, percentage of the study population presenting with lesions, location of acro-ischemic lesions, a summation excerpt, and whether the study found a link between these lesions and COVID-19 infection. A test subject then wrote an inclusive literature review using the AI-curated table, while a control subject wrote an inclusive literature review without the AI-curated table.

RESULTS: With the assistance of an AI, the reviewer was able to extract 38 relevant literature as well as the useful parameters of each publication. Once extracted, the reviewer was able to more quickly construct a literature review using the curated table than possible with traditional literature review. The final review found that adults infected with COVID-19 are more likely to develop severe and symptomatic ischemic lesions requiring medical management while children develop more localized pernio-like lesions on their extremities that resolved without treatment.

CONCLUSION: AI is able to locate relevant manuscripts and extract useful parameters from the text in order to expedite the literature review process. We demonstrate how AI allowed medical professionals to better synthesize the literature for this clinical question, and posit that it may hold potential for broader deployment and impact for addressing other clinical concerns as well.

Abstract Title: Understanding Attitudes Toward Contraception and Barriers to LARC Use in the Teenage Population

Investigator(s): Coons, JT, Vignali, LH, Yi, Z, Lawrence, SW, Sriraman, NK
Department(s): Pediatrics

Abstract

Introduction: Long-acting reversible contraceptives (LARC), such as intrauterine devices (IUDs) and subdermal implants, are recommended as the first-line contraceptive for all women, including adolescents. Despite high efficacy and satisfaction rates, LARC use among sexually active teenagers remains under 6% nationally. Our study aimed to identify barriers to LARC use in adolescent patients at an urban pediatrics clinic in Eastern Virginia.

Methods: Female patients ages 13-19, parents, and providers were asked to complete self-administered surveys. Surveys included demographic questions and questions regarding beliefs and attitudes towards three contraceptive methods: oral contraceptives, intrauterine devices, and implants.

Results: A total of 144 surveys were completed by patients (n=53), parents (n=40), and providers (n=51). Among the adolescents surveyed, 15 (28%) reported being sexually active and 22 (42%) reported ever having used a contraceptive. Adolescents reported using implants (26%), condoms (9%), and oral contraceptives (3%) as contraceptive methods. Few adolescents had general knowledge about IUDs, with 14% rating the statement "I know basic information about IUDs" to be somewhat or extremely true compared to 36% for implants and 49% for birth control pills. Adolescents' choice to use a contraceptive method was significantly correlated with perceived parental support ($r > 0.6$) and beliefs in the method's side effects ($r > 0.5$). Parents were most likely to recommend birth control pills (38%) to their child, followed by IUDs (23%) and implants (15%). Providers were most likely to recommend birth control pills (76%), followed by implants (64%) and IUDs (44%).

Conclusions: Contraceptive preference and knowledge level varied between teen patients, parents, and providers. Most adolescents did not know basic information about all three contraceptive methods, suggesting a need for enhanced education and provider communication regarding contraception and sexual health.

Abstract Title: Peritoneal dialysis patient with disseminated Nocardial infection involving the peritoneum, central nervous system, and lungs

Investigator(s): Jessica Corder, MS4; Catherine Derber, MD
Department(s): EVMS Internal Medicine- Infectious Disease

Abstract

INTRODUCTION
Nocardiosis is an infection caused by the gram-positive aerobic actinomycete *Nocardia* species. Found mainly in soil and vegetation, this species is identified by its branching-rod appearance and weak acid-fast staining. While *Nocardia* is ubiquitous in nature, its pathogenicity is relatively low, making it an uncommon cause of disease. Therefore, the majority of infections occur in immunocompromised hosts. The primary site of infection is the lungs which may lead to pneumonia and abscess formation. In immunocompromised populations, *Nocardia* can then spread widely to other organs, with a high affinity for neural tissue. Nocardiosis is known to cause disseminated, relapsing and remitting infection despite appropriate antibiotic therapy.

CLINICAL FINDINGS
This case discusses a 75-year-old man with bullous pemphigoid on long-term immunosuppressants who presented with bacterial peritonitis. He was treated with a short course of antibiotics, and dialysate cultures subsequently grew Nocardia. One month after his initial diagnosis and treatment, the patient presented to the emergency department with sepsis. His peritoneal catheter was subsequently removed, he was started on broad spectrum antibiotics, and his immunosuppressive regimen was decreased. Nocardia was identified during this hospitalization. The patient developed a new oxygen requirement prompting a CT of the chest which showed a right upper and right lower lobe infiltrate. Given Nocardia's predilection for the brain, a CT of the head was performed showing numerous nodular lesions. The patient underwent multiple antibiotic changes with eventual transition to oral trimethoprim-sulfamethoxazole for long-term maintenance therapy. An expectorated sputum sample was not obtained until two weeks into his antibiotic therapy and showed no growth. Repeat CT of the chest demonstrated improvement after one month of treatment, however he clinically worsened with increasing oxygenation requirements. After discussion with the medical team, his family opted for palliative care about a month into his hospitalization. The patient ultimately expired after a cardiopulmonary arrest a few months after his initial diagnosis.

CONCLUSION
Although uncommon, disseminated Nocardial disease should be considered in immunocompromised patients with shortness of breath and/or altered mental status. While pulmonary and disseminated Nocardial infection is well represented in the literature, peritoneal involvement has rarely been described. This case illustrates the factors that led to infection in this patient, the propensity for dissemination of this pathogen, and the high morbidity in immunocompromised individuals.

Abstract Title: Utilization of Artificial Intelligence Powered Literature Review to Answer Key COVID-19 Questions

Investigator(s): Nicole Crofton, Jamie Gergahty, Justin Zaremba, Jan Bremer, Maikel Boot PhD, Lucas Buyon, Paul Mooney PhD, Byron Wallace PhD, Michael Stolz, Dylan Vance, Amna Afreen, Zachary Landao DO
Department(s): Eastern Virginia Medical School, Wagner Macula & Retina Center, University Medical Center Hamburg-Eppendorf, Yale University, Harvard TH Chan School of Public Health, Kaggle, Northeastern University, Northeast Georgia Medical Center, Drexel University College of Medicine, Ross University Medica School, United States Marine Corps

Abstract

INTRODUCTION: As the COVID-19 pandemic persists, our ever-evolving understanding of this disease has resulted in an overwhelming influx of scientific data. Researchers, healthcare professionals, and policymakers across the globe have been faced with the challenge of complying and analyzing an impossible amount of information. The need for a robust AI-powered literature review is paramount for an efficient, actionable examination of the rapidly growing COVID-19 research. We herein report the efforts of the first large scale dataset of its kind within the United States, which was spearheaded by the White House Office of Science and Technology Policy. The CORD-19 is a consortium combining leaders in the fields of bioinformatics and artificial intelligence (AI) to combine custom search tools, text extraction algorithms, and expert curation to rapidly summarize the over 200,000 pieces of COVID-19 literature that it encompasses.

METHODS: The CORD-19 dataset was created after a call to action by the White House Office of Science and Technology Policy to create a machine-readable collection of coronavirus literature. Natural language processing algorithms were used by AI to extract relevant parameters from the CORD-19 dataset to answer 98 COVID-19 related questions. A team of over 250 medical and scientific volunteers from global institutes curated live literature reviews of the manuscripts the algorithms pulled. The relevant publications for each question were summarized in a tabular format. Search tools used for relevant literature reviews included PubMed, Google, and COVID-19 specific search engines such as covid19-research-explorer.appspot, semantic scholar, SciSight and covidex.

RESULTS: The CORD-19 dataset was utilized to expedite the analysis of massive volumes of research in real-time to aid in the mitigation of the COVID-19 pandemic. These AI were then used to curate concise tables in an easily readable, question-specific format that was then placed on the Kaggle website (Google Cloud subsidiary). These tables were automatically updated as the literature evolved to present the most recent research concerning COVID-19. Examples of the parameters that were extracted from the manuscripts include date of publication, journal, title of the manuscript, odds ratio, relative risk, hazard ratio, study design, sample size, measure of evidence, target population, and relevant excerpts from the studies. A link to each manuscript was also included alongside each manuscript so the viewer could access more details of the study results.

CONCLUSION: COVID-19 brings a high demand for useful, actionable research, as medical professionals and the larger scientific community seek to understand, predict, and solve the issues that arise from a global pandemic. AI-generated and professionally curated data tables greatly help expedite the literature review process, giving researchers actionable and current information on COVID-19 changes. The AI tools developed are now being utilized by medical journals, research institutes, and non-government organizations across the world.

Abstract Title: Parental Awareness of Rear-Facing Child Safety Seat Guidance

Investigator(s): Taylor Dobyns, BS, CPhT, MD Candidate; Emily Gordon, MPH; Ann Edwards, MS, CPST; Charles Springer, MD Candidate; Kelli England, PhD, LCP, CPST
Department(s): Pediatrics, Community Health & Research Division, Eastern Virginia Medical School

Abstract

INTRODUCTION
Approximately 75% of car crashes are frontal, which applies forward collision force to the driver, passengers, and contents of the car (Ragland et al. 2001). The crash forces applied to a child in a forward-facing seat propel the head, neck, arms, and legs forward while the body is restrained, leading to spinal stretching and other injuries to the child's still developing body (Durbin 2011). Children under two years old are especially vulnerable to these crash forces (Durbin 2011). However, if the seat is rear facing, the seat absorbs most of the forward force in a frontal car crash, supporting the spine and keeping the skeletal system in alignment (Durbin 2011). In order to prevent these injuries in young children, various state laws and best practice recommendations have emerged. The American Academy of Pediatrics recommends that children ride in a rear-facing safety seat to a minimum of age two years or longer, even up until the age of four years, provided that the child is still within the weight and height requirements of the rear facing seat. Virginia State Law effective July 1st, 2019 states that children are to ride in a rear-facing safety seat until the age of two or the child reaches the minimum weight limit for a forward-facing safety seat as prescribed by the manufacturer of the safety seat.

METHODS
Parents of children under thirteen in the state of Virginia were recruited online. Participants were each given an Amazon gift card for their participation in a virtual focus group ($40) or completion of an online survey ($15). Focus group and survey data were collected regarding parental knowledge, perceptions, and barriers to extended rear-facing positioning. A moderator's guide was developed to hold three focus groups via BlueJeans, a video conferencing platform. A member of the research team led each group (group n sizes = 6, 7, 8) through the interview questions, with assistance from a second research team member who took notes. Sessions were recorded and transcribed for analysis in NVivo qualitative data analysis software. Mixed methods survey data were also collected from 31 participants using Qualtrics, a secure online survey software, which were analyzed using both NVivo and SPSS analysis software.

RESULTS
A total of 52 parental responses are being analyzed and coded into four important categories of information regarding perceptions of rear-facing child safety seat guidance: knowledge of child safety seat recommendations, reactions to child safety seat recommendations, compliance with recommendations, and general parent safety seat questions. The team is in the process of identifying themes that emerge from the data as concepts are coded. Preliminarily, parents indicated various levels of understanding of the law, and these were divided into the following categories: awareness of the law and knowledge of the law. Awareness of the law indicated that a parent understood there is a law regarding rear facing but may not have known exactly what the law dictated, whereas knowledge indicated a parent had an understanding of the law that may or may not be complete. Additional barriers and perceptions are currently being coded.

CONCLUSION
Parental understanding of the most current rear-facing child seat laws and best practice recommendations are key for both safety and prevention of injuries amongst children. Once analysis is complete, these data can further be used to address knowledge gaps and barriers to rear facing, and these issues in adherence can be targeted in future communications.

Abstract Title: The Masquerading Acute Liver Injury

Investigator(s): Steve D'Souza MD, Jay Patel MD, Maurice Marcuard MD, Sami Tahhan MD FACP
Department(s): Internal Medicine, Eastern Virginia Medical School and Orange Park Medical Center; Gastroenterology, Palisades Medical Center

Abstract

INTRODUCTION: The presence of abnormal liver function tests has a broad list of differential diagnoses and is commonly seen in patients with medication side-effects. Hepatotoxicity is associated with many checkpoint inhibitor immunotherapeutics and requires immediate initiation of steroids; however, it is important to consider alternate etiologies for transaminitis. We present a case of a patient with presumed medication related hepatotoxicity found to have an extrahepatic etiology to their liver injury.

CLINICAL FINDINGS: A 69 year-old female with a medical history significant for metastatic pancreatic cancer status-post resection by pancreaticoduodenectomy (Whipple procedure) presented to the emergency room with complaints of progressive nausea, weakness, malaise, lower extremity edema, dark urine, and abdominal distension. She denied fevers, chills, and abdominal pain. She recently stopped taking pembrolizumab (Keytruda) at the recommendation of her oncologist due to abnormal liver enzymes, but reported progression of her symptoms. In the emergency room, vitals were normal.

Physical examination was notable for a chronically ill and frail appearing female with scleral icterus, a distended abdomen, and bilateral lower extremity edema. Laboratory studies were notable for significantly elevated transaminases, but decreased compared to four weeks prior, as well as markedly elevated total and direct bilirubin. She was admitted for evaluation of post-hepatic obstructive pattern.

Computed tomography of her abdomen and pelvis with contrast showed increased intra- and extra-hepatic biliary dilation as well as postsurgical changes. The patient underwent endoscopic retrograde cholangiopancreatography with endoscopic ultrasound, and endoscopic biliary decompression was attempted but unsuccessful due to her anatomy. Interventional radiology was consulted for percutaneous transhepatic cholangiography, and the patient successfully underwent biliary cannulation into the small bowel and stent placement. During this procedure, it was noted that there was a stricture of the biliary-enteric anastomosis.

CONCLUSION: This case illustrates the complexity of managing patients with pancreaticobiliary disease. There are many possible complications of the biliary-enteric anastomosis component of pancreaticoduodenectomy (Whipple procedure), including biliary stenosis, bile leak, bleeding, and infections. Biliary strictures are uncommon, with one analysis reporting a 2.6% occurrence rate.

The majority of patients who are treated with pembrolizumab have cholestasis prior to medication initiation, and medication related cholestatic injury is common, reported as 14% in one analysis.

This case demonstrates the potential dangers of succumbing to premature diagnostic closure and biases. Confirmation bias causes one to specifically seek information that supports initial conclusions. Other types of bias involve the overvaluation of irrelevant information and persistence of initial beliefs despite new information (anchoring bias). By being open to alternative diagnoses, we were able to recognize the obstructive pattern of liver injury. While infrequent, anatomic causes must remain on the list of differential diagnoses.

Make sure you date your diagnosis for a while before you feel wedded to it.

Abstract Title: BLZ945 Depletion of Perivascular Macrophages in Acute SIV-infected Macaque Brain

Investigators: Jinbum Dupont, Julian Hattler, Dr. Woong-Ki Kim
Department: EVMS Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION
Despite successful highly active antiretroviral therapy (HAART), HIV-associated neurocognitive disorders (HAND) continues to be an issue for many HIV infected individuals; even in patients with undetectable viral loads. In this study, we investigated the effect of BLZ945 on perivascular macrophage levels in SIV-infected rhesus macaque brains. BLZ945 is an orally administered inhibitor of colony stimulating factor 1 receptor (CSF1R) which is found in high levels on perivascular macrophages and is responsible for cell proliferation and survival. Perivascular macrophages are a known reservoirs for HIV in infected individuals even when their plasma viral load is suppressed by HAART.

METHODS
Six acutely SIV-infected, CD8 depleted, rhesus macaques were organized into a low dose group orally administered 10mg/kg/day, a high dose group orally administered 30mg/kg/day, and a control group receiving 0mg/kg/day of BLZ945 from Novartis. The treatment was administered for 21 days before necropsy. Formalin fixed paraffin embedded tissue sections from the hippocampus, basal ganglia, frontal cortex, occipital cortex, parietal cortex, thalamus, MB1, and PVC1 of each animal were stained using immunohistochemistry (IHC) for CD206 and P2RY12 and imaged using light microscopy. Fifteen images at 10x magnification were randomly generated from each slide. The average number of perivascular macrophages, counted by hand, across the fifteen images was used to quantify the perivascular macrophage levels for each section. The microglia levels were quantified using the average percentage area of the fifteen images for each section. All statistics were run in GraphPad prism 7. The results were compared to determine the effect of BLZ945 on perivascular macrophage and microglia levels.

RESULTS
Analysis of the IHC staining showed notably less CD206 staining of perivascular macrophages and slightly less P2RY12 staining of microglia in the brain tissue of the high dose treated animals, and less CD206 staining of perivascular macrophages and nearly the same amount of P2RY12 staining of microglia in the brain tissue of the low dose treated animals compared to the untreated brain tissue.

CONCLUSION
Based on the results, BLZ945 successfully depleted perivascular macrophages with minimal effects on microglia, with a more pronounced effect at high doses. This suggests a possible way to help reduce levels of HIV reservoirs in perivascular macrophages found in the brain of infected individuals.

Abstract Title: "A Comparison Study of Spanish-speaking and Non-Spanish-speaking Patient Populations in a Student-Run Free Dermatology Clinic"

Investigator(s): Taylor Dyson, MS3, M.S., Stafford Brown, MS3, M.S., Alexandra Leader, MD, MPH, Edward Prodanovic, MD

Department(s): Dermatology

Abstract

INTRODUCTION

In 2015, the Health Outreach Partnership of Eastern Virginia Medical School Students (HOPES) Clinic established its Dermatology Clinic to meet the dermatological needs of the uninsured population of Hampton Roads, Virginia. In 2016, EVMS medical students established ***Clínica Comunitaria Esperanza*** within the HOPES Clinic system to provide healthcare for uninsured, Spanish-speaking residents of Hampton Roads, Virginia.

METHODS

A chart review of patients seen in the HOPES Dermatology clinic since its inception on January 15, 2015 to the most recent, in-person clinic date, November 21, 2019, was conducted using the Practice Fusion electronic medical record. The Spanish-speaking patients were given the designation of "ESP" within Practice Fusion. The following variables were recorded in a password-protected Excel spreadsheet: age, sex, race, city of residence, date of first visit, date of most recent visit, reason for first visit, vitals (height, weight, body mass index, blood pressure) at first visit, number of vitals taken over the course of patient care, services provided, diagnoses, medications, additional patient needs, as well as the number of clinic visits, no-shows, and cancellations. The data values corresponded with a data dictionary. The data recorded for the Spanish-speaking and the non-Spanish-speaking patient populations were compared.

RESULTS

The HOPES Dermatology Clinic has seen 140 patients since January 15, 2015 to its most recent, in-person clinic date, November 21, 2019.

Non-Spanish-speaking

123 patients were non-Spanish-speaking. The patients' ages ranged from 19 to 67 years. 81 of the 123 patients were female. The most common diagnosis was seborrheic keratosis. 18 of 123 patients were diagnosed with seborrheic keratosis. 68 of 123 patients were prescribed medications.

Spanish-speaking

17 patients were predominantly Spanish-speaking. The patients' ages ranged from 13 to 57 years. 12 of the 17 patients seen were female. The most common diagnosis was keratosis pilaris. 3 of 17 patients were diagnosed with keratosis pilaris. 13 of 17 patients were prescribed medications.

Similarities between Populations

The majority of patients live in Norfolk, Virginia. The majority of both clinic populations was female. The majority of patients were seen for one visit. Race was recorded for less than 3% of patients in both populations. The most common reason for first visit was rash. The most frequently prescribed medication was Triamcinolone 0.1% ointment. 21 of 123 non-Spanish-speaking patients were prescribed Triamcinolone 0.1% ointment. 3 of 17 Spanish-speaking patients were prescribed Triamcinolone.1% ointment. The most frequently provided service was cryosurgery. 17 of 123 non-Spanish-speaking patients received cryosurgery while in the clinic. 3 of 17 Spanish-speaking patients received cryosurgery in the clinic.

CONCLUSION

The Non-Spanish-speaking and the Spanish-speaking patient populations of the HOPES Dermatology Clinic had many similarities, such as the most commonly prescribed medication and the most commonly provided service. The Non-Spanish-speaking and Spanish-speaking patient populations of this clinic differed in the most common diagnosis, the frequency of how often the most common service was provided, and the frequency of how often the most common medication was prescribed.

Abstract Title: The Role of Hydrogen Peroxide in Cathodic Voltage Controlled Electrical Stimulation as a Treament for Peri-prosthetic Joint Infections

Investigator(s): Catherine Eccleston, Caelen Clark
Department(s): University at Buffalo, Department of Orthopaedics

Abstract

INTRODUCTION: Peri-prosthetic joint infection (PJI) is a devastating complication associated with joint arthroplasty. It has led to functional incapacitation, increased pain and hospital stays, and even increased mortality. The treatment of PJI is made extremely difficult by the formation of biofilms on the implant. A mature biofilm consists of bacteria surrounded by an extracellular matrix rich in polysaccharides, which increases its resistance to antibiotic treatment The current standard treatment for PJI is two stage exchange arthroplasty, which involves the removal forthe infected implant and a period of mechanical deficiency while the infection is resolved. This is extremely debilitating for patients, and thus, there is a lot of motivation to develop new treatment methods that do not require removal of the implant. Cathodic Voltage Controlled Electrical Stimulation (CVCES) is one such treatment. CVCES is being investigated as a method for the minimally invasive treatment of PJI. In this technique, the implant serves as the cathode in a three electrode configuration, and a constant voltage is applied. Although this has been demonstrated both in vitro and in vivo, a complete understanding of the mechanism of the antibacterial effect of CVCES is still required. One of the proposed contributing factors for the antibacterial activity of CVCES is the electrochemical production of Hydrogen Peroxide (H2O2). This occurs when oxygen gets reduced during the cathodic stimulation. In these experiments, the effect of H2O2 against MRSA was determined to see if it plays a role in the antimicrobial effects of CVCES.

METHODS: This study examined the effect of external additions of H_2O_2 on the viability of MRSA (clinical isolate, strain NRS70). A range of concentrations from 5μM -100μM were evaluated against MRSA in both the planktonic and biofilm state. The primary variable was colony forming units (CFU/mL) of MRSA present after treatment with H_2O_2, and the secondary variable was the minimum concentration at which H_2O_2 was bacteriostatic/bactericidal. These experiments were done in a 24-well plate ***in vitro*** model.

RESULTS: The bacteriostatic and bactericidal concentrations of H2O2 were determined for MRSA in the planktonic form. H2O2 was bacteriostatic at 15 μM and bactericidal at 25 μM. However, H2O2 was ineffective once the mature biofilm had formed. MRSA continued to grow on these plates, even at the highest concentration of H2O2.

CONCLUSION: Since H_2O_2 alone was effective against MRSA in the planktonic form but ineffective once it formed a biofilm, this indicates that H_2O_2 may be able to prevent infection in orthopaedic implants. However, it is ineffective once a biofilm is present. These results point to other factors contributing to the effectiveness of CVCES such as the alkaline environment or the generation of hydrogen gas. These results support the study hypothesis that H_2O_2 would be effective against MRSA in its planktonic form but ineffective in its biofilm form.

Abstract Title: Pulmonary Alveolar Proteinosis in a chronic smoker

Investigator(s): Alsiddig Elmahdi
Department(s): Department of Veteran Affairs

Abstract

INTRODUCTION: Pulmonary Alveolar Proteinosis (PAP) is a disease characterized by the accumulation of surfactant components within alveoli. The pathophysiology of PAP is thought to stem from the inability of macrophages to clear these surfactant components. This can be due to autoantibodies against GM-CSF, genetic mutations in surfactant components or genetic mutations in GM-CSF. Exposure to factors that impair alveolar macrophage function can cause secondary PAP. This can be due to inhalation exposures or infections. Whole Lung Lavage (WLL) is the mainstay of treatment for symptomatic PAP. Inhaled GM-CSF can be used in cases where WLL is not well tolerated. PAP is rarely seen in smokers.

CLINICAL FINDINGS: A 65 year-old-male veteran chronic smoker with COPD presents with cough productive of clear sputum. On exam, the patient had minimal crackles and bilateral finger clubbing. PFTs showed mild obstructive ventilation defect with minimal impairment of diffusion capacity. Non contrast CT showed bilateral parenchymal fibrosis and a mosaic pattern in the lung fields. CT also showed hyperlucent areas consistent with emphysema. Patient did not improve with steroids. Repeat CT showed worsening of the mosaic pattern with persistent parenchymal fibrosis. Bronchoscopy of the lungs showed inflamed upper lobed with thick white secretions. Treatment was initiated with high dose corticosteroids and PCP prophylaxis

After 2 months of treatment, shortness of breath worsened. The patient's cough was now productive with brownish sputum. CT showed a diffuse groundglass appearance to the lungs with scattered small rounded areas of parenchymal sparing which could represent blebs. The groundglass opacification had worsened compared to the previous study. Considerations included pneumocystis or viral pneumonia versus pulmonary hemorrhage, or drug toxicity or idiopathic interstitial pneumonia. There was no adenopathy or pleural effusion. Patient now required 4L O2 with transfer to CT surgery for open lung biopsy

Biopsy showed fibrotic changes which was negative for inclusion bodies. Patient became hypoxic and ABG showed respiratory Alkalosis. O2 sat was in the 40s. CTA was negative for PE. He was started on 14L O2 and transferred to the ICU. He underwent another lung biopsy in 2 weeks. Biopsy showed PAS positive eosinophilic material filling the alveolar spaces consistent with Pulmonary Alveolar Proteinosis. After diagnosis, whole lung Lavage was performed over the course of 2 weeks.

Patient was discharged with improvement of symptoms. Follow up chest CT showed persistent bilateral patches of interstitial thickening and groundglass opacities consistent with residual areas of pulmonary alveolar proteinosis

CONCLUSION: This case illustrates the potential for PAP in chronic smokers with interstitial lung disease and respiratory failure. Although PAP is rare, it is important to keep it in mind interstitial fibrosis that is unresponsive to treatment. Moreover, secondary symptoms can be significantly alleviated with Whole Lung Lavage.

Abstract Title: Changes in liver fibrosis and islet morphology in response to sleep fragmentation in murine models of NASH and diabetes

Investigator(s): Ravin, Fisher, Manasa Vallabhaneni, Sezgi Arpag McIntosh, Anca Dobrian
Department(s): Physiological Sciences

Abstract

INTRODUCTION: Stress induced by sleep fragmentation has been identified as a contributor to the metabolic dysregulation. Stress can lead to the dysfunction of multiple metabolic pathways which play a role in the development obesity and co-morbidities such as insulin resistance, type 2 diabetes and fatty liver disease. To determine mechanistic pathways linking sleep dysregulation with metabolic dysfunction adequate animal models and sleep dysregulation paradigms are critically needed. In my project I used two mouse models: db/db mice, a strain that develop early obesity and accelerated insulin resistance and type 2 diabetes due to lack of the leptin receptor; and, the DIAMOND mouse model, a stable isogenic strain that develops progressive fatty liver and NASH when fed high fat diet and fructose water. Using these models we applied a short-term sleep fragmentation (SF) paradigm and determined effects on liver fibrosis and islet functional remodeling. This data will provide important information for therapeutic windows of intervention targeted to ameliorate liver fibrosis and to improve islet function in mouse models of disease exposed to sleep dysregulation paradigms.

METHODS: SF was applied for two weeks, 6 hours/day, every two minutes. As controls we used age matched mice for each of the strains, that did not receive the SF protocol.. We used 3 cohorts of DIAMOND male mice kept on the special western diet from 8 weeks of age, for 18 wks, 26wks and 40wks of age. They were randomly assigned to SF protocol or used as controls (n=5-6/group). These time points were selected based on different disease stages in this model that were previously published (from fatty liver to steatohepatitis with extensive fibrosis). As a type 2 diabetes model we used db/db male mice at 8 weeks of age that were randomly assigned to SF or control groups (n=3-4/group). Starting at this age, db/db mice became severely hyperglycemic and hyperinsulinemic, before they transition to the diabetic insulin dependent stage, around 15 weeks of age. We collected the livers and pancreas post-mortem and generated formalin-fixed, paraffin embedded blocks that were used to generate 4uM thick section for analyses. To analyze the extent of fibrosis in DIAMOND mice sections, we used 12 images collected from 2 non-serial sections of 2 different lobular areas (n=3 images/section). The sections were stained with Sirius Red and images were analyzed using an ImageJ plug-in software developed to analyze liver fibrosis. Data was expressed as a summation of percent fibrotic areas from all slides analyzed for each of the mice. Data was analyzed using t-test to establish differences between SF and control groups at each time point. To determine islet morphometry in db/db pancreas, we used a similar sampling approach. Islets were stained using a hamster anti-mouse insulin antibody and a FITC-labeled secondary antibody. Images were taken using a fluorescent microscope and islet area was measured using the ImageJ software. Islet size distribution was calculated and differences were analyzed using the unpaired Student t-test. Islet size distribution was used as a surrogate for islet functional remodeling.

RESULTS: SF increased liver fibrosis in DIAMOND mice by 2.8-fold (p-value<0.05) in early liver disease stages (18 weeks on diet). An increase in average fibrotic areas by ~2.5-fold (p-value<0.05) was also found in mice with advanced fibrotic disease after SF compared to controls. No significant changes were found in 26 weeks mice. Interestingly, the increase in fibrosis at early stages of disease was accompanied by increase in macrophage numbers and remodeling (please see poster by Vallabhaneni, M. et al). In db/db mice in the pre-diabetic phase there is an increase in islet size (hypertrophy) and limited islet neo-genesis (newly formed, small size islets). In mice subjected to SF there was a ~50% reduction in the percent of islets with areas $<5{,}000\mu m^2$ and a ~35% increase in hypertrophic islets with areas $>20{,}000\mu m^2$.

CONCLUSION: In this project I documented increased fibrosis in mice following SF in early stages of steatohepatitis and in advanced NASH with bridging fibrosis. Pathways involved in the early effects are likely caused by increased inflammation (Vallabhaneni poster). However, changes in late stages of disease are likely influenced by different mechanisms, possibly related to stellate cell hyper-activation leading to extensive matrix production. In db/db mice, the neo-islet formation and the hypertrophic remodeling of islets appear to be impacted by sleep fragmentation. Future studies will involve therapeutic approaches targeting relevant pathways in SF-induced disease exacerbation.

Abstract Title: Utilizing a Quality of Life (QOL) Tool to Examine the Presence of Fatigue in Subjects with Diabetes

Investigator(s): Steven Forte BS, Joshua F. Edwards MPH, Carolina M. Casellini MD, and Henri K. Parson, PhD

Department(s): Strelitz Diabetes Center for Endocrine and Metabolic Disorders, Eastern Virginia Medical School, Norfolk, VA
Healthcare Analytics and Delivery Science Institute at EVMS

Abstract:

INTRODUCTION: Chronic fatigue occurs in up to 45% of aging Americans. Fatigue can affect many aspects of quality of life (QOL) including mood and physical functioning, and has been associated with different comorbid conditions. Approximately 10.5% of the United States population over the age of 18 live with diabetes mellitus (DM), and nearly 50% of them will develop neuropathy. It is uncertain whether DM patients, and more specifically DM patients with diabetic neuropathy, experience chronic fatigue. Our objective is to assess the impact of diabetes and neuropathy on the development of fatigue and investigate the influence of other sociodemographic factors on fatigue.

METHODS: This is a cross-sectional study comparing 400 patients with Type 1 (T1DM) or Type 2 Diabetes Mellitus (T2DM), with 75 healthy controls (HC). In order to investigate the presence of fatigue in these 2 populations the self-administered, 35 item, validated Norfolk Quality of Life Fatigue Questionnaire (QOL-F) was administered to all participants. We are presenting preliminary findings from 75 HC and 253 DM patients who completed the questionnaire. Sociodemographic factors including age, race, gender, weight, BMI, and waist-circumference were also collected. Analysis of variance was performed to identify differences between the groups and linear regression models were conducted to identify factors influencing the presence of fatigue.

RESULTS: Two hundred and fifty three T1DM and T2DM subjects (mean age: 60.63±11.37, 65% African American, 35% Caucasian, 62.3% women, mean diabetes duration: 14.7±10.37y, mean BMI 33.49±7.81, 7.5% T1DM, 92.5%T2DM) were included. DM subjects had higher QOL-F scores when compared to HC (50.85±28.89 vs 24.74 ± 18.75, $p<0.0001$). No significant difference in overall fatigue was found between women and men in the DM group (52.94±30.65 vs 47.22±25.60; $p=0.11$), or between African Americans and Caucasians (50.59±28.75 vs 50.88±29.48, $p=0.94$). Diabetic patients with neuropathy reported greater fatigue than those without neuropathy (54.79±28.84 vs 40.86±23.88, $p=.0003$). Paradoxically, older age was found to correlate with improved fatigue ($r=-0.27$, $p<.0001$). BMI did not significantly correlate with fatigue ($r=0.01$, $p=0.81$).

CONCLUSION: This preliminary data provides further evidence that diabetic patients experience greater fatigue than their non-diabetic counterparts. Additionally, this study suggests fatigue is more prevalent in diabetic patients with neuropathy. Our data suggests that the QOL-F tool can be used to discriminate between factors that are associated with greater fatigue and factors that are not associated with greater fatigue in the diabetic population.

Abstract Title: Psychological Stress during the COVID-19 Pandemic and Central Serous Chorioretinopathy

Investigator(s): Mathilde Franklin, MS, Kapil Kapoor, MD, Alan Wagner, MD
Department(s): Eastern Virginia Medical School Department of Ophthalmology, Norfolk, VA. Wagner and Kapoor Research Institute, Virginia Beach, VA.

Abstract

Introduction*:* The relationship between the psychological stress of the COVID-19 pandemic and the development of central serous chorioretinopathy (CSCR) was analyzed at the Wagner Macula & Retina Institute.

Methods*:* This is a retrospective, cross-sectional study. All newly diagnosed CSCR cases were identified. Cases were compared between the pre-pandemic timeframe (January 2015—February 2020) and the COVID period (March 2020—May 2020). Medical records were then reviewed for previously reported risk factors.

Results*:* There was an average of 3.4 monthly CSCR diagnoses, with the greatest number in May 2020 (10 cases, 99.23 percentile). The year 2020 had the highest monthly case rate, which was significantly different from 2015, 2017, and 2018 (P = 0.004). Analyzing the cases using three-month rolling sums, January through March 2020 had the largest number of cases (21 cases, 99.21 percentile). Recent psychological stress was present in 29.4% of the COVID-era and only 9.27% of the pre-COVID patients (P = 0.025).

Conclusions*:* The relationship between a worldwide pandemic in the development of CSCR has not been previously reported. While the most significant number of monthly cases occurred during the pandemic, there was a relative increase shortly before the designated pandemic start-date. Larger, retrospective studies are warranted to evaluate the significance of these findings.

Abstract Title: A Rare Case Of Emphysematous Gastritis

Investigators: Ritsa Frousios, Jody King, MD
Department: EVMS Internal Medicine

Abstract:

INTRODUCTION: Emphysematous gastritis was first described by Fraenkel in 1889. Few cases have been reported up to this date. It is defined as intramural gas in the stomach with diffuse gastric wall inflammation secondary to disruption of gastric mucosa and invasion by gas forming organisms. Early recognition and conservative management are key therapeutic measures.

CLINICAL FINDINGS: A 67-year-old male with newly diagnosed lung cancer, interstitial lung disease, hypertension and systolic heart failure presented with an acute one-day history of hematemesis. On admission patient was hypotensive, tachycardic, and afebrile. Physical exam was unremarkable for abdominal tenderness. Initial labs showed a hemoglobin level of 4.9g/dL and White blood cell count of 15.2 K/uL. Lactic acid was 5.9 mmol/L with a high anion gap metabolic acidosis. Abdominal scan showed gastric distention, diffuse mural edema, and intramural air suggestive of severe emphysematous gastritis with no definite extraluminal free air. The patient was started on Pantoprazole drip, fluid resuscitation, vasopressors, and transfused 5 units. Empiric antimicrobials included Piperacillin/Tazobactam, Metronidazole, and Fluconazole. A nasogastric tube was placed for bowel rest and to monitor for active bleeding. Surgical intervention was deferred due to lack of evidence of gastric perforation. White count responded to antibiotics therefore plans for endoscopy were also deferred. Four days later, the patient showed clinical improvement with stabilization of his hemoglobin. A repeat abdominal CT scan on day 7 showed complete resolution of gastric abnormalities. He completed a 7-day course of Piperacillin/Tazobactam and a 14-day course of Fluconazole.

CONCLUSION: Intramural air trapping can happen along the gastrointestinal tract but is least common in the stomach. Local acidity and good vascularization protect gastric mucosa from bacterial invasion. Insulting agents such as caustic ingestion or alcohol in the setting of an immunocompromised state can disrupt the gastric wall and predispose to the invasion of bacteria. Organisms commonly involved are *Streptococcus*, *Escherichia coli*, *Enterobacte*r, *Clostridium*, *Pseudomonas, Staphylococcus aureus*, *Sarcina*, *Candida*, and *Mucor*. Other predisposing factors include malrotation, bezoar formation, abdominal surgery, and nonsteroidal anti-inflammatory use.

One must differentiate between emphysematous gastritis and gastric emphysema. The latter is a benign condition caused by barotrauma and is defined by air in the stomach wall without evidence of systemic toxicity. Patients with gastric emphysema do not usually present with acute abdomen unlike those with emphysematous gastritis, and prognosis is usually excellent. Radiologically, emphysematous gastritis is characterized by an irregular mottled appearance, compared to the thin linear lucencies seen in gastric emphysema.

No definitive diagnostic criteria exist. Previous studies diagnosed patients based on nonspecific clinical symptoms such as nausea, vomiting, epigastric or left upper quadrant pain, hematemesis and fever. Inflammatory markers and leukocytosis are usually present. Computerized tomography is the gold standard to distinguish intramural gas from intraluminal gas. Radiographic evidence of gas in the portal vein generally portends a worse prognosis, with an estimated mortality exceeding 75% when present. Treatment includes antimicrobials, proton pump inhibitors and supportive measures. Surgery is reserved for cases with medical therapy failure or gastric perforation. The mortality rate can range up to 60%, so early identification is paramount to successful management. An aggressive medical approach allows a favorable evolution in 40% of the cases. However, a risk of gastric stricture as sequel is reported in about 20% of the cases.

Abstract Title: Characterization of 24-Dehydrocholersterol Reductase Overexpressing B Cells in a Novel Mouse Model

Investigator(s): Gauronskas, Phillip J., MS[1]; Mubacher, Marion, PhD[1]; Ma, Shelby, MS[1]; Waseem, Tayab C.[1]; Fernandez-Hernando, Carlos, PhD[2]; Galkina, Elena V.[1]

Department(s): [1]Microbiology and Molecular Cell Biology; [2]Comparative Medicine, Yale School of Medicine

Abstract

INTRODUCTION: Atherosclerosis is a chronic inflammatory disease that develops largely from the overaccumulation of modified low-density lipoprotein (LDL) and formation of atherosclerotic plaques within medium to large-sized arteries. Monocytes infiltrate these blood vessels, differentiate into macrophages and eventually become overburdened with modified LDL. These processes result in overaccumulation of intracellular desmosterol and an anti-inflammatory signaling cascade within these cells. Nevertheless, the highly pro-inflammatory atherosclerotic environment overtime dominates and drives cholesterol –loaded macrophages to a pro-inflammatory phenotype. 24-Dehydrocholesterol Reductase (DHCR24) is a crucial enzyme necessary for both the Kandutsch-Russell and Bloch Biosynthesis pathway for cholesterol synthesis. DHCR24 regulates intracellular desmosterol levels by converting it into cholesterol. B cells display subset-specific roles in atherosclerosis with B1 and Marginal zone B cells being atheroprotective and follicular and Innate response activator B cells playing a pathological role. There are no data on the role of desmosterol in B cells, however, our lab has found evidence suggesting that loading of B cells with desmosterol can result in decreased intracellular Ca^{2+} in response to B Cell Receptor (BCR) engagement, and decreased antibody production against DNP-Ficoll, suggesting desmosterol may regulate B cell phenotype and functions. Moreover, we have found that depleting intracellular desmosterol in B cells through DHCR24 overexpression increases production of antibodies against DNP-Ficoll and increases intracellular Ca^{2+} flux after BCR engagement. Here, we confirmed that our newly established $DHCR24^{fl/fl}$ /$CD19^{cre/+}$ mouse model has B-cell specific upregulation in both mRNA and protein levels of DHCR24. We found that DHCR24 overexpression does not significantly affect B cell response to toll-like receptor (TLR)2 or TLR4 ligands, nor does it significantly alter populations of B cell subsets under homeostatic conditions.

METHODS: $DHCR24^{fl/fl}$/$CD19^{cre/+}$ and $DHCR24^{fl/fl}$/$CD19^{+/+}$ mice were sacrificed and single cell suspensions were prepared from spleens. To examine B cell response in the stimulation with TLR2 or TLR4, splenocytes were cultured in sterile RPMI-1640, supplemented in 10% FBS, 1% penn/strep, GlutaMAX, and -mercaptoethanol. Splenocytes were then treated with either 3 μg/ml of anti-mouse IgM $F(ab')_2$, 1 μg/ml of LPS, 1 μg/ml of Pam3CSK4, or otherwise left unstimulated, and were incubated overnight at 37 °C and 5% CO_2. The cultures were then stained with the following fluorochrome-conjugated antibodies for B cell activation markers: CD86-eF450, MHC-II-APC, CD69-PE, CD40-FITC, and CD19-PE-Cy7. For B cell subset characterization, splenocytes were stained with fluorochrome conjugated antibodies: B220-eF506, CD23-APC, CD43-PE, CD5-eF450, and CD19-PE-Cy7.

RESULTS: We detected significant increases in ***Dhcr24*** mRNA expression in $DHCR24^{fl/fl}$/$CD19^{cre/+}$ B cells compared to $DHCR24^{fl/fl}$/$CD19^{+/+}$ B cells. In line with qPCR data, protein levels for DHCR24 were significantly greater in $DHCR24^{fl/fl}$/$CD19^{cre/+}$ B cells compared to $DHCR24^{fl/fl}$/$CD19^{+/+}$ B cells. In our preliminary data, we found no significant differences between $DHCR24^{fl/fl}$/$CD19^{cre/+}$ and $DHCR24^{fl/fl}$/$CD19^{+/+}$ B cells in the distribution of B cell subsets in $DHCR24^{fl/fl}$/$CD19^{cre/+}$ mice including total population of $CD19^+$ B cells, Marginal-Zone (MZ) B cells ($CD19^+$/$CD43^-$/$CD23^-$), Follicular (FO) B cells ($CD19^+$/$CD43^-$/$CD23^+$), B1a ($CD19^+$/$CD43^+$/$CD5^+$) or B1b ($CD19^+$/$CD43^+$/$CD5^-$). Additionally, there were no significant changes in B cell activation between $DHCR24^{fl/fl}$/$CD19^{cre/+}$ and $DHCR24^{fl/fl}$/$CD19^{+/+}$ B cells when stimulated with Pam3SCK4, LPS, or anti-mouse IgM $F(ab')_2$.

CONCLUSION: While overexpression of DHCR24 affects Ca^{2+} and long-term B cell –dependent antibody production, it has no effects on B cell subset development nor B cell activation after stimulation via TLR2, TLR4 or BCR engagement. Thus, DHCR24 may play an important role in specific B cell functions associated with BCR signaling.

Abstract Title: The People vs. Dr. AI: Legal Implications of AI in Medicine

Investigator(s): Jamie Geraghty; Justin T. Zaremba; Evan DaBreo MD; Spencer Baldwin JD; Serge Andreou MS; Alexandra Urman MPH; David Schoolcraft JD; Tayab Waseem PhD; Jose Morey MD
Department(s): Eastern Virginia Medical School, University of Virginia Department of Anesthesiology, Cerebrate Law PLLC, Urman Consulting, Ogden Murphy Wallace PLLC

Abstract

INTRODUCTION: As Machine Learning (ML) in medicine rapidly grows more sophisticated and accurate, the uncertain liability rules surrounding its use hampers its integration into the field. Determining the legal liability standards for ML algorithm adoption in a healthcare setting is crucial to its advancement. Multiple ML algorithms have been approved by the FDA and are being utilized in clinical settings today. Each unique ML algorithm type presents a unique set of advantages and challenges to regulate. Using established tort law, we break down how physicians can be protected from liability when using FDA approved ML algorithms in their practices. We aim to outline a liability system for transparent and opaque ML algorithms that may be codified by policymakers that can then alter the current Standard of Care (SOC), so that physicians may incorporate the use of a cost effective and efficient technology into their clinical practice without being overly fearful of liability.

METHODS: A literature review was conducted on FDA ML algorithms and devices. AI algorithms were broken down based on static vs dynamic and then further stratified as transparent or opaque. Tort law regarding liability within other fields of AI as well as current case law within healthcare was collected.

RESULTS: Many AI products have now been approved by the FDA, leading to the integration of AI into health systems and hospitals at an increasing rate. The presence of AI in medicine is rapidly expanding, particularly in the fields of ophthalmology, radiology, dermatology and pathology. At the time the literature review was conducted there were more than 86 FDA approved AI devices/algorithms. Multiple studies have now shown that AI is equivalent if not superior to dermatologists in diagnosing melanomas and carcinomas. Deep learning algorithms have been shown to be comparable to expert pathologists in classifying and distinguishing between carcinomas. AI has also been approved to diagnose diabetic retinopathy and does so with sensitivities exceeding 91%. SOC is largely circumstantial and is apt to change. In Helling v. Carey(1974), the Supreme Court changed the medical standard of care. However, this is uncommon and the SOC tends to be defined as providing “minimally competent care.” The 1976 Medical Devices Amendment Act established preemption as a legal protection of medical devices from liability under regulations different from federal regulations. Medtronic, Inc. v. Lohr (1996) and Riegel v. Medtronic, Inc (2008) upheld that if medical devices undergo FDA approval then they are protected under preemption.

CONCLUSION: Liability in relation to AI is a rising issue in which there are no clear guidelines. SOC differs in different contexts, leaving room for interpretation regarding the level of care provided. Generally, under tort law, physicians must provide the same level of care as a competent physician in the same specialty to avoid liability. Therefore, if an AI system, transparent or opaque, is statistically better at making a specific decision, and the physician does not find any obvious flaw with the decision, then the physician should not be reasonably held liable for an unfavorable outcome. Alternatively, if a physician disregards recommendations by an AI system that results in patient harm, there may be a duty to incorporate AI’s into SOC guidelines. The legal recourse then depends on the scenario. Medical device makers are currently protected from product liability claims if they have received pre-market approval from the FDA. This however creates problems with dynamic ML algorithms. Is it possible to maintain preemption status if the product is constantly changing? The answer is not clear. In the future, the FDA will need to create a new framework on how they regulate, approve and periodically review AI devices to ensure patient safety.

Other safeguards, such as warnings from the AI algorithm, as well as physician training of proper use, should be used to minimize the potential risks AI pose. Under these guidelines, physicians should be free to utilize AI that matches or exceeds the diagnostic capabilities of physicians without undue worry. This will help encourage advancements in medicine while maintaining sufficient protection for patients. Future papers should further examine the FDA approval process of ML algorithms as well as the potential biases present in these algorithms.

Abstract Title: Diagnostic challenges of a refractory peripapillary leak with intraretinal lesion

Investigators: John Goté MS, Patrick Commiskey MD, Zachary A. Koretz MD, Jay Chhablani MD

Department: Eastern Virginia Medical School, UPMC Eye Center, University of Pittsburgh

Abstract

INTRODUCTION: Here, we present a case of a persistent peripapillary leak with intraretinal lesion without any obvious features of perifoveal exudative vascular anomalous complex (PEVAC), polypoidal choroidal vasculopathy (PCV), or central serous chorioretinopathy (CSCR).

Perifoveal exudative vascular anomalous complex (PEVAC) is a recently noted pathology, described as having a large isolated perifoveal aneurysm, minor hemorrhages, intraretinal exudation, and an accumulation of small hard exudates, without any retinal or choroidal vascular changes. On structural optical coherence tomography (OCT), a circular hyperreflective lesion is notable with local intraretinal cystic abnormalities around the PEVACs.

Polypoidal choroidal vasculopathy (PCV) is a maculopathy associated with pigment epithelial detachment (PED), retinal detachment, and subretinal bleeding due to an inner choroidal vasculopathy with leaky, polyp-like aneurysms commonly present in peripapillary location. Though PCV and AMD share morphological similarities and are treated similarly with photodynamic therapy and/or intravitreal anti-VEGF injections, visual outcomes are more favorable with PCV.

Central serous chorioretinopathy (CSCR) is a common retinopathy due to hyperpermeable choroid vasculature leading to subretinal fluid accumulations in the macula. Focal PED and an expanding hyperfluorescence of leaky fluid are classically appreciated on OCT and intravenous fluorescein angiography (IVFA) respectively.

CLINICAL FINDINGS: A 76-year-old man with no significant past medical history presented with gradual painless loss of vision in the right eye, worsening over the previous 4 months. Visual acuity at presentation was 20/60 in the right eye and 20/20 in the left eye. Dilated fundus exam revealed peripapillary hard exudates suggestive of prior subretinal fluid in the right eye, with peripapillary atrophy in both eyes (Figure 1A-B). In the right eye, indocyanine green angiography (ICGA) demonstrated focal hypofluorescence in the temporal peripapillary region with faint hyperfluorescent spots in the fovea (Figure 1C-F). IVFA demonstrated pooling hyperfluorescence in the same temporal peripapillary region. On OCT, subretinal bands with intraretinal hyperreflective spots were seen. Fluid and hard exudates were observed within the outer nuclear layer without a notched pigment epithelium detachment or other retinal pigment epithelium disturbances present. Notably, there was a singular hyperreflective circular lesion with a hyporeflective core in the temporal peripapillary region of the outer retina on OCT (Figure 1G). OCT angiography demonstrated a normal outer retina with areas of focal hyperreflectivity in the deep capillary plexus with corresponding hyporeflectivity in the choriocapillaris. On multimodal imaging there was no evidence of polypoidal choroidal vasculopathy (PCV), central serous chorioretinopathy (CSCR), or perifoveal exudative vascular anomalous complex (PEVAC). Given the presence of peripapillary focal leak associated with subretinal fluid, we treated the areas of focal hyperfluorescence noted in the right eye on ICGA with micropulse laser with 5% duty cycle. At 1 month after the micropulse treatment, there was no significant change in visual acuity or reduction in fluid (Figure 2A). At that point, Navilas-guided threshold focal laser treatment was performed on the same area. At 1 month after the focal laser treatment, there was persistent fluid on OCT (Figure 2B). ICGA imaging showed persistent leakage at the same location, and a second Navilas-guided focal laser treatment was applied to the areas of leakage near the optic disc. At 1 month following the third laser intervention (3 months since presentation), BCVA improved to 20/60 in the right eye and 20/30 in the left eye, however on OCT there was persistent intraretinal fluid in the right eye near the fovea so the eye was treated with two monthly intravitreal bevacizumab injections (Figure 2C-D). One month after second bevacizumab injection, BCVA was 20/60 in the right eye with persistent fluid on OCT and leakage on ICG (Figure 2E). A third focal laser treatment was performed and subsequently the patient was lost to follow up.

CONCLUSION: This case is presented for a discussion regarding a potential diagnosis and management strategy

Abstract Title: Outcome of Angiographic Intervention in the Reduction of Pediatric Hepatoblastoma Rupture

Investigator(s): John P. Greco, James B. Vogler MD, Anthony Pang, Adam Trusty, Harlan L. Vingan MD
Department(s): Department of Radiology, Eastern Virginia Medical School, Norfolk, VA

Abstract

Introduction: Previous studies have shown the growing effectiveness and role of image-guided intervention in the management of massive hemorrhage secondary to trauma. In a review of outcomes for 114 patients with traumatic liver injuries, Gaarder et al. showed that the introduction of angiography and embolization in addition to damage control surgery reduced the laparotomy rate from 58% to 34% and lowered the complication rate by 40% (including abscess, biloma, and bile leak) with a stable survival rate of 89-90%. (1) In one retrospective series, Johnson et al. demonstrated that in seven patients that received angiography after damage control surgery for liver injury, embolization was successful in all seven patients with no rebleeds. (2) This case report expands on the unique role that angiographic intervention can serve in the management of hemorrhage specifically in the setting of pediatric hepatic tumor rupture.

Case Description: We present a case of a 2-year-old male child who arrived at the emergency department with rupture of an existing hepatoblastoma associated with massive intra-abdominal hemorrhage that was successfully reduced with endovascular embolization and coiling of tumor vasculature branching from the left hepatic artery. The patient initially presented to the emergency department in acute distress with tachycardia, hypotension, and additional signs of hypovolemia after abdominal trauma. Chest radiograph (Fig. 1a) and CT imaging (Fig. 1b) on admission revealed evidence of rupture of a previously existing 9.7 cm x 7.7 cm heterogenous mass in the left hepatic lobe characteristic of a hepatoblastoma. The patient was transfused with packed red blood cells and an emergent laparotomy was performed with unsuccessful resolution of hemorrhage. The patient then underwent angiography which demonstrated active extravasation from multiple branches of the left hepatic artery (Fig. 2a). Particle embolization with 200-500um and 500-700um embospheres (Fig.2 b) as well as endovascular coiling of extravasating vessels was performed successfully stopping the bleeding arising from the left hepatic artery and vessels surrounding the tumor (Fig. 2c). The rest of the mass was resected, and the patient was transferred to the pediatric intensive care unit for further evaluation and management.

Discussion: This case highlights the utility of angiographic intervention techniques in the acute management of pediatric hepatoblastoma rupture. Endovascular embolization and coiling can be effective means of reducing hemorrhage secondary to traumatic tumor rupture. Current literature demonstrates the significant role that angiographic embolization can play in the management and control of acute hepatic hemorrhage secondary to trauma, however, this case highlights the specific utility of image-guided intervention in reducing hemorrhage in pediatric hepatic tumor rupture. Angiography gives a detailed and accurate view of extravasating tumor vasculature providing the opportunity for embolization to be performed selectively in bleeding vessels. Endovascular coiling can be performed quickly and efficiently to minimize patient blood loss from hemorrhage improving chances of survival. Clinically, endovascular techniques such as those described above can have a significant mortality benefit in conjunction with damage control surgery as shown in current literature and might even serve as an important adjunct in the first-line management of acute pediatric trauma in the future. There are obvious limitations of this case including the fact that the patient remained in poor condition after the procedure due to widespread tumor metastasis which obscures the efficacy of the intervention in improving survival. Other limitations include the fact that this case only shows potential efficacy of angiographic intervention in hepatic mass hemorrhage and does not provide evidence of efficacy in non-hepatic organ rupture. Further investigation aimed at assessing outcomes of angiographic intervention in the management of non-hepatic tumor rupture should be performed to further establish the unique role of image-guided endovascular embolization and coiling in hemorrhage control.

Abstract Title: Detecting Early Tumor Relapse in High-Risk Triple Negative Breast Cancer

Investigator(s): Gagan K. Gupta, Amber L. Collier, Dasom Lee, Richard A. Hoefer, Vasilena Zheleva, Lauren L. Siewertsz van Reesema, Angela M. Tang-Tan, Mary L. Guye, David Z. Chang, Janet S. Winston, Billur Samli, Rick J. Jansen, Emanuel F. Petricoin, Matthew P. Goetz, Harry D. Bear, Amy H. Tang

Department(s): Leroy T. Canoles Jr. Cancer Research Center, Department of Microbiology and Molecular Cell Biology

Abstract

Triple-negative breast cancer (TNBC), characterized by the absence or low expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (HER2), is the most aggressive subtype of breast cancer. TNBC accounts for about 15% of breast cancer cases in the U.S. and is known for high relapse rates and poor overall survival (OS). Chemo-resistant TNBC is a genetically diverse, highly heterogeneous, and rapidly evolving disease that challenges our ability to individualize treatment for incomplete responders and relapsed patients.

Currently, neoadjuvant chemotherapy (NACT) is a standard treatment for women with high-risk TNBC. A completed course of NACT results in two possible outcomes: pathologic complete response (pCR) or pathologic incomplete response (pIR). pCR is a reliable clinical prognostic biomarker associated with improved outcomes and long-term survival. Additionally, pCR has excellent prognostic value in patients with aggressive breast cancers like TNBC. Conversely, patients who have a pIR have an increased risk of early tumor relapse. Patients with a pIR may be further risk stratified clinically using the Residual Cancer Burden (RCB) classification. However, many TNBC patients with similar RCB classes may experience dramatically different clinical outcomes. Therefore, additional precision and prognostic biomarkers are needed to stratify high-risk TNBC patients with a pIR post-NACT. Importantly, new and more effective therapeutic strategies need to be developed to control and eradicate these multidrug-resistant malignant TNBC tumors.

Human seven in absentia homologue (SIAH) is a promising new therapy-responsive prognostic biomarker and a major tumor vulnerability in TNBC. SIAH is an evolutionarily conserved RING-domain E3 ligase and the most downstream signaling gatekeeper indispensable for proper K-RAS/EGFR/HER2 signal transduction. Abnormal K-RAS/EGFR/SIAH pathway hyperactivation is highly prevalent in high-risk, locally advanced, and relapsed TNBC. Activation of this major tumor-driving pathway is responsible for uncontrolled tumor growth, local spread, systemic dissemination, and correlates with chemo-resistance. Based on its evolutionary conservation and significance as the most downstream signaling module indispensable for K-RAS signal transduction, $SIAH^{ON/OFF}$ expression is a precision biomarker and a reliable readout of K-RAS/EGFR/HER2 pathway activation/inactivation post-NACT. We showed that $SIAH^{ON/OFF}$ expression is a binary code in residual TNBC tumors that can be used to stratify patients, augment RCB classification, forecast tumor relapse, and predict patient survival after first line NACT in a pilot retrospective study.

Multidrug-resistant high-grade TNBC is a genetically diverse, highly heterogeneous disease that challenges our ability to individualize and optimize precision therapy. Persistent K-RAS/SIAH/EGFR pathway activation endows TNBC with therapy resistance and increases the risk of metastasis and early relapse. As such, we developed a K-RAS/SIAH-centered biomarker discovery program and a synergistic multi-institutional anti-SIAH research initiative at six medical institutions with the intended goal of designing novel and potentially life-saving anti-SIAH-based anti-K-RAS targeted strategies to control and eradicate multidrug-resistant and intractable TNBC mammary tumors in the future.

Abstract Title: Management of endograft associated infected type IV thoracoabdominal aortic aneurysm with cryopreserved aortoiliac graft reconstruction

Investigators: Kevin Guy MS2, Brian Grant MBBS, Jean Panneton MD
Departments: Eastern Virginia Medical School, Division of Vascular Surgery, Norfolk, VA

Abstract

Introduction:
Aortic Graft Infection (AGI) is a rare complication associated with Endovascular Aneurysm Repair (EVAR). The rate of AGI after EVAR in the published literature is approximately 0.16%-1.3%.[1,2,3]. AGIs represent an extremely challenging problem, with perioperative mortality rate between 30%-60%.
Treatment strategies include extra-anatomic bypass followed by explantation of the infected graft, rifampin-soaked prosthetic replacement, neoaortoiliac system (NAIS) procedure, as well as aortic cryopreserved allografts (CPA). This case illustrates a unique situation in which a CPA was used to reconstruct an aneurysmal paravisceral aorta after extra-anatomic bypass and explantation of infected aortic endograft.

Case Presentation:
A 62 year-old man with familial adenomatous polyposis, hypertension, hyperlipidemia, mild myotonia congenita presented as an outpatient 5 months after undergoing EVAR for an infrarenal AAA complaining of left leg pain. In the interval following his EVAR, he underwent open ileocecectomy for an endoscopically unresectable polyp. This procedure was complicated by wound infection and intra-abdominal abscess formation, for which he had a percutaneous drain place. Cultures grew E. Coli. He also subsequently developed C. difficile colitis. CTA obtained for his leg pain showed suprarenal aortic degeneration, suspicious for AGI.
The patient then underwent axillo-bifemoral bypass in preparation for explantation of his infected endograft, which was uncomplicated. 3 days later, the patient underwent open thoracoabdominal EVAR explant and visceral reconstruction with CPA, utilizing the 4 iliac branches of the CPA for visceral arterial reconstruction. The endograft was then explanted, native iliac arteries ligated, and omentoplasty performed. His recovery was complicated by hemorrhage from inferior epigastric artery requiring surgical ligation, as well as AKI that resolved with supportive care. Tissue cultures grew Bacillus spp. and he was discharged on cefepime and daptomycin. He was seen in follow up twice in the subsequent 2 months and is recovering well.

Conclusion:
Cryopreserved aortoiliac allografts offer low rates of recurrent infection as well as versatility in the setting of paravisceral aortic reconstruction, and therefore should be considered in the treatment of complex AGI.

Abstract Title: Visualizing extracellular vesicle-cell interactions using high-resolution microscopy

Investigator(s): Tyree Hamilton, Nigeste Carter, Anca Dobrian, Ph.D. Frank Lattanzio, Ph.D
Department(s): Department of Physiological Sciences

Abstract

INTRODUCTION: Extracellular vesicles (EVs) are a heterogeneous group of lipid bilayer-enveloped particles that carry a versatile cargo comprised of proteins, lipids, nucleic acids and metabolites. EVs are released by virtually every cell type and can potentially be internalized by circulating cells, endothelial cells lining the blood and lymphatic vessels or parenchymal cells. They represent a new form or inter-cellular communication. The EV field is a young and vibrant field with many unanswered questions and in need of novel technical approaches and tools. The technical challenge to study these entities,that vary in size from 20nm to 1um is related to their small size and heterogeneity. Therefore, it is important for the researchers that study EV biology to have adequate research reagents and tools. Imaging techniques are key to understand EV-cell interactions and their cellular uptake and fate. For the smallest EVs, classical fluorescent microscopy does not have the resolution potential for single particle visualization. Super-resolution microscopy is one of the approaches that allow imaging of single EVs. IN my research project I used a recent addition to our imaging core: the high resolution microscope Nanoimager-S (ONI, UK). As a proof of concept I seek to determine the interaction between EVs produced by various endothelial cells and PC3ML prostate cancer cells.

METHODS: PC3ML Cell PreparationTrypsinized a culture of PC3ML cells per protocol and utilized cell counter to calculate the number of cells needed to be seeded. The number of PC3ML cells available was 2.86 x 106, and the number of cells needed was 7.5 x 104, so 26µL of cells were seeded in each of the 4 wells of an Ibidi 4-Chamber slides. 500 µL of the physiological relevant media was used to fill the wells.

Extracellular Vesicle Preparatim: Fluorescent Labeling

Used a 1:200 dilution by adding 0.5 µL of lipophilic DiD dye to 1OOµL of EV mix derived from endothelial cells and incubated for 10 minutes at 37°C. Following the incubation period, 1OOµL of 1% BSA was added to the mix to stop the dye loading.. Following the incubation period, the mixture was setup in an overnight dialysis against ultrapure water at 4°C.

PC3ML Cell Uptake of DiD Labeled Extracellular Vesicles

After removing the DiD labeled EVs from the overnight dialysis each well was treated with 67.5 µL at different time points : 30 minutes, 1 hour, 2 hours, and 4-hour incubation at 37°C. Following the last incubation period, each well's media was aspirated, washed one time with PBS before addition of 500µL imaging media.

High-Resolution Microscopy

After warming the microscope stage to 37°C, each well of the Ibidi 4-chamber slide was imaged using the Nanoimager-S (ONI, UK). Each image acquisition was comprised of 3000 images using the transilluminator to capture the cell and a 640 laser to image the fluorescently labeled EVs.

RESULTS: The goal of these experiments was to image the location of the EVs at different incubation times and to determine the amount of EV taken up by cells after different incubation times. Based on the results from the particle tracking in ONI's NIM software, the number of particles/cell was recorded. A large number of particles were adhered to or in close proximity of plasma membrane, after 30 min and 1hr incubation. With increase in incubation times, the intracellular location of the particles increased and gradually shifted their positioning away from the plasma membrane and towards the center of the cell. Using the LysoTracker green dye, we managed to determine co-localization of internalized particles with lysosomes. Only a small fraction of the particles showed co-localization, at any given time point. Experiments are in progress to refine the quantitative aspect of our study.

CONCLUSION: Using this technique we were able to visualize live interactions of EVs and cells in a time-dependent manner. We also determined intracellular localization of the particles following their uptake. This is a promising technique to study live cell interactions with EVs and to address biological mechanistic questions. Given the interest of several investigators at EVMS in EV biology, this proof-of-concept set of experiments performed in premiere using the ONI Nanoimager is an important first step for implementation of this novel technology.

Abstract Title: A case of linearly distributed spiradenomas

Investigators: John Hardy, Kate Kimes DO, Wendi Wohltmann MD, James Neiner MD
Departments: Eastern Virginia Medical School, San Antonio Uniformed Services Health Education Consortium

Abstract

INTRODUCTION: Spiradenomas are cutaneous adnexal tumors originating from sweat ducts that are thought to be of eccrine origin. Consistent with most other cutaneous adnexal tumors they commonly present as solitary, well-defined nodules on the head and neck, though other locations have been reported, as seen in our case. The nodules vary in size, ranging from 0.5-5cm in diameter, with colors ranging from blue to black to normal skin color. One of the distinctive features of spiradenomas is their tendency to be painful, as was the case with our patient. They most commonly arise between the ages of 15 and 35. Diagnosis can only be made by biopsy which shows well-circumscribed basophilic nodules with hyalinized basement membranes and a trabecular pattern. Spiradenomas are relatively benign neoplasms however when multiple are found on a patient, it should raise suspicion for a CYLD cutaneous syndrome eg. familial cylindromatosis, multiple familial trichoepithelioma, and Brooke Spiegler syndrome.

CLINICAL FINDINGS: We present the case of a twenty-year-old female diagnosed with multiple spiradenomas located in a linear distribution on her right lower extremity. The patient presented to the dermatology clinic for evaluation of several papules on her right medial thigh. She noted that they had been present since age twelve and were slowly increasing in number. Her main concern was the fact that they were painful especially while shaving but otherwise they were asymptomatic. On clinical examination, there were approximately twenty discrete blue, rubbery papules in a linear distribution starting on the distal thigh and extending to the proximal lower leg. The lesions had a notable absence of overlying hair growth compared to the surrounding skin, and they were tender to palpation. Similar lesions were not present anywhere else on the skin or mucosal surfaces. A punch biopsy demonstrated no epidermal changes with well-circumscribed basophilic nodules in the deep dermis. There were scattered ducts present and the nodules were peppered with lymphocytes. Cytokeratin 5 and 6 immunohistochemical (IHC) staining highlighted the lesional cells, consistent with a primary cutaneous adnexal neoplasm. Carcinoembryonic antigen (CEA) IHC staining highlighted the ductal lumen. These findings were consistent with spiradenomas and based on the distribution, the diagnosis of linear spiradenomas was made. Treatments including surgical excision and CO2 laser were offered to the patient and she elected for watchful monitoring. CYLD cutaneous syndromes such as Brooke Spiegler syndrome almost always involve the head and neck. As such the unique location and distribution of the tumors made this diagnosis unlikely, however the possibility was discussed with the patient and she was advised to return to the clinic with any new tumor development. We speculate that the most likely cause of this form of distribution is genetic mosaicism, with a sporadic mutation during development resulting in a line of cells that are susceptible to mutation.

CONCLUSION : We report this case to review the unique features of spiradenomas as well as to show an atypical presentation of the disease. Although spiradenomas are considered to be very rare, the clinical presentation can resemble many other conditions. As such it is important to keep this tumor as well as the closely related cylindroma on the differential when evaluating a patient with a new papule or nodule, solitary or otherwise. We also hope that this report will serve as a reminder that spiradenomas can present anywhere on the body and are not solely confined to the head and neck. Finally, this case reviews the general characteristics of the various CYLD cutaneous syndromes that clinicians should keep an eye out for when evaluating a patient with a confirmed diagnosis of a spiradenoma.

Abstract Title: Trauma-Informed Approach to Healthcare in Correctional Settings

Investigators: Abby Hargis, Maria Maslyanko
Department: Department of Diversity and Inclusion

Abstract

INTRODUCTION: As of 2019, 231,000 women and girls on average were incarcerated in the United States at a given moment, with 101,000 individuals located in local jails and 99,000 in state prisons. Because of the growing number of incarcerated women in the US, there is significant demand for healthcare aligned with the specific socio-economic, emotional, and medical needs of this population. Most incarcerated women share lifetime exposure to certain forces that underlie their offenses. Upon admission to jail, 68% of females have a mental health diagnosis compared with 41% of males[2]. In one study, 90% of women who are incarcerated were found to have a history of prior sexual, physical, or emotional trauma including intimate partner violence[2]. Many incarcerated women also carry with them to jails and prisons the responsibility of being the primary caregivers to their families[2]. The chronic stress experienced by women prior to and throughout incarceration influences menstrual bleeding, vaginal discharge, pelvic pain, risk of STI, and risk of unplanned pregnancies[2]. The National Commission for Correctional Health Care calls for standardization of medical care for female inmates, specifically in the realm of trauma-informed healthcare[2]. Routine medical procedures such as breast exams and pelvic exams are sensitive procedures that could be re-traumatizing for patients[2]. It is essential for medical professionals caring for incarcerated women to utilize a lens of trauma-informed methodology when conducting patient history and physical exams[2].

METHODS: This research was designed as a secondary data and literature review of publications from organizations such as Prison Policy Initiative, National Inventory of Collateral Consequences of Conviction (NICCC), National Commission on Correctional Health Care, and the National Institute of Health. A set of recommendations were developed in order to accommodate the need for trauma-informed healthcare within the justice system, as well as outside of it.

RESULTS: Analysis of information collected during the current research initiative showed a strong need for trauma-informed healthcare within the justice system. While trauma-informed training exists in certain residency programs, such as in OB/GYN, not all physicians are trained to interview and examine patients with a history of trauma. Eastern Virginia Medical School (EVMS) should include an additional clinical skills teaching session during the genitourinary physical exam training which would utilize standardized patients in order to educate medical students on 1) How to elicit possible history of trauma and 2) How to modify the GU physical exam in the case of a positive history.

CONCLUSION: In order to promote the highest quality of medical care for individuals with a history of incarceration or trauma, EVMS should integrate trauma-informed healthcare training into the undergraduate medical curriculum, specifically during the genitourinary physical exam teaching session. More work on the methodology of trauma-based physical exams and interview techniques is necessary for further development of the curriculum.

ABSTRACT TITLE: Straight Through CT

INVESTIGATOR(S): Joshua Harris, Hayden Salts MD, Sarah Shaves MD
DEPARTMENT(S): Diagnostic Radiology EVMS

Abstract

INTRODUCTION: Computed Tomography (CT) images commonly undergo processing after initial acquisition. Reformatting is a standard image processing that displays the images in different planes than the original image reconstruction. These reformats assist the diagnostician in obtaining an accurate diagnosis. Proper image reformatting has been shown to affect image quality, radiologist reading times, and pathology detection 1-5. Unfortunately, variability in CT reformatting produces radiological studies with a significant amount of axis deviation which degrades image quality and causes difficulty with interpretation. This project aims to improve image quality by educating radiological technologists within our department on the importance of assessing the patient's position during image reformatting.

METHODS: Twenty-five head CT scans were evaluated for the degrees of off axis rotation on the coronal and sagittal reformats. The degrees of rotation around the vertical, Z axis (top to bottom) and longitudinal, X axis (front to back) were recorded. Rotation around the lateral, Y axis (side to side) had minimal bearing on imaging and was not included. Measurements were taken from the Foramen of Monroe to the cortical surface using the IMPAX angle tool. After recording the results, a presentation on the importance of accurate reformats and an explanation on how to produce them was given to the radiologic technologists at Sentara Norfolk General Hospital. One week later, twenty-five additional head scans were obtained and were again assessed for deviation around these axes. Basic statistical evaluation was performed including mean, median and mode followed by an unpaired t-test.

RESULTS: After one week from the initial intervention, we expected the average deviations to decrease; the data confirmed our hypothesis. We compared our results with an unpaired t-test. Before the intervention, the means of vertical axis and longitudinal axis were 6.0 and 4.0 degrees, respectively. After the intervention, the means had decreased to 4.0 and 3.2 degrees. Despite a 50% decrease, the vertical axis deviation (6.0 vs 4.0) was not statistically significant (p=.12). The longitudinal axis deviation (4.8 vs 3.2) reached statistical significance with a p-value of.02.

CONCLUSION: Although the vertical axis deviation changes were not significant, the longitudinal axis deviation improvements suggest the intervention may have been effective. We believe that further follow-up with repeat assessments will prove beneficial in improving vertical axis deviation. Both vertical and longitudinal deviations have an effect on image quality in the sagittal and coronal planes, so even with the statistically significant improvement in longitudinal axis deviation the post images were objectively better.

Abstract Title: Effect of Non-uniform Cyst Distribution in Lymphangioleiomyomatosis on Pulmonary Function

Investigators: Amir M. Hasani, Brianna Matthew, Mahshid Goljamali, Yun-Ching Chen, Mario Stylianou, Mehdi Pirooznia, Angelo Taveira-DaSilva, Marcus Y. Chen, Han Wen, Joel Moss
Departments: EVMS, National Hearth, Lung, and Blood institute, Bethersda, MD

Abstract

Introduction: Pulmonary diseases may present with cysts that are distributed randomly or localized in the upper, middle, or lower regions of the lung. Although Lymphangioleiomyomatosis (LAM) has been identified as a diffuse lung cystic disease with a homogeneous distribution, we now show that LAM patients have a greater lung involvement in the middle areas of the lung, perhaps related to the proposed lymphatic origins of LAM.

Methods: A group of confirmed LAM patients (n =104, all-female, age: 49.7±11.2 years) were enrolled consecutively in a clinical study at the National Institutes of Health; a chest CT scan was obtained. The lung was divided into three regions: the top quarter (TQ), the middle half (M2Q), and the bottom quarter (BQ). Regional cyst scores were measured. We used the Wilcoxon signed-rank test to assess the uniformity of cyst distribution. We performed principal component analysis among the regional cyst scores with linear modeling for the correlation between these components and lung function tests.

Results: The cyst scores of the top and bottom quarters of the lungs were significantly lower than that of the full-lung value ($p < 0.001$ and $p=0.037$), whereas that of the middle half was significantly greater than that of the full-lung ($p < 0.001$). This pattern held up in patient groups with full-lung cyst scores of 5-15% ($p = 0.029$ and $p = 0.003$, respectively). Linear modeling showed that FEV1 and FEV1/FVC were predicted by a combination of the full-lung cyst score ($p < 0.001$) and the difference between the mid-half and the rest of the lung ($p < 0.001$ and $R2 = 0.57$). For patients with the same full-lung cyst scores, those with higher middle lung involvement tended to have a lower FEV1 and FEV1/FVC ($p < 0.001$), but not DLCO ($p = 0.54$).

Conclusion: LAM is a heterogenous cystic lung disease, which frequently, the upper and lower regions are less involved than the middle portion of the lung. FEV1 and FEV1/FVC but not DLCO were affected by cyst distribution.

Abstract Title: Racial disparities in pre-pregnancy obesity and gestational diabetes in Virginia Mothers-Results from 2009-2018 Pregnancy Risk Assessment Monitoring System Data

Investigator(s): Katharine Hawkes, MPH[1], Lauren Truwit[1], Cherell Rivers, MPH[1,] Sophia Wang, MPH[1,], Clay Porter, MPH[1] Kenesha Smith, MSPH, PhD[2], and Hongyun Fu, PhD [1,]

Department(s): 1) EVMS School of Health Professions, 2) EVMS School of Medicine, 2) EVMS Department of Pediatrics 3) Virginia Department of Health

Abstract

INTRODUCTION: The United States has the worst maternal and child health (MCH) indicators among industrialized countries, with African American women carrying a disproportionate burden of negative outcomes. It is widely acknowledged that intrauterine exposure to maternal obesity is associated with adverse MCH outcomes. This study examines factors associated with pre-pregnancy obesity and gestational diabetes in Virginia mothers using the Virginia Pregnancy Risk Assessment Monitoring System Data (VA-PRAMS).

METHODS: This study included a sample of 7,201 mothers that participated in the 2009-2018 VA-PRAMS – a probability based sample survey which collected a wide range of information from new mothers about their socioeconomic background; experiences before, during, and after their recent pregnancies; and health outcomes. Multivariate logistic regression was used to examine factors associated with pre-pregnancy obesity (BMI $\geq$25) and gestational diabetes, adjusting for confounding factors and sampling weights.

RESULTS: Overall, 20.8% of mothers were obese before pregnancy, 8.6% had hypertension, and 5% had gestational diabetes, with rates in pre-pregnancy obesity (33.9%) and hypertension (12.4%) significantly higher in African American women; rates in gestational diabetes were higher in Hispanics (6.2%) and women of Other race/ethnicities (9.1%). Pre-pregnancy obesity (OR: 1.17, 95% CI: 1.01 – 1.37) and gestational diabetes (OR: 1.66, 95% CI: 1.25 - 2.21) were associated with increased odds of having pre-term birth.

CONCLUSIONS: Findings demonstrate significant racial disparities in pre-pregnancy obesity and gestational diabetes in Virginia mothers and an association with negative birth outcomes. The increased trend in obesity among childbearing women highlights the need for targeted interventions.

Abstract Title: Characteristics and health status of Virginia mothers who received progesterone treatment for prematurity prevention-findings from the 2016-2018 PRAMS

Investigator(s): Katharine Hawkes, MPH[1], Hongyun Fu, PhD[1] and Kenesha Smith, MSPH, PhD[2], (1)Eastern Virginia Medical School, Norfolk, VA, (2)Virginia Department of Health, Richmond, VA
Department(s): School of Health Professions

Abstract

INTRODUCTION: The effectiveness of progesterone treatment in preventing premature birth is controversial, although the treatment has been promoted for use among pregnant women with histories of spontaneous premature birth and were pregnant with just one baby. This study explored factors related to unsuccessful treatment outcomes among Virginia mothers who received weekly progesterone shots, using data from the 2016-2018 Pregnancy Risk Assessment Monitoring System.

METHODS: The VA-PRAMS collected information about mothers' experiences before, during, after their recent pregnancies. This analysis included a subsample of 157 mothers (5.4%, 157/2,901) who reported weekly 17P shots during their most recent pregnancy. Sample characteristics were presented and Chi Square analysis was used to examine the differences in preterm birth rates by mothers' socioeconomic background and health profiles.

RESULTS: The majority (58.6%) of mothers were above 30-years-old; 38.2% were White, 34.4% were Black, 20.4% were Hispanic, 55.4% were married, 45.9% had a high school diploma or less education, 39% had private insurance, 48.4% received WIC; 30.6% had pre-pregnancy obesity, 15.9% had high blood pressure, 14.6% had gestational diabetes, and 36.9% had preterm birth. The rates of preterm birth were higher in Black women (44.4%), mothers who had high blood pressure (48.0%) and gestational diabetes (47.8%) ($P<0.05$).

CONCLUSIONS: Findings indicated high rates of preterm birth in mothers receiving progesterone treatment, particularly among Black mothers and mothers with chronic health problems. More population-based research is needed to inform health care providers of the populations most affected by poor outcomes as well as effective strategies to improve treatment outcomes.

Abstract Title: Performing TransCarotid Artery Revascularization (TCAR) Outside of Manufacturer's Instructions for Use is Safe but has Higher Reintervention Rates.

Investigator(s): Stephen Hayes, Christopher Murter, MD, David Dexter, MD, Animesh Rathore, MBBS, Rasesh Shah, MD, and Jean Panneton, MD
Department(s): EVMS Vascular Surgery

Abstract

INTRODUCTION
TransCarotid Artery Revascularization (TCAR; Silk Road, Sunnyvale, CA) has emerged as a safe and effective technique for revascularization for carotid artery stenosis in high risk surgical candidates. The applicability is limited by the manufacturer's instructions for use (IFU) and patient selection warnings (PSW). We studied perioperative and short-term outcomes between TCAR procedures compliant with IFU versus outside IFU.

METHODS
We retrospectively evaluated patients undergoing TCAR procedures performed within a single multispecialty group between December 2015 and February 2020. Patients without adequate pre-operative cross-sectional imaging were excluded. IFU criteria include common carotid artery (CCA) diameter ≥ 6 mm, distal internal carotid artery (ICA) landing zone diameter of 4-9 mm, adequate femoral venous access, carotid bifurcation to clavicle length ≥ 5 cm, and absence of severe disease at the CCA puncture site. PSW included extensive calcification of the target lesion, presence of intraluminal thrombus, and ICA/CCA tortuosity. Primary endpoints included perioperative (30-day) major adverse events (ipsilateral stroke, transient ischemic attack (TIA), death, or myocardial infarction (MI)) and perioperative complications. Secondary endpoints included restenosis and ipsilateral reinterventions.

RESULTS
We identified 217 TCAR procedures (85 symptomatic, 132 asymptomatic) performed among 209 patients (69.4% male, mean age 71.9). 198 procedures were within IFU, while 19 (8.8%) had at least one IFU violation. 69 of 198 within IFU patients (35%) had at least one PSW violation. The most frequent IFU violations were length from clavicle to bifurcation (n=6), distal ICA diameter (n=5), and CCA puncture site disease (n=5). In the IFU violation group there were higher incidences of urgent or emergent procedures (26% vs 15%, p =.004) and prior ipsilateral CEA (42% vs 16%, p=.006). The perioperative (30-day) major adverse event rate was 3.2% (n=7), including 3.0% within IFU (n=6; 3 strokes, 2 TIAs, 1 death) and 5.3% outside IFU (n=1 death), (p=0.63). There was one conversion to endarterectomy in each group ($p<0.05$). There were no significant differences in perioperative bleeding, cranial nerve deficit, carotid dissection, or post-operative bradycardia/hypotension. There were no clinically significant MI's or contralateral strokes perioperatively. Mean follow up time was 1.2 ± 1.0 years. Follow up data >30 days was available for 196 of the 217 procedures. Rates of carotid reintervention were 10.5% off IFU and 2.5% on IFU, which was statistically significant in Kaplan-Meier log rank test (p=.04). Other short-term outcomes (stroke, TIA, MI, and in-stent restenosis) were equivalent. PSW violations were not associated with any significant difference in perioperative and postoperative outcomes.

CONCLUSION
This study suggests that performing TCAR in well-selected patients when patient anatomy is in violation of the manufacturer's IFU has similar major adverse event rates and other perioperative complications. The IFU violation group had higher rates of carotid reintervention. Larger sample size and long-term follow up data is needed to identify risks of specific anatomic violations as well as long-term outcomes.

Abstract Title: Corneal Complications Post Cosmetic Iris Explantation

Investigator(s): Jody He, Vikas Chopra, MD
Department(s): Ophthalmology, University of California, Los Angeles

Abstract

INTRODUCTION

Medical tourism has introduced many complications to patients who were once healthy. By touting quick fixes and the "safety" of their devices, companies have lured patients into traveling abroad and undergoing procedures that are dangerous, not medically necessary, and not FDA-approved.

A prime example of this is the cosmetic iris implant, a device advertised to change one's iris color without the need for colored contact lenses. Although the cosmetic iris implant does change one's iris color, the uninformed patient takes on far more risk than benefit. Common complications of the cosmetic iris implant include substantial uveitis, secondary glaucoma, and corneal decompensation.

This case report will discuss one patient's corneal complications post-cosmetic iris implantation and subsequent explantation.

CLINICAL FINDINGS

A 24-year-old female presented to our clinic one year after bilateral cosmetic iris implants in Portugal. She had recently been diagnosed with bilateral uveitis. Her visual acuity at her first appointment was 20/20 in her right eye and 20/150 in her left eye. Her intraocular pressure was 18 mmHg in her right eye and 36 mmHg in her left eye. She also had a history of LASIK in both eyes.

After an extensive work-up with an endocrinologist, it was suspected that the etiology of the patient's uveitis was due to the cosmetic iris implants. Steroid drops did not resolve the inflammation and the patient had now developed glaucoma and corneal decompensation in her left eye. The patient traveled back to Portugal to have the cosmetic iris implants extracted.

After explantation, the patient's left eye was left with pupillary and iris membranes, severe chronic angle-closure glaucoma, and corneal decompensation. She has had two failed corneal transplants to date in her left eye and is discussing replacing her failed graft with either a third corneal transplant or a keratoprosthesis. Her most recent uncorrected visual acuity was 20/800 in her left eye.

CONCLUSION

In this case, a 24-year-old female without visual complaints elected to undergo "safe" cosmetic iris implantation that resulted in multiple subsequent surgeries and permanent loss of vision. Any patient interested in cosmetic iris implants should be strongly discouraged from consenting to the procedure.

Abstract Title: Interprofessional Telehealth Education Program: Assessment of Student Perception

Investigators: Rachel Holmes, BA; Christopher Sommer, MS; Carmen Ingram-Thorpe, MPH; Bruce Britton, MD; Justin Tondt, MD.
Departments: Department of Family Medicine, Eastern Virginia Medical School, Norfolk, VA. Carolyn Rutledge, PhD. School of Nursing, Old Dominion University, Norfolk, VA.

Abstract

Introduction: Interprofessional collaboration has gained importance in recent years as healthcare needs diversify and Interprofessional Collaborative Skills has been added as a 2020 LCME Standard for medical school accreditation. Telehealth has become crucial when office visits are not possible, historically due to access barriers, currently due to the ongoing pandemic, and for future unforeseen barriers. To address these changes and prepare students for future healthcare developments, ODU and EVMS designed an Interprofessional Education (IPE) program for students to develop both their interprofessional collaboration and telehealth skills. A mixed methods study design surveyed the effectiveness of the IPE Telehealth program, which includes family and pediatric Nurse Practitioner, Clinical Nurse Specialist, Doctor of Physical Therapy, speech language pathology, clinical counseling, athletic training, dental hygiene, social work, pharmacy, and 4th year medical students.

Methods: Evaluation tools include a pre- and post- program evaluation, Comfort Level with Telehealth, and a Readiness Assessment for IPE, which was originally the IPE Comfort Scale but was updated to the Interprofessional Attitudes Scale in 2017. The scales included twenty-two 5-point Likert Scaled items, open-ended questions assessing learners' attitudes and suggestions for program improvement (2 questions in 2015, increased to 9 by 2018); a demographic question asking learner's profession was added in 2018. The 5-point Likert scaled items were analyzed in aggregate and by profession, when available after 2018. SPSS was used to perform descriptive and inferential statistics. Qualitative responses were analyzed via constant comparative analysis for consensus and major themes were identified.

Results: To date, survey data from 1027 students has been analyzed. Six major themes were identified across professions: 1) Interprofessional teamwork practice promotes awareness and understanding of other health professions (OHP), 2) Hands-on workshops provide interactive telehealth practice, 3) Clear instructions and objectives prepare students for IPE Telehealth sessions, 4) IPE Standardized patient training is utilized as a tool to address self-biases, 5) Authentic experiences provide an environment for immediate feedback, 6) SP group interaction promotes communication and skill development. Quantitative data supports these 6 themes; on a 1-5 Likert Scale, students report a mean increase in knowledge of OHP (4.68), Telehealth technology (4.44), Realism (4.55), Feedback (4.47), Clinical Skills (4.37), and Skill Development (3.82).

Conclusion: Student attitudes, beliefs, and self-reported skill development in IPE and telehealth improved following completion of the immersive program. Further analysis of this data will include breakdown of data by profession, and comparison between program setting. Educators may consider further investigating student behaviors, attitudes, and beliefs toward IPE and telehealth longitudinally, beginning earlier in the healthcare curriculum.

Abstract Title: Community Stroke Awareness Survey in Hampton Roads, Virginia

Investigator(s): Kevin Houston, Caroline Chessare, David Le, Padideh Ghorbani, Abigail Fariscal, Zachary Smith, Daniel Connelly, David Melton, Sarah Cullen
Department(s): EVMS Community-Engaged Learning – Community Stroke Awareness

Abstract

Introduction: A 2015 report by the Virginia Department of Health indicated stroke as the 4th leading cause of death for Virginians. Today, stroke remains a leading cause of morbidity and mortality in the United States with recent studies reporting an incidence of ischemic stroke increased in young adults by up to 23% in one decade. With a growing incidence of stroke in young adults, utilizing an online forum to both communicate and obtain information is imperative to the future health of this population. In order to better understand the local population a web-based stroke questionnaire was implemented to gain real-time data on how best to meet needs in Hampton Roads, Virginia.

Methods: A web-based survey of 21 questions was created focusing on: demographic variables, personal risk factors, clinical knowledge of stroke, and community motivation for learning. The survey was conducted through the SurveyMonkey software platform and distributed through a local hospital system's community-leader outreach directory and social media platforms using a single standardized template. The survey was open to residents of Hampton Roads over the age of 18.

Results: A total of 211 individuals of Hampton Roads across 8 cities responded to the survey. Demographic results: relatively equivocal distribution across the age ranges, female (75%), Caucasian (86%). Personal risk factors results: 95% without a personal diagnosis of stroke, personal chronic diseases of hypertension (25%), high cholesterol (19%), obesity (19%), and diabetes (8%). Clinical knowledge results: 93% of participants correctly identified the brain as the main body part affected in a stroke. 65% reported awareness of the FAST/BEFAST although only 46% of those could name 3 or more of the mnemonic. 72% indicated calling EMS if they or someone they knew was presenting with stroke symptoms, while only 3% of respondents indicated noting the time last well. In regards to free-recall of risk factors of stroke: 72% total responded with various risk factors and subgroup analysis revealed top responses of hypertension (69%) and smoking (44%). Community motivation results: 80% agree or strongly agree that "it is important that they know the signs and symptoms of stroke" and 70% indicate they prefer to receive stroke information from their doctor's office and 59% prefer on social media.

Conclusions: The data collected has provided several key areas for future investigation, educational opportunities, and implementation of stroke awareness initiatives. Notable findings including a high proportion of individuals not identifying the FAST/BEFAST mnemonic or prioritizing a time-last-well of those presenting with stroke. Both of these have been well-documented to be integral in receiving acute stroke care and guiding treatment modalities once at a healthcare center. Next, a large proportion of respondents have identified stroke awareness to be important and when correlated with risk factor identification show an area amenable to improvement. Furthermore, there is a preference among respondents for physician and social media-mediated modalities for future education. Lastly, there seems to be a large component of demographic responses from female, Caucasian residents in Hampton Roads which may be due to a higher proportion of access to the web-based questionnaire. This survey, although with limitations, helps us to better understand the landscape of stroke awareness in Hampton roads and how to better implement education to the local community in years to come.

Abstract Title: In-Vivo Preclinical Model of Glioblastoma Multiforme Induced Seizures

Investigators: Kendall Howard[1], Katherine Vinokuroff[1,3], Esther Pototskiy[1,3], Kendall Major[1], Deepak Sharma[1], Veronique Andre[4], and Alberto E. Musto[1,2]
Department: Department of Pathology and Anatomy, Eastern Virginia Medical School Old Dominion University, College of Biomedical Sciences
Early Solutions, Neuroscience Therapeutic Area, UCB Belgium

Abstract

INTRODUCTION: Glioblastoma Multiforme (GBM) is a highly malignant cancer in the brain that is highly resistant to treatment, rapid infiltration, and epileptic like seizures (Prakash et al. 2012; Vertosikc et al. 1991). The seizures in GBM patients have been particularly resistant to anticonvulsant medications and further increase the rate of mortality (Scott and Gibberd, 1980, Rosati et al., 2009, Glantz et al. 2000; Englot et al., 2012; de Groot et al., 2012). There is currently no clear understanding as to how GBM leads to increased neuronal network disorganization and how it mediates the development of seizures.

METHODS: U87MG cells (5 x 10^5 cells in 5 uL serum-free DMEM) that were marked with firefly luciferase were stereotactically implanted via a microsurgery into the right dorsal hippocampal region of female BalbC (nu/nu) mice that were approximately 6 to 8 weeks of age. Post operative weights, neurological outcomes, responses to pain, and reflexes were gathered twice a week for the duration of the study to ensure the animal's wellbeing. Tumor growth was monitored weekly using the IVIS fluorescence imaging system. Approximately after 15 days of tumor growth, animals were injected IP with 10mg/kg of PTZ every 5 minutes until the animal achieved tonic clonic seizures or received 60mg/kg in total. On day 17, animals were injected with Midazolam (MDZ) one hour before injection 35mg/kg of PTZ to measure seizure susceptibility. Control animals were injected with saline instead of MDZ. Seizure severity was calculated using the Racine scale. Seizure latency and frequency were also calculated.

RESULTS: All animals included in the study showed consistent tumor growth, but animals who started exhibiting visible neurological deficits were not included as data points for this study. All animals included in the study also had to have maintained a healthy weight to be included in the dataset.

Our results show a statistical significant difference ($p=0.0119$) of seizures susceptibility of animals with tumors versus those without. However, there was no significant difference ($p=0.0791$) in the maximum racine score reached in animals with a tumor and those without, but there was a statistically significant difference ($p=0.0015$) in the latency to the maximum racine score. Animals treated with 35 mg/kg of PTZ countered with MDZ and saline vehicles, showed statistically significant data for MDZ being an effective anticonvulsant against seizures ($p= 0.0003$).

CONCLUSION: In the future, this new model of evaluating seizure activity can be utilized as a tool to safely and effectively investigate various neurological diseases and corresponding treatment compounds. It has demonstrated potential use in future studies using other pharmaceutical therapies. During our research using an intracranial model of GBM progression, it was seen that MDZ may help mediate the progression of seizures and may be a viable option for the treatment of seizures in GBM patients.

Abstract Title: Anxiety and Depression in Hispanic and Non-Hispanic African American Obese Children in the United States

Investigators: Mackenzie Hunt, Arianna Jensen-Wachspress, Nicole Holt, MPH, DrPH
Departments: EVMS Pediatrics

Abstract

Intro
Social behavioral determinants of health are critical considerations for behavioral change, such as reducing the prevalence of childhood obesity. Mental health factors like anxiety and depression can influence one's determination and behavior. We aim to investigate the association between anxiety and depression and obesity in African-American and Hispanic children in the United States.

Methods
We investigated the prevalence of anxiety and depression among non-Hispanic African-American and Hispanic obese (BMI > 85th age and sex-specific percentile) children ages 0-17 years (N=10,839). We used 2017 data from the National Survey of Children's Health (NSCH). We also sorted the 2017 data by state level to investigate the prevalence in the states with the top 35% rates of obesity: South Carolina, Alabama, Texas, Oklahoma, Iowa, Kansas, Missouri, Arkansas, Louisiana, Mississippi, Tennessee, Kentucky, and West Virginia.

Results
At the national level, out of 10,839 children, 27.4% were found to be obese (BMI > 85th percentile of age and sex-specific CDC guidelines). Of 11,315 children, 6.9% (10,839) of African American children and 11.1% of Hispanic children were obese. Of 11,256 children (N), 6.1% noted ever having anxiety and depression. At the state level, 31.8% of 2,733 children were obese, with 6.1% of 2,842 children noted ever having anxiety and depression. Of 2,853 children, 10.8% of African American children and 8.3% of Hispanic children were obese. A two-way chi-square statistical test was performed at both levels ($p = 0.05$). All variables were found to have a non-significant relationship ($p > 0.05$).

Discussion and Conclusion
We did not find a significant association between childhood obesity and anxiety and depression in African-American and Hispanic children ($p > 0.05$) in comparing the national frequencies to the compilation of state frequencies. In order to determine a statistically significant association between the prevalence of anxiety and depression among obese African-American and Hispanic children, we therefore recommend a future study focusing on this population demographic among the aforementioned states. An ideal future study would further examine aspects of social determinants of health among the study population. Such a specific study would contribute to the scientific community, inform policy makers and further determine allocation of funds for childhood obesity intervention programs that include a mental health component.

Abstract Title: Conducting A Youth Engagement Program Promoting Positive Lifestyles and Relationships Among High School Students in Public Housing in Norfolk, Virginia.

Investigators: Caitlin Jefferson; Emily Gordon, MPH; Andrew Plunk, PhD, MPH
Department: EVMS Pediatrics

Abstract

INTRODUCTION The Eastern Virginia Medical School (EVMS) Division of Community Health and Research (CHR) engineered a youth engagement program focusing on building and maintain mentoring relationships with youth from disadvantaged communities in Norfolk, VA.

METHODS Initially, the youth engagement program connected teens from public housing in Norfolk, VA with mentors from Eastern Virginia Medical School and Old Dominion University. Students ranged in ages from 12-16. Alongside leaders from the CHR, students met weekly with their mentors and as a large group. Students were led through various interactive activities and discussions throughout the course of the summer term. As the program transitioned into fall, students began to focus on creating projects representative of issues they felt affected their disadvantaged communities more greatly than others. The students met once a month to work with their mentors. Topics included smoking, violence, and lack of encouragement in school settings. Mentors and CHR leaders regularly contacted students and their families to assess their progress and immediate needs. In lieu of recent events, the youth program has transitioned to virtual conduct. Focus of topic discussion has centered around current events and lessons from the Botvin Life Skills curriculum. Students have remained in contact with program leaders and mentors as they have adjusted to meeting in a virtual setting.

RESULTS Through engagement with the CHR and mentors, students were able to develop skills such as communication methods, de-escalation techniques, and safe health practices. Mentors and program leaders served as a constant point of contact for the youth. As students worked with issues directly affecting their underrepresented communities, they became more engaged and were given the opportunity to take the lead on a project they created. This led to the students planning creative outlets such as posters, video presentations, and in person demonstrations to relay important messages. Progression in the program has resulted in maintained relationships between the youth and program mentors and leaders.

CONCLUSION The future goals of this program are centered around streamlining meeting virtually for the foreseeable future, reintroducing interactive virtual components to the program, and expanding student resources, all while maintaining the relationships the program has built with the youth.

Abstract Title: The Creation of a Curriculum Map for Medical Education

Investigator(s): Dr. Don Robison, Kaivalya Dandamudi, Mark Johnson, Tacora Lemelle
Department(s): EVMS Curriculum and Instruction

Abstract

INTRODUCTION

Curriculum mapping is a widely accepted modality for displaying curriculum and educational standards, but the penetrance of curriculum mapping within medical education remains limited. While a curriculum map has many functionalities, our primary intent for creating one at Eastern Virginia Medical School (EVMS) was for students, professors, and faculty/staff to have complete transparency of the medical school curriculum, see where things occur in a four-year timeline, and have direct access to curriculum content. Additionally, we wanted to deliver this information to the intended parties in a visual manner for ease of understanding as well as allow easy access to the map for ease of use.

CLINICAL FINDINGS

While significant changes were made in the development of the curriculum map, this report will not be able convey whether or not they are positive changes in terms of usability. Usability testing will occur in Fall 2020. The timeline for creating the map itself was significantly expedited by the employment of three rising second year medical students during the summer break. In order to create the EVMS Curriculum Map, individual lecture objectives, module objectives, and overall Liaison Committee on Medical Education (LCME) competency objectives were linked to one another and ultimately tied to an assessment. As for individual lecture content, each lecture was manually associated with keywords and diseases that were taught in each lecture were associated with specific symptoms. These keywords and symptoms were created using a combination of lecture content, clinical presentations within First Aid, and clinical objectives for third and fourth year medical students and are all searchable within the Curriculum Map. In this format, all users are able to easily access the map and the individual session materials while also being able to search for specific content. The EVMS curriculum map attempts to create a similar effect to Wikipedia and Google in which tangible in-house lecture material becomes both specific and relatively instantaneous.

CONCLUSION

One of the benefits of having a functional and usable curriculum map is that it will also allow users to match up class and module objectives with National Board of Medical Examiners (NBME)/LCME objectives in a more efficient way compared to Curriculum Management & Information Tool (CurrMIT). This provides reassurance to professors and students that the content being taught serves a purpose. A curriculum map also allows professors and students to identify gaps in content/knowledge as well as instances of “over-teaching” in the pre-clinical years. By being able to identify these discrepancies, the current curriculum can be refined in order to deliver the best possible education to students.

Abstract Title: Mental Illness Through A Cultural Lens: Analyzing Trends in the Endorsement of Mental Health Related Symptoms in Hampton Roads Refugees

Investigators: Aaliyah Joseph, BA Brynn Sheehan, PhD, Lydia Cleveland, MPH, Ibrahim Maroof, Alexandra Leader, MD, MPH
Department: EVMS Pediatrics

Abstract

INTRODUCTION/STUDY QUESTION: Individuals from collectivist cultures, which emphasize conformity and group cohesion, such as those from Afghanistan and Syria, have been shown to endorse more somatic than psychological symptoms when discussing mental illness in healthcare settings. This study tested if having origins in a collectivist culture influenced the endorsement of more somatic vs psychological symptoms among adult refugees in Hampton Roads, VA.

METHODS: A retrospective study was conducted on 497 individuals who recently immigrated to Hampton Roads, VA and completed the Refugee Health Screener-15 (RHS-15). All participants were from countries that are traditionally collectivist in nature. The RHS-15 tool includes 4 items that assess somatic symptoms and 10 items that assess psychological symptoms. Items assess the frequency with which participants experience particular health symptoms and range from 0 (*Never*) to 4 (*Almost Always*). Analyses were conducted to assess whether somatic or psychological symptoms are experienced more frequently, the association between both types of symptoms, and whether individuals from different countries endorse similar somatic and psychological symptoms.

RESULTS: A paired-samples *t*-test revealed that more psychological symptoms (M= 0.77, SD = 0.77) were reported than somatic symptoms (M = 0.68, SD = 0.82), t = -3.59, p <.0001. A strong positive association ($\chi 2$ (1) = 49.65, p <.0001) was found between psychological and somatic symptoms, suggesting that endorsing one type of symptom was associated with endorsing the other type of symptom. Individuals from three of the four most represented countries in the sample shared the most reported symptom, "too much thinking/too many thoughts," which is a diagnostic proxy for depression on the RHS-15 scale.

CONCLUSION/DISCUSSION: Contrary to study predictions, findings suggest that refugees in this sample do not present more somatic symptoms but rather present more psychological symptoms associated with mental illness. Furthermore, the endorsement of the same depressive symptom among refugees from different countries highlights the need to expand research to better understand the contributing factors. Lastly, the results suggest that somatic symptoms are not preferentially endorsed among this group since somatic and psychological symptoms are often endorsed concurrently. This understanding is important for clinical practice among the growing refugee population in Virginia.

Abstract Title: Catheter Directed Thrombolysis with subsequent Thoracic Outlet Decompression has superior outcomes when treating Venous Thoracic Outlet Syndrome

Investigators: Mihir Karande, David Dexter, MD, Chris Murter, MD, Animesh Rathore, MD MBBS, Jean Panneton, MD
Department: EVMS Vascular Surgery

Abstract

Introduction: Thrombotic venous thoracic outlet syndrome (vTOS) has traditionally been managed with catheter directed thrombolysis (CDT) and/or anticoagulation (AC) (CDT ± AC) followed by surgical thoracic outlet decompression (TOD). There is no one clear treatment strategy regarding the combination and timing for CDT, AC and TOD for the management of vTOS. We sought to evaluate outcomes of various treatment approaches for the management of vTOS and examine difference in outcomes of the timing of TOD relative to CDT or AC.

Methods: A retrospective review was performed within a single hospital system of patients presenting with vTOS between January 2012 and April 2020. Treatment included CDT ± AC with TOD, CDT ± AC without TOD, TOD + AC, or TOD alone. Patients undergoing TOD were further classified as early versus delayed based on an interval of < 10 days or >/= 10 days from CDT and/or AC. We evaluated these patients for complete symptom resolution (CSR), which was defined as the absence of pain, swelling, cyanosis, and/or venous collaterals in the affected upper extremity. Statistical analysis was performed with chi-squared analysis using SPSS software.

Results: Of the 75 patients diagnosed with vTOS, 67 had complete follow-up data. There were 30 patients who received CDT ± AC followed by TOD, with 9 patients having CDT ± AC followed by early TOD and 21 patients having a delayed TOD. 10 patients received CDT ± AC without TOD and 14 patients had TOD alone. 13 patients were part of the TOD + AC cohort, with all of them having delayed TOD (Figure 1). At the time of the initial follow-up, 86.7% (26 out of 30) with CDT ± AC with TOD reported CSR compared to 30% (3 out of 10) with CDT ± AC without TOD, 69.2% (9 out of 13) with TOD + AC, and 50% (7 out of 14) with TOD alone (p=0.003). 90.4% (19 out of 21) CDT ± AC with delayed TOD had CSR as compared to 77.8% (7 out of 9) CDT ± AC with early TOD (p=0.563). Of note, one patient in the CDT ± AC with early TOD group required Percutaneous Transluminal Angioplasty for re-intervention.

Conclusion: In our retrospective study, a combination of catheter directed thrombolysis and anticoagulation followed by thoracic outlet decompression offered a significantly better symptom resolution compared to other modalities. There was no significant difference between the early (<10 days) versus late thoracic outlet decompression in symptoms resolution. A larger sample size of patients in a multicenter setting with complete follow-up data is needed.

Abstract Title: Interlukine -12 induces vascular hypersensitivity to vasoconstrictors in obesity with type 2 diabetes

Investigator(s): Khalid Matrougui
Department(s): Physiological Sciences

Abstract

INTRODUCTION: Vascular smooth muscle cell **(**VSMC) hypersensitivity to vasoconstrictors is clinically significant vascular pathology in obese type 2 diabetic (T2D) patients because it leads to heart failure, hypertension, peripheral artery disease, and delaying wound healing. This becomes particularly significant because obese type 2 diabetic patients are highly vulnerable to Covid19. A recent study showed that excess visceral fat, even in lean people, is as detrimental as being obese with T2D, thereby implicating visceral fat in a number of chronic diseases, such as cardiovascular complications. Yet, a key knowledge gap is the lack of understanding of mechanisms by which omental fat, in obese T2D patients, causes VSMC hypersensitivity to vasoconstrictors. Current therapies neither halt nor reverse obesity/T2D and obesity/T2D-induced VSMC pathology. Thus, there is a critical unmet need to identify mechanism-based, treatable targets to improve VSMC function in obesity with T2D. There is a strong association between omental fat and cardiovascular diseases in both obese T2D patients and T2D animal models. A variety of cytokines and adipokines are increased in T2D, which could affect VSMC function. Significantly, interleukin-12 (IL-12) is increased in adolescent and adult T2D patients and in obese T2D mice. Importantly, IL-12 administration to non-obese mice leads to diabetes, liver toxicity and fibrosis, kidney damage, and atherosclerosis, supporting a detrimental role of IL-12 increase in the etiology of diabetes and abnormalities of multiple tissues and organs. In this study we will determine the role of IL-12 release from omental fat from obese T2D mice in vascular hypersensitivity to vasoconstrictors.

METHODS: Mesenteric resistance arteries (MRA) are isolated from control mice (C57/Bl6) or $rB2^{-/-}$ (IL-12 receptor knockout) mice, mounted in Myograph and then incubated with omental fat from obese T2D mice (db^{-}/db^{-}) or obese T2D mice lacking the gene coding for IL-12 ($db^{-}/db^{-IL\text{-}12\text{-}/\text{-}}$). After equilibration period, Mesenteric resistance arteries are stimulated with a dose-response of phenylephrine or thromboxane (U46619) with and without Apilimod (0.1μM). In another set of experiments, mounted mesenteric resistance arteries from C57/Bl6 are stimulated with dose-response of exogenous IL-12. To determine the mechanism by which IL-12 induces hypersensitivity to vasoconstrictors, we stimulate cultured VSMC and intact mesenteric resistance arteries with exogenous IL-12 and then run Western blot analysis for ERK1/2 and Src tyrosine kinase.

RESULTS: Omental fat from obese T2D mice or exogenous IL-12 induces MRA hypersensitivity to vasoconstrictors.Omental fat from $db^{-}/db^{-IL\text{-}12\text{-}/\text{-}}$ mice did not induce MRA hypersensitivity to vasoconstrictors The inhibition of IL-12 or the use of arteries from $rB2^{-/-}$ mice blunts the effect of omental fat and exogenous IL-12 on MRA hypersensitivity to vasoconstrictors. IL-12 increases ERK1/2 and Src tyrosine kinase phosphorylation in cultured VSMC and intact MRA

CONCLUSION: Omental fat from obese T2D mice releases IL-12, which induces MRA hypersensitivity to vasoconstrictors likely through ERK1/2 and Src tyrosine kinase mechanism. Thus, targeting IL-12 or its downstream signaling could be a therapeutic strategy to overcome VSMC pathology in obesity with T2D.

Abstract Title: Identify Potential Improvements for Hypertension Management at a Local Safety Net Clinic

Investigator(s): Kirklan Kathe, Catherine Eccleston, Cody Daniel, Jason Dukes MD
Department(s): Department of Internal Medicine

Abstract

INTRODUCTION

Hypertension affects more than 45% of adults in the United States and is a leading risk factor for cardiovascular disease (CD) and the country's leading cause of mortality. Despite the widespread diagnoses and treatment of hypertension in America, the condition remains poorly controlled with more than 75% of diagnosed adults unable to maintain normotensive blood pressures. The Sentara Ambulatory Care Clinic (ACC) addresses racial and social disparities in chronic disease outcomes like CD from hypertension by providing uncompensated care to adult residents in Norfolk, Virginia who are low-income, uninsured or underinsured through Medicare and/or Medicaid. The ACC recognized hypertension control as a key longitudinal metric to inform quality improvement (QI) research. This QI initiative aims to identify quantitative trends in patients with uncontrolled hypertension that inform clinic stakeholders.

METHODS

A literature review of quality improvement initiatives for hypertension management was undertaken and the most recent American Heart Association guidelines were discussed in monthly meetings with a QI group of ACC staff who support patient care. The EVMS Free Clinics Extract process generated a list of 605 ACC patients diagnosed with hypertension for at least 6 months in the year before January 21, 2020. A chart review was undertaken to analyse blood pressure medications, number of blood pressure medications, length of prescription adjusting for refills, days before scheduled follow up, if a patient presented for follow up.

RESULTS

Of these patients, removing duplicate charts, 249 (41%) were identified whose last reported in office blood pressure was >140/90 in ages 18-59 or >150/90 for ages 60-85. Within this sample of patients with uncontrolled hypertension at last office visit, 26% did not have follow up occur by scheduled date. Several patients called in refills for medications if time had elapsed past a scheduled follow up that did not occur. During this time period 36% of this sample obtained sufficient insurance to have care provided outside of a safety net clinic.

Conclusions

Under or uninsured patients who receive care for hypertension at the ACC clinic face obstacles in having regular care. Qualitative discussions with clinic staff indicate several social determinants of health impact hypertension control. This project identifies prevalent trends to improve hypertension management in future QI interventions.

Abstract Title: Screening for Social Determinants of Health in Early Childhood Mental Health Consultation

Investigator(s): Daniel Katz, Mary Margaret Gleason, Sam Egger
Department(s): Psychiatry

Abstract

INTRODUCTION

The American Academy of Pediatrics recommends psychosocial evaluation beginning in infancy and throughout a child's development. Part of this recommended evaluation includes adverse social determinants of health (ASDoH), which has been linked to "toxic stress" in children. This type of stress disrupts an individual's stress response and has been shown to have long-term consequences on mental and physical health. As there are evidence-based interventions designed to help children with emotional and behavioral difficulties manage stress, as well as support programs available to families in poverty, screening and identifying those in need is critical.

Solutions that have demonstrated positive results involve creating integrated medical communities, connecting medical health experts with community members who care for children, such as teachers, families, and pediatricians. One such program is the New Orleans-based Tulane Early Childhood Collaborative (TECC), in which mental health experts provide training to pediatric providers, as well as remote or on-site consultations which vary based on need. The purpose of this paper is to describe ASDoH and clinical needs of the young children in this consultation program, and assess the program's environmental screening platform in identifying children in need of mental health care.

METHODS

The study covers 568 families in greater New Orleans provided early childhood mental health consultations by TECC between January 2015 and March 2019. Some children were seen as part of routine well child care and the majority were seen as part of a clinical consultation about a mental health issue. In all, 568 parents received a version of one or both of the two questionnaires: Safe Environment for Every Kid Parent Questionnaire (SEEK) and Early Childhood Screening Assessment (ECSA). A questionnaire about trauma was added partway through the project.

RESULTS

Results from the SEEK show 56.3% of children had experienced at least one ASDoH. In families who received the trauma questions, 17.1% experienced at least one traumatic event. A positive SEEK had 77.4% sensitivity in identifying children with a positive clinical screen. Among children with a positive SEEK, 62.4% had a clinical ECSA. A positive trauma report had a sensitivity of 29.6% in identifying children with a positive clinical screen. Among children with a positive trauma report, however, 76.3% had a clinical ECSA.

CONCLUSION

This paper provides a descriptive analysis of ASDoH in a large population of young children and assesses the prevalence and predictive value of these experiences in identifying children in need. Over half of the population had been exposed to ASDoH and over 15% had experienced a traumatic event. The SEEK correlated well with clinical scores on several measures. This certainly demonstrates the pervasiveness of damaging environmental factors in our most vulnerable individuals. In clinical practice, universal screening with a measure like the SEEK could identify children with modifiable ASDoH as well as a substantial proportion of children with a mental health concern. It should be noted that the SEEK alone is not sufficient to effectively screen for mental health concerns and the AAP's recommendation to screen for social emotional problems can promote early identification of children in need.

Abstract Title: Efficacy of Porcine Small Intestine Submucosal Graft Tympanoplasty

Investigators: Timothy Kearney, MS; Andrew E. Bluher, MD; Stephanie Moody-Antonio, MD
Department: CHKD Department of Otolaryngology

Abstract

Background: Tympanic membrane perforations adversely affect patient quality of life, contributing to otorrhea, infections, ear pain, water avoidance, and conductive hearing loss. The FDA recently approved the Biodesign® **porcine small intestine submucosal (SIS) graft, which offers the advantage of reduced operative time and site morbidity associated with autogenous graft harvest.**

Aims: (1) Compare outcomes between tympanoplasties that use autologous temporalis fascia versus those that use SIS grafts. (2) Identify clinical factors that may predict surgical success or surgical failure, as defined by persistent perforation.

Study Design: Retrospective case control study

Setting: Tertiary pediatric hospital

Methods: Patients aged 2-16 years old who had a medial graft tympanoplasty performed by the senior author from 9/1/16 to 9/1/18 with either autogenous fascia or SIS xenograft were eligible for inclusion. Patients who had a concurrent mastoidectomy or ossicular chain reconstruction were excluded. Patients who had a tympanoplasty using an SIS graft were included as cases, while age-matched patients who had temporalis fascia graft tympanoplasties were included as controls. Data regarding perforation size, grafting technique, graft location and mucosal descriptors were also obtained.

Results: Preliminary data shows a perforation healing rate of 72.7% in the Biodesign® **group (N=11) and a perforation healing rate of 84.2% in the control group (N=38). Data analysis which seeks to find any correlation between surgical success and patient age, initial perforation size, or perforation location is currently in progress.**

Conclusions: Further research is needed to confirm the efficacy of xenografts in a clinical setting.

REQUIRED:

Define Professional Practice Gap & Educational Need: There remains a need to critically evaluate xenografts for their efficacy in tympanoplasty.

Learning Objective: Xenografts may have lower efficacy for medial graft tympanoplasty in a pediatric tertiary care setting.

Desired Result: Surgeons will continue to remain cognizant of potential for worsened tympanoplasty outcomes when using xenografts in pediatric tertiary care settings, pending further data.

Level of Evidence – IV

Indicate IRB or IACUC: IRB number: 19-05-XX-0144. Approved by Eastern Virginia Medical School Institutional Review Board.

Abstract Title: AAV-PCSK9 mouse model of hypercholesterolemia does not serve as a useful model of metabolic syndrome

Investigator(s): W. Coles Keeter[1], Jerry L. Nadler[2], Elena Galkina[1]
Department(s): [1]Department of Microbiology and Molecular Cell Biology, [2]New York Medical College

Abstract

INTRODUCTION
Atherosclerosis is the major etiological culprit that leads to cardiovascular disease, which remains the leading cause of mortality in the United States. Atherosclerotic models include germline deletions of either apolipoprotein E (***ApoE***) or low-density lipoprotein receptor (Ldlr) in C57BL/6 mice. We previously established the ***Ldlr***$^{-/-}$ mouse on a custom high-carbohydrate, high-cholesterol diet (DDC) to model atherosclerosis, glucose intolerance, and insulin resistance. An emerging model to study atherosclerosis utilizes a single injection of adeno-associated virus (AAV) that expresses a gain-of-function mutation of proprotein convertase subtilisin/kexin type 9 (PCSK9), which degrades hepatic LDLR, leading to elevated plasma cholesterol and advanced atherosclerosis when paired with high-fat diet. Therefore, we investigated whether this model recapitulates the metabolic deficiencies seen in the ***Ldlr***$^{-/-}$ model of atherosclerosis and metabolic disease.

METHODS
Male C57Bl/6 mice (n=10 per group) received i.v. injection of either AAV-PCSK9 (PCSK9-DDC) or saline (B6-DDC) and were placed on DDC diet for 20 weeks, with a third group of age matched chow-fed mice (B6-Chow) as an additional low fat diet control (chow diet). Insulin tolerance and glucose tolerance tests were performed at 19 weeks post-injection. AAV-PCSK9 transduction was assessed via post-sacrifice plasma cholesterol measurement. Histological analysis was conducted on pancreas sections to determine changes in islet size and percent islet area via insulin immunostaining. Islet LDLR expression was also determined via immunostaining.

RESULTS
Despite elevated plasma cholesterol and advanced atherosclerosis in the PCSK9-inejcted DDC fed BL/6 mice compared to DDC fed BL/6 mice, both groups showed similar profiles of insulin resistance and impaired glucose clearance, while BL/6 mice fed chow diet expectedly had normal responses. PCSK9-injected DDC fed BL/6 mice displayed higher levels of basal glucose prior to the ITT in comparison with DDC fed BL/6 mice, however these values were more comparable after a longer fasting period prior to the GTT between both groups. Similar to the results from the ITT/GTT experiments, BL/6 mice fed DDC and PCSK9-injected DDC fed BL/6 mice displayed comparable islet size, percent islet area, and insulin staining. These values were all significantly greater than BL/6 chow diet controls, as expected. DDC feeding led to an increase in islet LDLR expression, while the PCSK9-injected DDC fed BL/6 mice expressed a slight yet significantly lower level of islet LDLR, which is likely attributed to increased circulating PCSK9 acting on the islets.

CONCLUSION
Overall, the addition of elevated circulating levels of total cholesterol due to AAV-PCSK9 expression in DDC fed BL/6 mice does not support the development of additional glucose intolerance when compared to DDC fed BL/6 mice indicating that the AAV-PCSK9 model on DDC diet does not serve as a suitable murine model of atherosclerosis and associated metabolic syndrome.

Abstract Title: Quantification of Severity in Infantile Hemangioma: A Pilot Study

Investigator(s): Christine Kim, MS2; David Darrow, MD, DDS, FAAP
Department(s): Otolaryngology, Pediatrics

Abstract

INTRODUCTION: Infantile hemangioma (IH) is the most common childhood tumor, occurring in approximately 5% of infants. It rapidly grows for the first 6 months after birth (proliferative phase) and gradually regresses over the next 4-5 years (involution phase). Most IHs are benign and need no additional treatment. However, a subset of IHs may result in ulceration, pain, functional compromise, permanent disfigurement, and even death. Because these lesions are diverse in their appearance and behavior, a grading system for IHs similar to those for cancer is necessary to predict which lesions are likely to require treatment and to determine the effectiveness of treatment. In order to meet this need, the Hemangioma Severity Scale (HSS) was developed by Haggstrom et al (2012). However, there are flaws with this system, namely, the HSS does not consider the degree of surface skin involvement, color intensity, and height of the hemangioma. Additionally, the incorporation of associated anomalies into the HSS skews the severity of the hemangioma itself, rendering the score less useful in measuring the response to therapy. Accordingly, we developed the QUAntification of Severity in Hemangioma (QUASH) IH scoring system which is more easily applied and incorporates these characteristics. In addition, the QUASH only considers only features of the hemangioma itself. The purpose of this study is to confirm the validity of the QUASH, determine whether the QUASH score correlates with clinicians' subjective judgement of hemangioma severity, and to compare scores obtained from the QUASH to HSS.

METHODS: In Phase I, a pilot study was performed with 4 physicians assessing photos of 27 IHs. Each physician judge was asked to first grade the hemangiomas on a scale of 1 to 5 based on the associated degree of cosmetic and/or functional impairment and the likelihood of medical or surgical intervention. The scoring formula was then applied and a QUASH score determined. Data analysis included intraclass correlation for grades and for each of 8 QUASH scoring domains, interrater reliability of the total scores, and determinant analysis for cutoff points in the scores for each hemangioma grade.In Phase 2, in progress now, anatomic subsites have been better defined and the severity more evenly distributed over the 5 grades of hemangioma severity. At least 3 physicians from different specialties will be asked to score photos of 120-140 IHs based on the QUASH and HSS scoring systems. Each judge will score the hemangiomas twice at an interval separated by 1 to 4 weeks to evaluate intra-rater reproducibility. The physicians will also be asked, as in Phase I, to provide a gestalt grade and to compute a QUASH score. Determinant analysis will again be used to establish cutoff points in the scores for each hemangioma grade.

RESULTS: In the Phase I pilot study, intraclass correlation coefficients for grades and for the 8 hemangioma characteristics were >0.9 with p-values of <0.001 (a strong concordance is indicated by a coefficient of >0.7). The distribution frequency of hemangioma grades among the raters was fairly consistent based on "gestalt," but improved when using the QUASH score. Correlations between the gestalt-based grade and the score-based grade varied among the judges from moderate to strong (intraclass correlation coefficients ranging from 0.5 to 0.77 among the judges) with p-values of <0.004 for all 4 judges.

CONCLUSION: The Phase I pilot study suggests that the QUASH scoring system is reliable and that it correlates with subjective judgements of hemangioma severity. In Phase 2, we hope that better definition of affected subsites, improved diversity of case selection, and inclusion of "before and after" case photos will improve on our previous results and demonstrate that, compared to HSS, QUASH is a more useful system for establishing IH severity and studying outcomes of treatment for IH.

Abstract Title: Evaluating the Educational Needs of Essential Procedures in Global Surgery and Surgical Care

Investigators: Brianna E. King, MSc, Kathleen Casey, MD, Alexandra Leader, MD, MPH, Bibiana Gama, Leslie Toledo, MPH

Department: EVMS Global Health

Abstract

Unreliable access to safe surgical care is a global public health crisis. In response, organizations around the world have created partnerships with under-resourced communities to address gaps in surgical training and care. Physicians for Peace is a non-profit organization focused on educating and mentoring medical providers in specialties such as burn surgery training, intensive care training, urology reconstructive surgery training, essential surgery training and pediatric surgery, through community partnerships. In 2015, the World Bank published a list of 44 surgical procedures deemed essential to population health. By utilizing organizational partnerships, survey analysis can assist in identifying priority essential procedures for specific patient populations.

The aim of this study is to assess participants' perspectives of their clinical settings with respect to skills/training, availability of functional equipment, and availability of equipment/supplies/drugs for essential department-specific procedures. While gathering this information, additional participant insight will be gained on the frequency and accessibility of facility-led and self-led continuing medical education, and online learning accessibility.

This survey was sent to Physician for Peace partners that primarily work in Surgery, Trauma/Emergency, Obstetrics, or Anesthesia departments. Additional survey participants were gathered by referrals from a list of non-surveyed Physician for Peace partners. Other referrals were obtained from survey participants when asked to provide the contact information for the head of the department, if not the survey participant themselves. Results and referrals will be continuously monitored and updated. The survey was adapted from the WHO surgical assessment tool, WHO situational analysis tool, and The Essential Surgery Package: Procedures and Platforms as deemed by Disease Control Priorities 3rd edition. In conjunction with these tools, the questionnaire collects demographic information such as participant country, hospital, department, and job role. Participants also have the option to fill out the survey for more than one department due to multispecialty positions.

Participants self-evaluate and report if they perform procedures deemed essential to their specialty, choose from a list of reasons if procedures are not performed, and can express an interest in learning more about specific procedures. Further educational needs are evaluated by asking participants if they participate in continuing medical education, what resources they have access to, and what further training they would like to receive. Specialty-specific questions regarding scope and limitations of practice will allow insight into the educational needs of survey participants, which can ultimately positively influence the quality of patient care.

Surveying partners will allow insight into the perspective of their clinical setting, procedural performance, and educational training. This information will allow organizations like Physicians for Peace to expand their educational resources to meet partners' specific needs. By surveying healthcare providers in essential surgical procedures, organizations can further address gaps in educational needs leading to more reliable access to safe surgical care.

Abstract Title: Pneumocystis Pneumonia in a COVID-19 World: Not All Ground Glass Opacities Are Due to COVID-19!

Investigator(s): Allen Ko MD, Steve D'Souza MD, Benjamin Goodman MD FACP, Sami Tahhan MD FACP
Department(s): Internal Medicine

Abstract

INTRODUCTION: Cough with findings of diffuse ground glass opacification (GGO) on computed tomography (CT) appropriately raise suspicion for coronavirus disease 2019 (COVID-19). However premature closure and anchoring may mask other etiologies such as infection with Pneumocystis jirovecii pneumonia (PJP), leading to inadequate treatment and risking patient harm.

CLINICAL FINDINGS: A 27-year-old female with medical history significant for intermittent asthma presented with one month of exertional shortness of breath, fevers, hoarseness and dry cough. She had been evaluated thrice at emergency departments for similar complaints, during which she was discharged with trials of steroid tapers and a course of azithromycin. Due to the global pandemic, she was tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during one visit with a negative result. Social history was notable for infrequent tobacco use. She reported one male sexual partner within the past year, remote history of Chlamydial infection and no other known history of sexually transmitted infection.

Physical examination demonstrated tachycardia, hoarseness, no wheezes, and decreased bilateral breath sounds with oxygen saturation of 80% that improved to 100% on supplemental oxygen. Labs revealed mild transaminitis and normal white blood cell count and differential. Chest radiography showed bilateral infiltrates. D-dimer was mildly elevated, and chest CT angiography showed no embolism but had significant bilateral diffuse GGO. Further testing revealed elevated serum inflammatory markers and the patient was admitted for suspected COVID-19 and placed on intravenous steroids. Respiratory viral panel was positive for enterovirus and SARS-CoV-2 testing was negative twice 24 hours apart. On the second day of admission, HIV testing resulted positive and the patient was started on trimethoprim-sulfamethoxazole (TMP-SMX) for presumed PJP.

The patient's presentation with severe hypoxia and initial lab and CT findings did not correlate well with enterovirus infection, and pulmonology was consulted for bronchoscopy to secure a definitive diagnosis. Additional labs demonstrated decreased CD4+ count of 30, elevated HIV viral load, positive Beta-D glucan assay, and an elevated lactate dehydrogenase level. Bronchoalveolar lavage confirmed the diagnosis of PJP via Grocott methenamine silver (GMS) stain. TMP-SMX and steroids were continued, and the patient was started on HIV antiretroviral therapy.

CONCLUSION: Clinical presentation for COVID-19 closely resembles that of PJP with hypoxia, elevated inflammatory biomarkers, lymphopenia, and bilateral infiltrates or GGO on imaging. Several cases have recently emerged in the literature that demonstrate concurrent PJP and COVID-19 in immunocompromised patients, making workup for both disease states important when there is high clinical suspicion.

This case illustrates the effect of the COVID-19 pandemic in confounding well established diagnoses such as PJP due to overlapping similarities in clinical, laboratory, and radiological features. The need for strict isolation procedures with suspected COVID-19 can delay diagnostic workup and treatment resulting in unnecessary morbidity and mortality.

Abstract Title: Neoadjuvant chemotherapy increases patient survival in lymph-node negative pancreatic cancer

Investigator(s): Zakary Kolkey, BS[1], Anthony Pang, BS[1], Michael P. Lee, MS[1], Alex LaFever, BS[1], Rick J. Jansen, PhD[2], M. Cameron Hayes, BS[1], Dennis A. Rowley, MD[3], Janet S. Winston[3], Brad W. Kirby, BS[4, 5], David Z. Chang, MD, PhD[6], Richard A. Hoefer, DO[5] and Amy H. Tang, PhD[1]

Department(s):

1. Leroy T. Canales, Jr. Research Center, Department of Microbiology and Molecular Cell Biology
2. Department of Public Health (Bioinformatics)
3. Pathology Sciences Medical Group (SNGH)
4. Sentara Tumor Registry
5. Sentara Cancer Network
6. Virginia Oncology Associates

Abstract

INTRODUCTION

The dismal prognosis of patients diagnosed with pancreatic cancer points to our limited arsenal of effective anticancer therapies. Surgical resection followed by chemo- and radiation therapy remains the current standard of care therapies for pancreatic cancer patients with resectable diseases. Despite aggressive and high-intensity systemic therapies, only incremental survival benefits were achieved in patients with surgical options. Due to the complications and major health impact of pancreatic surgery, timely completion of adjuvant chemotherapy is often delayed significantly in the post-operative setting. Accumulating evidence is in support of administering neoadjuvant chemotherapy (NACT) prior to surgery to treat pancreatic cancer. In this study, we examined whether incorporating chemotherapy in the neoadjuvant setting would offer any significant survival benefits to pancreatic patients treated at Sentara Hospitals.

METHODS

191 patients with resectable pancreatic cancer were identified from Sentara Tumor Registry and EPIC database between 2008 and 2014. All patients were reviewed using the hospital's electronic medical record system, and the length of disease was calculated from the date of initial diagnosis to the date of censoring or death. Death due to pancreatic cancer was confirmed by hospital death record and physician's last note. Statistical correlations of patients who received surgery and chemotherapies in neoadjuvant or adjuvant settings, and surgery alone were examined to predict patient survival.

RESULTS

Of the 191 pancreatic cancer patients, 45 underwent surgical resection only, 100 received surgery and adjuvant chemotherapy, and 46 received NACT and surgery. The overall median survival of these patients with node positive disease and node negative disease in the neoadjuvant setting is 24 months and 60 months, respectively ($p < 0.0088$). We find that NACT significantly increase patient survival in node-negative resectable pancreatic cancer in this cohort.

CONCLUSION

We found that it is beneficial to incorporate multi-agent chemotherapies in both neoadjuvant and adjuvant settings to treat lymph node-positive pancreatic cancer. We have found that pre-exempt NACT in lymph node-negative pancreatic cancer has increased 5-year survival. This retrospective study supports the notion that all pancreatic cancer should be treated aggressively with NACT as systemic diseases with and without detectable micro- and macro-metastases.

Abstract Title: Retrospective Evaluation of the Three-Step EIA/PCR Algorithm as an Effective Method for Detection and Treatment of Clostridium Difficile Infection

Investigator(s): Bakri Kulla
Department(s): Internal Medicine

Abstract

Background: *Clostridium difficile* infection (CDI) is the primary cause of infectious diarrhea in the United States. CDI can be life threatening as the symptoms range from diarrhea to toxic megacolon to death. Timely and accurate testing provides the guidance that physicians need to determine how and when to treat a patient. The local hospital system performed, what is considered, a less sensitive test (i.e., GDH/Toxin EIA) detection method until 2012. Starting July of 2013, laboratory service utilized a more sensitive, three-step algorithm to detect CDI. The algorithm detects glutamine dehydrogenase antigen (GDH), Toxins A and B, and proceeds with NAAT (PCR) testing for samples that have discrepant results (e.g., positive for only one test; GDH or Toxin A and B).

Our retrospective study was designed to determine rates of positive CDI and compare rates and outcomes of GDH (+)/Toxin (+) and GDH (+)/toxin (-) patients who were subsequently PCR (+) based on CDI severity stratification.

Methods: A retrospective chart review was performed for all patients that presented with hospital associated diarrhea, who were admitted to Sentara Norfolk General Hospital (SNGH) and subsequently tested for ***C. difficile*** from 9/1/2016 to 9/30/2017. Cases were detected using the three-step algorithm previously described. Multivariable Chi-square tests were performed to compare CDI with medical history**,** outcome measures, treatment-related variable, CDI treatment, and blood test lab values.

Results: From 9-1-2016 to 9-30-2017 a 1031 stool samples were tested for C.Diff, 853 [82.7%] were negative and 178 [17.3%] were positive, including 265 [25.7%] GDH positive tests and 94 [9.1%] toxin positive tests. Specifically, the rate of true positive [GDH+ and Toxin+] were 94 [9.1%], true negative [GDH- and Toxin-] 766 [74.3%], Indeterminate positive [GDH+ and Toxin- and PCR+] 84 [8.1%], and indeterminate negative [GDH+ and Toxin- and PCR-] 87 [8.4%].

For tests that are GDH+ and Toxin -, the PCR test serves as a proxy for the CDI test. Among this population, the PCR has a specificity rate of 98.8% and a sensitivity rate of 97.6%, with a false positive rate of 1.2% and false negative rate of 2.4%, $2(1) = 159.23$, $p < .0001$F.

In order to examine patient-level variables with CDI tests and outcomes, the first positive or first test from each patient was included to ensure independence of data points, resulting in 830 unique tests and patients. When comparing outcomes for true positive tests to indeterminate positive tests, groups did not differ on a variety of demographic (e.g., gender, age) and clinical variables (e.g., length of stay, ICU length of stay, diabetes mellitus, hypertension, end stage renal disease, heart disease, HIV, solid organ transplant, GI surgery, subsequent CDI case, readmission, proton pump inhibitor,H2RA, chemo, steroid, toxic mega colon, ileus, colectomy, and level of care), and various lab values (e.g., Creatinine, Albumin, and WBC). The groups were found to differ on initial treatment used, with true positive cases being more likely to receive both Metro ($p = .005$), and Vanco $p = .006$), treatment as compared to indeterminate positive cases.

Conclusion: When comparing outcomes of true positive tests to indeterminate positive tests, we found that the results of the groups did not differ considering a variety of demographic and clinical variables. We did find evidence that the groups differed in initial treatment used, with true positive cases being more likely to receive both Metro ($p = .005$) and Vanco ($p = .006$) treatment when compared to indeterminate positive cases.

Abstract Title: The Opportunistic Hiccup - A Unique Case Presentation of Candidal Esophagitis in Well-Controlled HIV Patient

Investigator(s): Bakri Kulla
Department(s): Internal Medicine

Abstract

Introduction:

Candida esophagitis is an infection which mostly occurs in the immunocompromised population. Medications or acquired illnesses can decrease the functionality of our immune system leading to opportunistic infections like candida esophagitis. Chemotherapy, systemic steroids, and AIDS are the common offenders that we see clinically. When we do see this in immunocompetent patients, proton pump inhibitor (PPI) use, gastroesophageal reflux, and inhaled corticosteroids are commonly blamed as the reason that patient developed the infection. With all this, it still can occur without any risk factors, although uncommon. We present a case where a patient with no active risk factors was found to have candida esophagitis.

Case report:

A 45-year-old Male with a medical history of well-controlled HIV with recent CD4 count 1,102 cells/μL on anti-retroviral therapy, hypertriglyceridemia, and well controlled type 2 diabetes who presented with melanic stool, hiccups, and bloating for five days. Two weeks prior to the admission, he was given a course of Doxycycline for a respiratory infection. He denied any dysphagia, odynophagia, nausea, vomiting, diarrhea, fever, chills, cough, and shortness of breath, chest pain, polyuria or polydipsia. His vitals were unremarkable and on physical there was no gross bleeding per digital rectal examination (DRE). In the ED his fecal occult blood test (FOBT) was positive. Initial lab workup revealed hemoglobin 13.1, WBC 13,000, platelet count 217,000, blood glucose elevated to 283 mg/dl, BUN 20, creatinine 0.9, triglyceride 354, LDL 158, cholesterol 251, liver enzymes were within normal range.

Based on his presentation of melena and elevated BUN/Cr ratio, he was felt to have UGI bleeding and was started on IV PPI. Esophagogastroduodenoscopy (EGD) was performed and revealed severe white, mucosal, plaque-like lesions coating the entire esophagus; few candidal patches were found in the hypopharyngeal area as well, and normal gastric and duodenal mucosa (Figure 1). A colonoscopy was done which as well showed normal colonic mucosa to cecum. He was diagnosed with candida esophagitis on the basis of the characteristic endoscopic findings and patient was started on oral Fluconazole.

He did well after completion of oral antifungal treatment with resolution of his presenting symptoms. Follow up endoscopy showed normal esophageal, gastric and duodenal mucosa (Figure 2).Following lab results demonstrated well controlled HIV and DM. His blood sugar ranged around 99 mg/dl and his HIV PCR was undetectable, CD4 count remained normal.

Discussion and conclusion:

Candida albicans compose a part of the normal oral flora and colonization may be present in up to 20% of the population. Hallmark presentation of Esophageal Candidiasis is odynophagia, dysphagia, and retrosternal chest pain. Oral thrush is seen in most patients with esophageal candidiasis and AIDS. Esophageal symptoms occur in up to half of all patients with AIDS, and Candida Esophagitis accounts for more than 50% of these cases. One study documented esophageal candidiasis in 48% of hospitalized patients with AIDS, although 40% of those infected individuals reported no esophageal symptoms. In rare cases, hiccups were noted to be the presenting symptoms as we saw in this case.

This case highlights the importance of vigilant history and workup to evaluate causes for Candida Esophagitis. Melena and Hiccups are uncommon symptoms of Candida esophagitis as noted in our patient occurring in 0.5% and rare case reports respectively.

Abstract Title: Intoxicated Donors and Heart Transplant Outcomes: Long Term Safety

Investigator(s): Justin Lansinger, BA[1], Ashleigh Long, MD, PhD[1], John M. Herre, MD, FACC[1], Amin Yehya, MD, FACC, FHFSA[1], Edward J. Sawey, MD[1], Amit P. Badiye, MD[1], Wayne Old, MD[1], Jack Copeland, MD[2], Hannah Copeland, MD, FACS, FACC[3], David A. Baran, MD, FACC, FSCAI, FHFSA[1]

Department(s):

1. Sentara Heart Hospital, Division of Cardiology
2. University of Arizona
3. University of Mississippi Medical Center, Cardiothoracic Surgery

Abstract

INTRODUCTION

The opioid crisis has led to an increase in donors and transplants, but questions remain about long term outcomes. Prior studies have relied on social history only without examining the toxicology results at the time of organ offer.

OBJECTIVES

Examine the long-term survival of heart transplants in the recent era, stratified by results of toxicologic testing at the time of organ offer, and compare to older historical variables.

METHODS

The United Network for Organ Sharing (UNOS) database was requested with the addition of the donor toxicology field. Between 2007 and 2017, 23748 adult heart transplants were performed. UNOS historical variables formed the UNOS Toxicology Score (UTS) and the measured toxicology results formed a Measured Toxicology Score (MTS). Survival was examined by the UTS and MTS, as well as Cox proportional hazards models incorporating a variety of factors.

RESULTS

The UTS did not correlate well with the MTS. There were donors with positive UTS and negative toxicology and those with positive MTS values but negative UTS. Survival post-transplant was equivalent across all categories of UTS and MTS. Cox proportional hazards models showed however only donor age and ischemic time were correlated with survival ($p<0.0001$).

CONCLUSION

Among donors accepted for transplantation, history or toxicology positive for a single drug, or a combination did not influence long term survival. Donor drug use is not a contraindication to utilization of otherwise acceptable organs, and increasing use of such donors should be emphasized as we manage the chronic organ shortage.

Abstract Title: Anti-Platelet therapy and Cognitive Function Outcome

Investigator(s): James Lau[1]; Saivarshith Peddireddy, MS[1]; Bahar Niknejad, MD[2]; Hamidreza, Okhravi, MD[2]; Mohan, Pant, PhD, Pstat[3]

Department(s): 1. Eastern Virginia Medical School 2. Glennan Center for Geriatrics and Gerontology, 3. EVMS-Sentara Healthcare Analytics and Delivery Science Institute (HADSI)

Abstract

INTRODUCTION: Alzheimer's Disease (AD) is the most common form of dementia characterized by Amyloid-Peptide (A) and Tau protein deposition in the brain. Currently, more than 26 million people are affected by AD and dementia and the prevalence is projected to quadruple by the year 2050. Emerging data suggest age-related change in platelet function contributes to the pathogenesis of neurodegenerative diseases, including AD. It has been hypothesized that increased activation and aggregation of platelets with aging mediate chronic inflammatory reaction, which is associated with increased rate of A peptide formation and deposition in brain and AD development. Animal models, especially transgenic mice, have shown the potential to highlight the interaction between platelets and molecular mechanism in AD. Studies on mouse models treated with Clopidogrel have shown decreased activation of platelets and formation of amyloid precursor proteins. To date there is paucity of longitudinal studies exploring the effect of anti-platelet medications on long-term cognitive function outcome in human subjects.

OBJECTIVES: We aimed to evaluate whether Clopidogrel and Aspirin, use separately vs in combination, is associated with a change in cognitive trajectory, measured by Clinical Dementia Rating (CDR) score, Mini-Mental State Examination and neuropsychological tests.

METHODS: We performed a retrospective longitudinal cohort investigating the effects of anti-platelet therapy on cognitive function in participants aged 50 or older with baseline normal or mild cognitive impairment (MCI) during a four-year follow-up interval. Participants with inconsistent antiplatelet use report or diagnosis of dementia on initial visit were excluded. The data for this study was obtained from the National Alzheimer's Coordinating Center (NACC) consisting of 31 Alzheimer's Disease Centers in the United States with longitudinal data obtained in annual comprehensive evaluations. In this study we included participants who were enrolled in NACC between January 2005 and December 2019. The study participants were assigned to four treatment groups of Clopidogrel use, Aspirin use, Clopidogrel plus Aspirin use and control group (no Clopidogrel or Aspirin use). The primary outcomes measures were change in MMSE and CDR global scores measured in time to clinical event. Secondary outcomes were change in neuropsychological tests selected to evaluate specific cognitive domains including executive function, attention, and memory.

RESULTS: A total of 1,521 participants were included in the analysis. At initial visit, 959 patients had no cognitive impairment and 562 had MCI. The distribution of study participants by treatment group included Clopidogrel group (n= 122, mean [SD] age 76.6 [8.5]), Aspirin group (n= 733, mean age 72.2 [8.0]), Clopidogrel plus Aspirin group (n= 86, mean age 73.9 [7.6]) and Control group (n=580, mean age 70.2 [8.9]). Cox proportional hazards regression analysis was used to compare the four groups after controlling for all confounding covariables. Aspirin group had a statistically significant effect with 32% reduction in risk of progression in cognitive decline (CDR global score measured in time to clinical event) compared to control group ($p<.005$). The Clopidogrel group and Aspirin plus Clopidogrel group had no significant effect on MMSE change or time to clinical event CDR global score.

CONCLUSION: Aspirin use reduces the rate of cognitive decline in patients with normal cognition or mild cognitive impairment. There was no evidence that clopidogrel had any cerebroprotective effect on cognitive function.

Abstract Title: Neuroendocrine Tumor of the Ampulla of Vater: A Rare Tumor of the GI Tract

Investigator(s): Brandon Lew, Daniel O'Neal, Richard Thomas
Department(s): Department of Radiology

Abstract

INTRODUCTION: Neuroendocrine tumors (NETs) at the ampulla of Vater are very rare, accounting for less than 0.3% of all gastrointestinal neuroendocrine neoplasms.[1] They typically present as low grade tumors and are often subtle in their clinical and laboratory findings when located at the ampulla of Vater. Diagnosis is typically established using ERCP with biopsy although imaging with CT and DOTATATE scans also plays an important role in identifying the tumor. Prognosis is generally favorable in these patients, with an estimated 5-year survival rate of 90%.[6] Treatment typically consists of a Whipple procedure or an endoscopic papillectomy (EP). Here we present a case report of a NET of the ampulla of Vater.

CLINICAL FINDINGS: A 49-year-old female with a history of GERD, Graves' disease, and hypertension presented with intermittent epigastric abdominal pain, nausea, vomiting, and dysphasia over the course of several months. A CT abdomen with contrast was obtained and she was noted to have a 2 cm mass projecting from the level of the ampulla into the duodenal lumen with associated extrahepatic common duct dilation up to 1.3 cm (Fig 1). A follow up MRI showed similar findings with pancreatic duct dilation up to 6 mm. EGD with EUS was performed for biopsy with staining revealing positive panCK, synaptophysin, chromogranin A, and CD56, with suspicion of a NET which was later confirmed (Fig 2). She obtained a DOTATATE PET scan for further evaluation which showed little to no radiotracer uptake in the primary mass and no metastatic disease (Fig 3). She underwent a pancreaticoduodenectomy for removal of the tumor with surgical pathology confirming NET. Her post-operative course was complicated by H. Pylori, delayed return of bowel function, nausea, and vomiting. She was started on appropriate triple therapy and required a gastrojejunal tube for feeds. Her postoperative complications eventually resolved with this treatment and she was discharged a month following her operation.

CONCLUSION: While NETs of the ampulla of Vater are rare with the literature reporting ampullary NETs encompassing 0.3% of gastrointestinal NETs, identification appears have increased in recent years, likely owing to increased imaging and endoscopic studies.[4] Patients typically present with jaundice (53%), abdominal pain (24%), pancreatitis (6.0%), or weight loss (3.6%).[3] Imaging through CT or MRI usually establishes the presence of a tumor while EGD with biopsy confirms the presence of a NET. NETs also typically show increased activity of DOTATATE PET. However, in the case of ours, there was little to no activity, suggesting a lack of somatostatin receptors on the tumor. Surgical resection has been recommended as the standard of cure for these tumors, although one case series has reported success with EP.[1] A cutoff of ≤ 2 cm was suggested the same study for consideration of an EP. In our patient who experienced a prolonged post-operative course, it is uncertain whether she may have benefitted from this alternative procedure. One case study found a complication rate of 18% in the endoscopic treatment of papillary carcinomas, largely due to acute pancreatitis.[5] It may be worth further investigation to better delineate the choice of one treatment over the other but this may be difficult because of the rarity of this tumor.

Abstract Title: Refugee Mental Health Symptomology: Evidence of Gender-based Differences

Investigator(s): Elizabeth Lindsay; Dr. Brynn Sheehan, PhD; Lydia Cleveland Sa, MPH; Ibrahim Maroof, MPH; Dr. Alexandra Leader, MD, MPH
Department(s): Global Health

Abstract

INTRODUCTION: Refugees face significant challenges before, during, and after migration that put them at higher risk for mental health distress and disorders. The Refugee Health Screener-15 (RHS-15) is a validated tool for identifying refugees who are at-risk for symptoms of post-traumatic stress disorder, anxiety, and depression and is administered to all adult refugees resettled by the federally appointed agency in Hampton Roads, Virginia. In the current study, we also categorized some of the items of the scale to indicate somatic and psychological mental health symptoms. The current study objective was to investigate whether the overall RHS-15 screening outcome and mental health symptoms differ by gender.

METHODS: Study data included the RHS-15 and demographic information which were obtained from the local resettlement agency. The first 14 items of the RHS-15 questionnaire are scored on a Likert-type scale ranging from zero to four, which indicates the frequency with which each symptom is experienced over the previous month. Four of these items were categorized as somatic symptoms (e.g., muscle, bone, joint pain), and ten items were categorized as psychological symptoms (e.g., feeling helpless, having nervousness or shakiness inside). Scoring of the overall RHS-15 followed the recommendation that a score of 12 on items 1-14 or a distress thermometer score of 5 indicates a positive screen. Data were analyzed using descriptive frequencies, chi-square tests, independent samples t-tests, and regression models.

RESULTS: The final sample included records of 497 refugees from 14 different countries who resettled in Hampton Roads from 2013-2018. 37.8% of the participants screened positive. A chi-square test revealed a significant relationship between gender and positive screen, $\chi^2(1)= 13.99$, $p < .0001$ (47.8% of females and 30.7% of males), with women having two times the odds of testing positive than men (*OR* = 2.067). For all men and women in the sample, two items that were indicated most frequently were “too much thinking or too many thoughts” and being “unable to cope”.

An independent samples t-test revealed that women reported significantly greater somatic symptoms, $t(438.07) = 3.97$, $p < .0001$ (*M* =.77, *SD* =.84) and psychological symptoms, $t(432.73) = 4.54$, $p < .0001$ (*M* =.90, *SD* =.80) compared to men (somatic *M* =.49, *SD* =.66; psychological *M* =.59, *SD* =.62). Regression models showed that on average, being female was associated with a.182 increase in somatic scores ($p < .0001$) and a.207 increase in psychological scores ($p < .0001$) compared to male’s scores.

Across all individuals screened, regardless of screening status, “muscle, bone or joint pains” was the most frequently reported somatic symptom. For the psychological symptoms, “too much thinking or too many thoughts” was reported as one of the most frequent symptoms by all gender and screening status groups. For females and males who screened negatively, feeling “unable to cope” was a shared strongly endorsed psychological symptom, while for those who screened positively, “feeling down, sad, or blue most of the time” was a shared strongly endorsed psychological symptom.

CONCLUSION: In Hampton Roads, female refugees were significantly more likely to have a positive screening result for mental health disorders on the RHS-15 than male refugees. Men and women seemed to report similar symptoms, with “too much thinking or too many thoughts” and being “unable to cope” most reported, though women reported experiencing symptoms with greater frequency than men. While this study found that being female was associated with greater reported somatic and psychological symptoms, the fractional increase may not be clinically significant since the item scale is scored using integers from zero to four. Symptoms that were strongly endorsed by each group, regardless of gender or screening status, include “muscle, bone or joint pains” and “too much thinking or too many thoughts.” Clinicians and resettlement workers in Hampton Roads can note these common symptoms to better recognize when a refugee might be experiencing compromised mental health.

Abstract Title: Multi-Scale Whole-Body Computational Modeling on Human Cholesterol Metabolism

Investigator(s): Timothy Liu[1,2], William Pei[2], Leo Zhu[2], Claire Velikonja[2], Radhakrishnan Mahadevan[2]
Department(s): Eastern Virginia Medical School[1], Chemical Engineering, University of Toronto[2]

Abstract

INTRODUCTION: LDL cholesterol, an important indicator of potential cardiovascular diseases, has complex interactions and pathways in many levels within the human body, ranging from genome-scale and molecular-level regulations to cellular metabolic pathways to transport phenomena between tissues to organ-system-level physiological interactions. Multi-scale whole body model is designed to capture these intricate dynamics and interactions of cholesterol regulation within the human body. This approach provides an ideal framework to incorporate and evaluate quantitative systems pharmacology, as computational modelling allows the identification of potential drug therapy, dosage optimization, as well as personalized medicine in a low-cost environment. The goal of this research is to consolidate and fine-tune the several existing literature cholesterol modelling approaches into a unified cholesterol model that can be used to evaluate physiological dynamics of the cholesterol species and pharmacological effects of cholesterol lowering drugs.

METHODS: A system of mathematical differential equations based on mass balances is developed to model the interactions of three lipoprotein species (VLDL, LDL, HDL) in four major compartments (liver, intestine, blood, peripheral tissues), their dynamics with LDL receptor (LDLR) and serum proprotein convertase subtilisin/kexin 9 (PCSK9), and the effects of statin, such as atorvastatin, and anti-PCSK9 antibody, such as alirocumab, therapies through quantitative systems pharmacology. Dynamic, constraint-based flux balance analysis is performed using the hepatocyte genome-scale model *iHepatocyte2322* to model the cholesterol metabolism with the focus on HMG-CoA reductase regulation within the liver cells. A model without statin and anto-PCSK9 antibody inputs is first developed to establish the baseline physiologic characteristics of cholesterol regulation modelling framework. Based on clinical recommendations, various daily dosages of statin between 10 mg to 80 mg and daily dosages of anti-PCSK9 antibody between 5 mg to 10 mg are selected to preliminarily evaluate the model's response to the two cholesterol lowering drugs on the market.

RESULTS: Simulation results demonstrate that for baseline cholesterol regulation based on the selected patient profile, steady state is generally reached at around day 40 and at 3.9 mM of blood LDL-C level, which is in the borderline high range and serves as a benchmark simulation for further pharmacological therapy models. The overall dynamics appears to be first order. Daily statin dosages between 10 and 80 mg per day are able to lower blood LDL-C level to the lower bound of borderline high and upper bound of near/above optimal blood LDL-C range, with the steady state dynamics similar to the baseline model. In contrast, daily anti-PCSK9 antibody dosages between 5 and 10 mg per day show little effects on lowering blood LDL-C level based on the model simulations. At clinically recommended dosages, statin, compared to anti-PCSK9 antibody, is more effective at lowering and controlling the blood LDL-C level in this preliminary model simulation.

CONCLUSION: The results from this study demonstrate that the developed modelling framework is capable of modelling LDL cholesterol regulation in the human body. At the same time, the modelling framework has potential applications in systems pharmacology for clinical decision making, dose selection in precision medicine, target selection in drug discovery. Different input and parameters within the model can be adjusted and/or expanded to further mimic additional variables that may influence cholesterol regulation within the human body. This paves the path to a precision medicinal approach where individual patient's health profile can be better simulated through modelling to better identify optimal therapies.

Abstract Title: Investigating the importance of pericyte subsets in the human brain

Investigator(s): Danielle Long, Diana Bohannon, Woong-Ki Kim
Department(s): Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION: Pericytes (PCs) have been shown to be essential players in blood-brain barrier (BBB) homeostasis through their production of extracellular matrix proteins, and their promotion of the upregulation of tight junction proteins (TJPs) with the Sonic Hedgehog (Shh) pathway. PCs and PC abnormalities have also been shown to be important in neurocognitive diseases such as white matter abnormalities in Multiple Sclerosis and altered amyloid beta transport in Alzheimer's disease. This review highlights difficulties in previous studies' differentiation of PCs from other perivascular cells in the human brain and suggests this previous confusion in regard to studying PCs is rooted in the presence of two PC subsets, smooth muscle actin (SMA) negative type-1 PCs (PC1) and smooth muscle actin (SMA) positive type-2 PCs (PC2). We further highlight the importance of investigating these PC subsets in the human brain based upon recent evidence of their active roles in BBB homeostasis and disease.

METHODS: This review article is supplemented with novel research findings in which formalin-fixed paraffin-embedded archival cortical brain tissues from juvenile uninfected (n=10), young adult uninfected (n=10), aging adult (n=10) and SIV-infected rhesus macaques with (SIVE, n=5) or without encephalitis (SIVnoE, n=4) were examined using multi-label, semi-quantitative immunofluorescence microscopy of Shh, netrin-1, PDGFRB, Glut-1, fibrinogen, MYH11, and SMA. IF staining was imaged on a Zeiss Azio Observer with AxioVision or a Zeiss 880 laser scanning confocal microscope with ZEN black and analyzed using ImageJ. All graphing statistics were performed using GraphPad Prism.

RESULTS: While PCs have been studied extensively, we found many instances of confusion and misuse of markers in the literature. This is partially due to studies being conducted in mice instead of humans, which convoluted the data because of differing vascular anatomy of the two species. By using rhesus macaques as a model for humans, we can study homeostatic and diseased models. In physiological conditions, an increase of PC2 are positively correlated with an increase in expression of Netrin-1, a protein that promotes Shh induced production of TJPs. Additionally, an aging rhesus macaque model showed an increase in PC2 with increasing age, as well as an increase in fibrinogen extravasation, an indicator of BBB breakdown.

CONCLUSION: In this review, we highlighted various instances of confusion between PCs and other perivascular cells, including perivascular macrophages, endothelial cells and smooth muscle cells, both due to the varied appearance of PCs and a misuse of differentiating markers. From this data, we created a list of markers used in cited literature to differentiate between these perivascular cells and identified which cell types express which markers. We distinctively classify two subsets of microvascular pericytes, PC1 and PC2 which have distinct roles in BBB homeostasis and disease. During homeostasis, PC2 associated vessels show increased immunoreactivity for Shh and its associated protein Netrin-1, which are traditionally associated with BBB repair. Additionally, our data shows that PC2 are increased in aging and disease models, which is supported by our evidence that an increase in PC2 is positively correlated with increased BBB breakdown. Ultimately, we conclude that there are different roles for PC1 and PC2 in the human neurovasculature; with PC1 being BBB supportive, and PC2 being associated with regions of BBB breakdown. From this review and recent evidence, it is evident that further study is needed into the role of PC subsets in disease and aging and to elucidate the true roles each type of PC in these processes.

Abstract Title: The effect of chronic obstructive pulmonary disease on chest trauma.

Investigator(s): Lopacinski AB, Grigsby CK, Rao AS, Collins JN
Department(s): Department of Surgery

Abstract

INTRODUCTION
Chest trauma is a significant source of morbidity and mortality, especially in the elderly population. Blunt chest trauma is the 2nd leading cause of death after traumatic brain injury in the trauma population. Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity that affects 16 million individuals and is the fourth leading cause of death in the United States. Unfortunately, despite the prevalence of these conditions, very little data describing outcomes for individuals with coinciding chest trauma and COPD exists. We aimed to quantify the impact of COPD in patients admitted with blunt chest trauma.

METHODS
We performed a retrospective cohort study on patients in the trauma registry at Sentara Norfolk General Hospital from January 1, 2014 to March 15, 2020. To make the data consistent across populations we focused on age 65 and above. Chest trauma patients are given aggressive multi-modal pain control and are evaluated and treated by our respiratory therapists. These patients have incentive spirometry measured and may have adjuncts used like chest physiotherapy, intrapulmonary positive pressure therapy, high frequency chest wall compression, and non-invasive ventilation. The COPD patients are treated with bronchodilators and corticosteroids as appropriate.

RESULTS
Our results show that COPD patients have a higher average length of stay than other patients (8.88 days versus 6.65 days, $p = 0.0027$). Days in the intensive care unit (ICU) were longer for those with COPD (3.10 days versus 1.98 day, $p = 0.0018$). These patients were more likely to have unplanned ICU admissions (13.2% versus 3.8%, $p = 0.00003$). Mortality is not significantly more (12.5% versus 7.4%, $p = 0.079$).

CONCLUSION
Our data suggest patients with underlying obstructive pulmonary disorders have stay longer in the ICU, overall longer hospital stays, and more unplanned ICU admissions. The mortality of these patients does appear that it may be higher, but with our sample was not significant. Taken together, there is strong evidence of higher morbidity for individuals with COPD. These patients may benefit from more aggressive treatment with multi-modal pain control and working with respiratory therapy.

Abstract Title: "Scratch Assay Analsis: A Comparison of Methods for Quantifying Cell Migration"

Investigator(s): Merete Lund, Diane M. Duffy, PhD
Department(s): Physiological Sciences

Abstract

INTRODUCTION: Cell migration is an important process involved in multiple activities including angiogenesis, the immune response, and even tumor growth. Tools to analyze characteristics of cell migration are critical to understanding the physiology of these processes. This project compared multiple approaches of cell migration assay data analysis to identify which technique was both the most accurate in comparison to a membrane-based migration assay and the most feasible in terms of time and extra equipment required.

METHODS: A cell migration scratch assay is an easily accessible approach to quantify cell migration. Monkey ovarian microvascular endothelial cells (mOMECs) were isolated as previously described (Trau, H.A., Davis, J.S., & Duffy, D.M., 2015). Cells were grown to confluency and two intersecting scratches made with a pipette tip to remove cells and create an empty area for remaining cells to migrate into. Cells were treated with basal media (control) or basal media containing the known migratory stimulus neurotensin (0.5, 5.0, or 50 μM NTS). Photos of scratched areas were taken at two-hour intervals for twelve total hours to capture how far the cells had advanced at each time point. The area of the scratch in each photograph was first calculated by hand by overlaying a grid of one by one-inch squares (method 1). A second attempt utilized ImageJ and the Wound Healing Tool macro to find the leading edge and calculate the area of the scratch (method 2). The third method built on the second method, but the photographs were adjusted in ImageJ utilizing additional macros and edges were defined using Gimp software (method 3). Using these methods and their corresponding data, the migration speed of cells under different treatment categories was determined utilizing a linear slope. Slopes were compared using ANOVA with 1 repeated measure.

RESULTS: The results of methods 1 and 3 resembled the results of the membrane-based migration assay the most in that the neurotensin treatments did have an increase in the migration speed as compared to the control. However, none of the methods showed significant differences between control and NTS treatments. Method 1 was beneficial in that it did not rely on the calculations of a computer to determine where the leading edge of the cells was. In this way, there was little risk of added error, but calculating the area was time consuming and required estimated guesses as the scratch area was not a perfect shape. Method 2 solved the issue of time – the program analyzed each photograph and displayed where it determined the leading edge to be and the area calculated in a matter of seconds. In comparing the computer's edge-finding technology and manual edge-finding, there was little difference at earlier time points, but more difference at later time points as the scratch areas became smaller. This required adjustment to the settings of the macro and thus added in the chance for additional error. Method 3 allowed the macro settings to be kept constant. Limitations to this approach included issues with keeping the light level and placement of the sharpie mark more consistent.

CONCLUSION: The three methods presented here all bring their own advantages and disadvantages in accurately calculating the cell migration speed using a scratch assay. In learning from the advantages and disadvantages of the first two methods, the third method is the most accurate and feasible approach. While there is still room for improvement in its application, this method allowed for simple analysis of cell migration assay without requiring additional tools or equipment.

Abstract Title: Standardizing patient preparation prior to radioiodine therapy

Investigator(s): Dr. Richard Lussier DO, Dr. Sarah Shaves MD FACR, Dr. Lester Johnson MD PhD FACR
Department(s): Radiology

Abstract

INTRODUCTION: Prior to radioiodine as definitive treatment of hyperthyroidism, elucidating the proper clinical history, screening patients for pertinent medications and providing expected outcomes prior to administering radioiodine is critical for good patient care. Discussion of risks and benefits, alternatives and expected outcomes is a part of standard informed consent. As radioiodine administration is not a common procedure, we recognized the need for a teaching tool for ensuring radiology residency trainees have the necessary experience to adequately prepare patients for the intervention.

METHODS: We will create a reference document which the resident physician will review during the patient encounter prior to radiodine therapy. The document will include a list of screening questions-including but not limited to: thyroid function tests, medications, prior imaging, and recent iodinated contrast. For women, pregnancy status, breastfeeding or history of hysterectomy must be documented. Thyroid medications and discontinuations dates must obtained. Surgical history and pathology should be reviewed with the patient. In addition, clinical outcomes including the desired outcome of hypothyroidism and the potential for repeat administration of I-131 should also be discussed with the patient. Safety protocols including proper distancing especially if there are children in the home and management of bodily fluids must be taught and the physician must be confident in the patient's understanding and willingness to abide by the safety measure prior to administration.

RESULTS: Radioiodine screening tool standardized discussion of risks of radioiodine of persistent or recurrent hyperthyroidism, thyroid storm, need for thyroid hormone replacement, potential risk to others from radiation exposure; benefits of not needing surgery; alternatives of doing nothing with continued symptoms and risks of hyperthyroidism or undergoing surgery; and expected outcomes of euthyroid state but with need for continued follow up.

CONCLUSION: Development of a standardized approach to screening patients prior to radioiodine treatment for hyperthyroidism allows for appropriate patient selection and detailed informed consent. In addition, an organized approach to screening for radioiodine therapy could be used in a simulated patient encounter as a training tool.

Abstract Title: Investigating the role of CD45-dependent B-cell functions in atherosclerosis

Investigator(s): Shelby Ma, Dr. Marion Mussbacher, Alina Moriarty, William Coles Keeter, Phillip Gauronskas, Dr. Elena Galkina
Department(s): Department of Microbiology and Molecular Cell Biology

Abstract

INTRODUCTION: Atherosclerosis is an inflammatory disease of the large and medium size arteries. While specific antigens in atherosclerosis are not well characterized, strong data show that immune responses are involved in atherogenesis. The role of B cells in atherosclerosis is B cell subset specific: B2 cells serve as proatherogenic, and B1 and Marginal Zone (MZ) B cells are atheroprotective subsets. B cell activation is dependent on B cell receptor (BCR) signaling along with a secondary signal such as CD45. CD45 is a protein tyrosine phosphatase that regulates antigen-induced BCR signaling. While evidence suggests that B cells play a role in atherosclerosis, it is not clear whether CD45-dependent BCR signaling is involved in the regulation of B cell activation and functions in this disease. The goal of this project was to test whether and how CD45 is involved in the BCR-induced activation of B cells in atherosclerosis.

METHODS: We took advantage of a transgenic mouse line, in which all B cells express low levels of CD45 (CD45L/L) due to a point mutation in CD45. We examined the phenotype of CD45L/L B cells using BCR-induced Ca2+ flux assay and a series of in vitro experiments. To test the effects of B cells expressing low levels of CD45 in atherosclerosis, we used two murine models. The first model induced acute atherosclerosis through a single injection of a recombinant adeno-associated virus vector (AAV) encoding a gain-of-function mutant form of proprotein convertase subtilisin/kexin type 9 (PCSK9). The second model induced lifelong atherosclerosis by a germline deletion of Apoe (*Apoe*$^{-/-}$ mice). Both groups of mice were fed Western diet (WD) for 18-23 weeks. Because CD45 is expressed on all leukocytes, we performed adoptive transfer of CD45L/L or control WT B cells into B cell-deficient (μ*Mt*$^{-/-}$ or μ*Mt*$^{-/-}$*Apoe*$^{-/-}$*)* recipient mice. B-cells were tested for activation levels and functions.

RESULTS: Examination of the phenotype of the CD45L/L B cells was consistent with previous reports. We found that low expression of CD45 attenuated BCR-induced activation of B cells as demonstrated by attenuated responses in Ca2+ flux assays and reduced phosphorylation of kinases SYK, BTK, and ERK. We also showed that low expression of CD45 favors differentiation of MZ B cells, B1a and B1b cells in the spleen under homeostatic conditions. In the first atherosclerotic model, CD45L/L B cells μ*Mt*$^{-/-}$ recipients showed increased plaque burden along with increased atheroprotective B1 and Breg B cells, decreased levels of atherogenic FO B cells, atheroprotective MZ B cells, and CD8+ Tregs vs WT B cells μ*Mt*$^{-/-}$ mice. These data suggest that CD8+Tregs, and to a lesser extent MZ and B1 cells, play a key protective role against lesion formation. In the second atherosclerotic model, μ*Mt*$^{-/-}$ *Apoe*$^{-/-}$ recipients that received CD45L/L B cells showed diminished atherosclerosis. These effects correlated with an increase in atheroprotective MZ B cells and a decrease in germinal center formation in CD45L/L μ*Mt*$^{-/-}$ *Apoe*$^{-/-}$ compared to μ*Mt*$^{-/-}$ *Apoe*$^{-/-}$ mice that received WT B cells, suggesting that MZ B cells is a powerful subset to protect against life-long atherosclerosis.

CONCLUSION: In summary, we confirmed and further extended data on the role of CD45 in B cell biology under homeostatic conditions. Low expression of CD45 leads to the attenuated BCR-induced B cell activation via the reduced activation of ERK, BTK, and SYK kinases and alterations in development MZ B cells, B1a and B1b cells. By investigating the total B cell populations, we can speculate that in advanced atherosclerosis, MZ B cells may play a bigger role in protecting against atheroprogression via the regulation of the germinal center formation. In contrast, in early acute hyperlipidemic conditions, it appears that loss of immunosuppressive functions of CD8+ Tregs is the driving factor for the promotion of atherosclerosis. The difference of these two models can possibly be attributed to the different immune responses seen in early atherosclerosis vs. advanced atherosclerosis. Early atherosclerosis can be characterized by a rapid activation of the immune response, while advanced atherosclerosis is characterized by chronic inflammation possibly allowing time for more antigen-dependent specific responses. Future studies that will be focused on a CD45-dependent role in antigen recognition by B cells and TLR-dependent functions of B cells will help to close a gap in our understanding of B cell role in cardiovascular disease and find a more targeted therapeutic approach to reduce the chronic inflammatory environment and slow atheroprogression without compromising the immune response.

Abstract Title: Accuracy of Ultrasound Diagnosis of Placenta Accreta During the First Trimester

Investigator(s): Dr. Ray Abinader, Ms. Natalie Macdisi, Dr. Alfred Abuhamad
Department(s): EVMS Maternal Fetal Medicine/ OBGYN

Abstract

Introduction: Low gestational sac implantation (LGSI) is an important marker for the diagnosis of placenta accreta spectrum (PAS) in the first trimester. Pregnancies with placenta previas but without PAS also have LGSI in early gestation. Diagnosis of PAS in the first trimester is highly beneficial as it allows for more reproductive choices, and early transfer to specialized centers for counseling and care. The objective of this study was to identify first trimester ultrasound markers to diagnose PAS in pregnancies with LGSI.

Study Design: This is a retrospective case-control study of pregnancies who delivered at our institution from 2009-2019. Cases represented pregnancies with PAS who delivered by cesarean-hysterectomy and had a first trimester ultrasound with LGSI. Controls represented pregnancies with persistent placenta previas without PAS, who delivered by cesarean section without post-partum hemorrhage and who had a first trimester ultrasound with LGSI. Patients with cesarean scar implantations were excluded. Sonographic images were reviewed by an investigator blinded to pregnancy outcome and sonography reports. Images were reviewed for presence of placental lacunae, with or without swirling on gray scale or color Doppler, abnormal utero-placental interface, and presence of increased uterovesical hypervascularity. Definitions of ultrasound markers followed national task force on PAS. Chi-square and T-test were used to investigate the association between variables.

Results: 21 cases and 46 controls met the inclusion criteria. Lacunae were present in 18/21 (85.7%) cases and in 7/46 (15.2%) of controls (OR 33.4; 95% CI, 7.7-144.4, $p<.0001$). Presence of 3 or more lacunae were 100% predictive of PAS with an average number of 5.0 lacunae in cases compared to 1.3 in controls ($p=0.019$). The average size of the lacunae was 9.88±3.7mm in cases and 4.41±0.56 mm in controls ($p<.0001$). Lacunae swirling on grey scale as well as positive lacunae color Doppler were 100% predictive of PAS ($p<.0001$). Presence of an abnormal utero-placental interface (abnormal retroplacental hypoechoic zone, abnormal uterovesical interface or thinning/absence of the retroplacental myometrium) were also 100% predictive of PAS ($p<0.0001$). Uterovesical and/or parametrial hypervascularity on color Doppler was present in 14/14 cases and only 1/12 controls ($p<.0001$).

Conclusions: Presence of 3 or more lacunae in pregnancies with LGSI in the first trimester is highly predictive of PAS. To our knowledge, this is the first study evaluating the predictive value of placental lacunae in early gestation in pregnancies with low gestational sac implantations.

Abstract Title: Unmet needs in high-risk and locally advanced HER2-positive breast cancer:

Author BlockInvestigators: Kendall Major [1], Amber L. Collier, MD[1], Dasom Caroline Lee, MD[1], Alex C Lafever, MD[1,] Mary L Guye, MD, FACS[2,3], Janet S Winston, MD[4], Billur Samli, MD[4], Rick J Jansen, PhD[5], Emanuel F. Petricoin[6], Harry D. Bear[7], Richard A Hoefer, DO, FACS[3,8], Amy H Tang, PhD[1*]

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Abstract

Metastatic breast cancer is the 2nd leading cause of cancer-related deaths in American women, representing 15% of cancer deaths in women. Early-stage breast cancer is amenable to standard of care (SOC) therapies and has an excellent prognosis; however, locally advanced and late-stage breast cancer has a poor prognosis despite intensive and well-established systemic therapeutic interventions. High-risk and high-grade HER2-positive breast cancer is a highly heterogeneous and rapidly evolving disease that has consistently challenged our ability to identify effective therapies and precision medicine to save these patients. A unique challenge facing patients with HER2-positive metastatic breast cancer is the prevalence of brain metastasis which can be seen in up to 30% of patients. The restrictive nature of the blood-brain barrier presents as an obstacle with drug delivery. Scientific breakthroughs that would enable us to effectively control locally advanced and therapy-refractory HER2-positive breast cancer remain elusive. Although there are multiple targeted treatments for HER2-positive breast cancer, the long-term prognosis is still poor. In addition, HER2-positive breast cancer frequently develops resistance to treatment, which confers a poor prognosis. Identifying and targeting the elusive, ever-changing, and locally advanced HER2-positive mammary tumor is important for identifying unique tumor biology, compensatory pathway activation, patient-specific tumor vulnerability, and fine-tuning targeted therapy and systemic therapy. We aim to identify and validate a central tumor-driving K-RAS/SIAH/HER2 signaling pathway in malignant HER2-positive tumors in hopes of controlling and eradicating chemo-resistant, anti-HER2-refractory, relapsed and locally advanced HER2-positive breast cancer. It is imperative that current targeted therapies and standard-of-care (SOC) treatment plans will be personalized and rationally optimized for each HER2-positive patient: administering precision medicine at the onset of 1st line therapy is critical to save more lives in the clinic. In this clinical study, we will study a local HER2-positive cohort Sentara-EVMS-VOA, and compare the survvial withb AJCC national average, validate a prognostic biomarker, $SIAH^{ON/OFF}$ binary switch, in high-risk HER2-positive breast cancer to stratify patients, identify treatment-resistant tumor clones with high molecular precision at single tumor cells, quantify therapy efficicy, forecast early tumor relapse, and predict overall survival in Hampton Roads Virgina.

Abstract Title: Ensuring Continuity of Women's Healthcare After Incarceration

Investigator(s): Maslyanko, M., Hargis, A.
Department(s): Medicine

Abstract

INTRODUCTION: According to the 2019 report published by Prison Policy Initiative, 231,000 women and girls are incarcerated in the United States at any given moment, with 101,000 in local jails and 99,000 in state prisons.The increasing female population within the United States correctional system requires specific accommodations for the healthcare needs of incarcerated women. Several social and economic determinants existing in the pre-incarceration lives of female inmates influence their specific healthcare needs upon arrival to incarceration. In comparison with non-incarcerated women, female inmates have higher rates of irregular menstrual bleeding, vaginal discharge, cervical cancer, and breast cancer. Although the onset of most medical needs of incarcerated women occurred before women reach imprisonment, many of these diagnoses require ongoing medical care throughout incarceration and even after release from confinement. Following release, there are several unique obstacles that stand between these individuals and proper medical care, including limited access to healthcare facilities, and lack of health insurance coverage. As a result, many people must simply discontinue any medical treatments they received while incarcerated upon release. The discontinuing of necessary medical therapies and prescriptions can lead to severe long-term consequences and detriment to an individual's health. As healthcare professionals, we must ensure a continuum of care following release from incarceration so that newly released inmates can receive the healthcare they need in order to lead successful and healthy lives.

METHODS: The design of the research was secondary data and literature review of articles published by such organization as The Prison Policy Initiative, National Inventory of Collateral Consequences of Convictions, National Commission on Correctional Health Care, and more. Demographically, the focus of this research project is specific to women's health in incarceration. While both males and females face significant struggles that relate to incarceration, the recent increase in the number and proportion of incarcerated females encouraged us to explore issues unique to female incarceration.

RESULTS: Research showed that, due to various social determinants of health, females present with a variety of OB/GYN healthcare needs while incarcerated. While the medical conditions are treated and monitored during confinement, many inmates have difficulty following up with medical providers after their release. The following recommendations have been proposed that would help to ensure continuity of care for newly released individuals in the Hampton Roads community: first, establish free clinic days in the Hopes Clinic, where the uninsured, previously incarcerated population would be able to receive basic healthcare services. Secondly, partner with local incarceration facilities to organize individual counseling sessions during out-processing, during which the inmates would be given clear education on their specific healthcare needs as well as where they can go to obtain care following release.

CONCLUSION: The above-mentioned steps would promote continuity of care for newly released individuals. It would also provide EVMS students an insight into the unique needs of previously incarcerated individuals, which would enhance the EVMS student contribution to the well-being of the Hampton Roads community. Future work should be focused on establishing a closer working relationship between local correctional facilities and EVMS, as well as other medical institutions, to fill the gaps in the healthcare needs of the local population.

Abstract Title: EVs from adipose tissue microvasculature modulate the metastatic potential of prostate cancer cells

Investigator(s): Alli Mathiesen MS, Michael Brown, Bronson Haynes PhD, Anca Dobrian PhD
Department(s): Department of Physiological Sciences, Eastern Virginia Medical School

Abstract

INTRODUCTION: Obesity increases prostate cancer (PCa) aggressiveness and adipose tissue (AT) is a rich source of extracellular vesicles (EV) known to contribute to pro-oncogenic effects in various malignancies. Our lab showed previously that EV isolated from human obese AT (ATEV) reduced invasion, increased proliferation and suppressed expression of MMPs in PC3-ML metastatic PCa cells. The miRNA contained in these EV were shown to target genes that control MMP activity, cell invasion, and proliferation; all hallmarks of metastasis. AT is a heterogeneous tissue that contains a significant number of vascular cells besides adipocytes and immune cells. Our lab is interested to determine the functional and molecular contributions of vascular endothelium derived EV to ATEV pool. Endothelial cells (EC) from human AT in pro-inflammatory conditions are known to produce EV that propagate dysfunctional features in naïve recipient EC and may contribute to metastatic progression in PCa cells *in vitro*. Twist1, a key mediator of prostate cancer aggressiveness, is elevated in both obesity and prostate cancer. The goal of this study was to determine molecular and phenotypic changes of PCa cells in response to EV produced by human adipose tissue endothelial cells (HAMVEC) exposed to pro-inflammatory conditions mimicking the state of chronic inflammation in obesity.

METHODS: In order to model reproducibly different phenotypes for PCa cells, PC3ML cells were engineered to express either diminished or increased expression of endogenous Twist-1. One Twist-1 allele was knocked out using CRISPR/Cas9 editing. These Twist-1 deficient cells bear a less invasive and proliferative phenotype. Twist overexpression was achieved by permanent genome insertion using a PiggyBac vector. Twist1-overexpressing cells are more invasive and have a pro-metastatic phenotype and high proliferative rates. Naïve PC3ML cells were exposed to EV harvested from HAMVEC treated with pro-inflammatory cytokines (PIC), termed EV_PIC, to mimic the obese AT environment. RNA was collected from HAMVEC, EV_PIC, and EV_PIC treated PC3ML. EV miRNA cargo and HAMVEC and PC3ML mRNA transcriptome was assessed using NanoString and IPA analysis. Proliferation was assessed via uptake of BrdU and scoring via fluorescent microscopy. Invasion was measured using a Matrigel transwell assay; cells were imaged and number of cells per field counted. Expression of mRNA was assessed by RT-PCR.

RESULTS: EV_PIC were found to contain a subset of miRNA that were shared by EV isolated from human obese AT, including miR-21, and miR29. These miRNAs target genes are key modulators of various pro-oncogenic pathways including tumor cell proliferation and invasion. The mRNA transcriptome of PC3ML treated with EV_PIC revealed a molecular signature indicating increased activity of several pro-oncogenic pathways predicted to be targeted by the miRNAs found in both EV_PIC and ATEV. EV_PIC increased proliferation in PC3ML expressing both wild type and elevated levels of endogenous Twist1. PC3ML invasion was found to be positively correlated to Twist1 expression. EV_PIC treatment increased invasion in PC3ML with reduced endogenous Twist1, but reduced invasion in PC3ML overexpressing Twist1. Both overexpression of Twist1 and treatment with EV_PIC increased the ratio of E-Cadherin to Vimentin, which is used clinically as a prognostic indicator.

CONCLUSION: Overexpression of Twist1 aggravated the malignant phenotype of PC3ML by dysregulating pathways directing sphingolipid metabolism and cell cycle regulation. EV_PIC are enriched in miRNAs that play various roles in cancer progression. MiR-21 has been identified as an oncogene and has been found to promote prostate cancer invasion and miR-29 has been demonstrated to act as an oncogene in pancreatic cancer by mediating epithelial-to-mesenchymal transition. PCa cells treated with EV_PIC develop a pro-oncogenic molecular signature consistent with metastatic progression. This signature is characterized by the predicted activation of pathways including TGF-, HOTAIR, and FAT10, all of which are associated with metastasis. PC3ML treated with EV_PIC i*n vitro* demonstrate increased mRNA expression of mesenchymal markers, increased proliferation, and reduced invasion. These functional changes are consistent with establishment of a secondary tumor site *in vivo*. Overexpression of Twist1 exacerbated the effect of EV_PIC on the molecular signature of PC3ML, resulting in dysregulation of multiple oncogenic signaling pathways. These data suggest that miRNA contained within EV from adipose microvasculature in a pro-inflammatory environment may confer pro-oncogenic properties on PCa cells *in vitro* which may provide insight into the link between obesity and increased incidence of prostate cancer.

Abstract Title: Extracellular vesicles' microRNA cargo in follicular fluid as a predictor of oocyte maturation in infertile patients

Investigator(s): Tamar Matitashvili, MD, Sezgi Arpag, MS, Alli Mathiesen, MS, Celia Gerard, PhD, Laurel Stadtmauer, MD, PhD, Anca Dobrian, PhD.

Department(s): Jones Institute for Reproductive Medicine; Department of Physiological Sciences

Abstract

INTRODUCTION: Altered expression of microRNAs in ovarian follicular fluid (FF) was proposed to be one of the factors affecting folliculogenesis and steroidogenesis. Extracellular vesicles (EV) are major carriers of miRNAs in virtually all body fluids, including FF. miRNAs carried by EVs are protected from degradation, have a longer half-life and a potentially selective delivery to target cells compared with free-circulating miRNAs. As a result, EV miRNAs emerge as promising biomarker candidates for various diagnostic or response to treatment paradigms. Our study objective was to define extracellular vesicles (EV) miRNA cargo in FF of infertile women, including patients with polycystic ovarian syndrome (PCOS), to determine correlations between EV miRNA cargo and oocyte maturation stage that could lead to discovery of novel biomarkers.

METHODS: Our prospective pilot study included 12 infertile women undergoing in vitro fertilization treatment (IVF) at Jones Institute. We enrolled 6 women diagnosed with PCOS based on Rotterdam criteria and 6 non-PCOS controls matched for age and body mass index (BMI). Patients in both groups underwent controlled ovarian stimulation using standard gonadotropin releasing hormone antagonist protocol.

FF was obtained from the first punctured follicle in each ovary during oocyte retrieval and was processed individually and matched with respective oocytes. EVs were isolated form FF using a commercially available kit. Following RNA extraction, miRNA composition was quantitated using the nanoString nCounter FLEX Analysis platform. Oocytes, isolated from the individual follicles, were evaluated by a trained embryologist for maturity stage after the removal of cumulus cells. Comparisons between the two groups were performed using the Kruskal-Wallis test and correlations between miRNA expression and clinical parameters were done using Spearman's non-parametric test.

RESULTS: No statistical differences were detected between the PCOS and control groups with regard to age, BMI, IVF cycle characteristics, number of oocytes retrieved and blastocytes. FF-EVs were similarly in numbers and total amount of mRNA cargo. Out of 828 human miRNAs screened in the FF, expression of 19 miRNAs were above the detection limit. 7 miRNAs (miR-502-5p, miR-603, miR-548aa, miR-548t-3p, miR-1246, miR-548n, miR-627-5p and miR-4531) were exclusively found in PCOS samples and 2 miRNAs (miR-21-5p and miR-411-5p) were detectable in the non- PCOS group only. MiR-1253 and miR-302d-3p were present in both groups and were significantly lower in the PCOS group ($p<0.03$). Difference in additional 4 miRNAs (miR-let-7i-5p, miR-1283, miR-603 and miR-502-5p) were borderline statistically significant ($p<0.06$).To examine association between follicular fluid EV-miRNAs and oocyte maturity we compared FF samples that had metaphase II (MII) oocytes to those that had metaphase I (MI) or germinal vesicle. FF that contained less immature oocytes had less miR-302d-3p compared to samples with MII oocytes ($p<0.01$). Using ingenuity pathway analysis (IPA) we identified 3930 potential miRNA-regulated target genes. One of the validated target genes of miR-302d-3p is FOXL-2, which is upregulated in the presence of miR-302d-3p. FOXL-2 is a transcription factor known to be involved in ovarian development. Knockout of FOXL-2 leads to formation of cystic follicles with an androgen predominant environment, which is a feature of PCOS.

CONCLUSION: Based on our pilot results, we propose to further validate miR-302-3p in EVs of the FF as a potential biomarker for prediction of fertility rates and oocyte quality in IVF patients, especially the ones diagnosed with PCOS. We will also focus in future studies on potential mechanisms related to miR-302d-3p-FOXL-2 axis as a key contributor to oocyte maturation. This and other miRNAs can reveal new pathways responsible for oocyte maturation arrest in PCOS patients.

Abstract Title: Methods for Evaluating Sudomotor Function: A Review.

Investigator(s): Robert McCauley, BS[1], Henri K. Parson, PhD[1], Carolina M. Casellini, MD[1]
Department(s): [1]Division of Endocrinology and Metabolism, Strelitz Diabetes Center and Neuroendocrine Unit, Department of Medicine, Eastern Virginia Medical School, Norfolk, VA, United States.

Abstract

INTRODUCTION: Sudomotor function refers to the control of sweat gland activity by the autonomic nervous system in response to various environmental and emotional stimuli. Sweat production is a vital thermoregulatory mechanism used by the body to prevent heat-related illness. In addition, sweat plays key roles in grip, microbial defense, and wound healing. Since sweat glands are primarily innervated by sympathetic cholinergic nerve fibers, the evaluation of sudomotor function can be utilized as a sensitive, non-invasive method for assessing the function and integrity of the autonomic nervous system. When used in conjunction with cardiac autonomic reflex testing, it can assist in the differentiation of various etiologies of generalized autonomic dysfunction, such as autonomic neuropathies, multiple system atrophy, and pure autonomic failure. It can also be utilized to quantify the severity of autonomic dysfunction, thus allowing for the surveillance of progression and regression of disease in response to treatment. In addition, sudomotor examination can provide early detection of somatic small fiber neuropathies as the peripheral somatosensory neurons responsible for temperature and pain sensation are structurally similar to sudomotor neurons, and thus are often affected concomitantly. Sudomotor dysfunction may also occur in central nervous system disorders, such as multiple sclerosis and ischemic stroke. Hence, sudomotor testing has utility in the localization and diagnosis of a broad spectrum of neurologic disorders. This review aims to discuss in depth commonly used methods of sudomotor assessment, including their procedure, clinical utility, benefits, and drawbacks.

MAIN BODY: The **Thermoregulatory Sweat Test (TST)** is considered the gold standard for objective measurement of both preganglionic and postganglionic sudomotor function. The test is performed in a temperature- and humidity-controlled setting and involves the application of an indicator dye over the ventral body surface, which changes color upon the onset of sweating. Prevalent neurological disorders have characteristic TST sweating patterns. While TST has proven to be a sensitive measure of sudomotor function, it requires highly specialized personnel and there is a limited availability of TST-standardized facilities. The **Quantitative Sweat Axon-Reflex Test (QSART)** utilizes iontophoresis of acetylcholine to measure the sweat response in a localized skin area. When combined with TST, QSART can differentiate between preganglionic and postganglionic sudomotor nerve lesions. Like TST, it requires highly specialized personnel and testing facilities, and the results can be impacted by numerous factors. While many researchers have reported QSART to be highly sensitive in detecting postganglionic small nerve fiber dysfunction, others have found it to have high variability, poor reproducibility, and a low diagnostic sensitivity. Electrochemical Skin Conductance (ESC) measures the capacity of the sweat glands on the palms and soles to release chloride ions in response to electrochemical activation. ESC, expressed in micro-Siemens (μS), is the ratio between the current generated and the constant direct voltage stimulus applied between the electrodes. Measurement of ESC is dependent on the glands capability to transfer chloride ions and reflects sympathetic small-C nerve fiber function. **Sudoscan**, which utilizes ESC, has shown to be useful in the detection of small fiber neuropathy in patients with and without type 2 diabetes mellitus, Low ESC values correlate strongly with increased severity of diabetic peripheral neuropathy, diabetic kidney disease, and metabolic syndrome. ESC measurements have shown to be highly reproducible and gender-independent. Limitations of ESC include a large inter-individual variability in sweat gland function, although this can be seen in varying degrees in all sudomotor function tests. **Neuropad** measures sweat production on the soles of the feet using a color indicator. The time required for a complete color change is inversely related to the humidity of the skin. It has only a moderate sensitivity for diabetic peripheral neuropathy, and thus is best suited as a screening test.

CONCLUSIONS: While TST and QSART are still considered the gold standards for assessment of sudomotor function, newer methods, such as Sudoscan and Neuropad, offer sensitive and more widely available alternatives for screening and monitoring response to treatment and are easier to apply in the clinical setting.

Abstract Title: Determining the association between perioperative opioid administration and the development of new persistent opioid use after minor surgical procedures.

Investigator(s): ENS Alexander Metzger, MS-4. LT Jacob Cole, MD. LT Gregory Booth, MD.
Department(s): Naval Medical Center Portsmouth Department of Anesthesiology

Abstract

INTRODUCTION: The opioid epidemic in the United States persists as a public health crisis in need of effective multidisciplinary solutions to relieve the burden of chronic opioid use and opioid-related deaths. Surgery is a portal through which patients can develop chronic opioid use, with a pooled 6.7% incidence of new prolonged opioid use after surgery. An estimation based on this incidence would predict that about 1.5 million post-surgical patients will develop prolonged opioid use in the United States annually. To combat this, studies have been performed to determine the numerous factors that predispose patients to new persistent opioid use. An intuitive and commonly-held assumption states that opioid consumption at any point of care increases a patient's risk for developing chronic opioid use. Therefore, it is widely believed that reducing total opioid administration in the perioperative setting, even while a patient is anesthetized, will reduce the risk of developing an opioid use disorder. However, there is currently little evidence to support this claim. In spite of this, many new practice guidelines and protocols advocate for perioperative opioid-sparing techniques such as multimodal or opioid-free analgesia. These techniques, which are much costlier than traditional opioid-based analgesia, have indeed shown to produce similar or improved outcomes regarding postoperative complications such as nausea, vomiting, ileus, and hyperalgesia, but no studies have examined whether these novel approaches lead to a reduction in chronic opioid use. The aim of this study is to address the fundamental question of whether opioid administration in the preoperative, intraoperative, PACU, or postoperative periods is associated with the development of new persistent opioid use.

METHODS: Our hypothesis is that the dose of opioid administration in each perioperative period is associated with the development of new persistent opioid use in opioid-naïve patients. We employ a common definition of new persistent opioid use, which is having at least one active prescription of opioid analgesic between 90 and 180 days postoperatively. We will perform a retrospective cross-sectional study of patients undergoing laparoscopic appendectomy and laparoscopic cholecystectomy at Naval Medical Center Portsmouth. We chose these procedures due to the similar, yet non-protocolized nature of the analgesia plan, resulting in varied dosages of opioid administration at the anesthesia provider's and surgeon's discretion. We will gather the sample from patients undergoing these procedures during a five-year period (December 1, 2014 – December 1, 2019) for a target sample size of at least 1500. Then, we will determine the number of patients from this sample who developed new persistent opioid use. Next, we will determine the total dosage of opioids prescribed in oral morphine equivalents (OME) for each patient in the preoperative, intraoperative, PACU period, and postoperative periods. Then, using these data, we will perform logistic regression analyses to determine whether there is an association between opioid dose in each perioperative period and the development of new persistent opioid use.

RESULTS: Currently, the project is in the process of extracting data from the patient sample. Thus, results for this project are pending analysis.

CONCLUSION: The results of this study could contribute to filling a significant gap in evidence-based perioperative analgesia practices. If the study determines that there is an association between dosage of opioids in certain perioperative periods and the development of new persistent opioid use, then this would support practice guidelines that emphasize the minimization of opioid administration in those time periods. If there is no association, then the results would contradict a widely-held assumption regarding perioperative opioid administration, and a more nuanced approach to analgesia delivery would be warranted.

Abstract Title: Prolonged Sleep Fragmentation Amplifies Atherosclerosis And Destabilizes Plaques

Investigator(s): Alina Moriarty[1], Dr. Tayab Waseem[1], W.Coles Keeter[1], Shelby Ma[1], Philip Gauronskas[1], Dr. Larry Sanford[2], Dr. Laurie Wellman[2], Dr. Elena Galkina[1]
Department(s): Microbiology and Molecular Cell Biology[1], Pathology and Anatomy[2]

Abstract

INTRODUCTION: Atherosclerosis is a chronic, inflammatory disease characterized by the hardening and narrowing of the small and medium sized arteries caused by the accumulation of fatty lesions and formation of atherosclerotic plaques. As the disease progresses, the composition of advanced atherosclerotic plaques increases in complexity and can become unstable and prone to rupture. Ruptured plaques are the main cause of the severe cardiovascular related events that are more likely to result in death. A large necrotic lipid core, increased infiltrating immune cells, and changes in collagen networks are key characteristics associated with vulnerable plaques. Sleep fragmentation (SF) is tightly correlated with the development of chronic low-grade inflammatory diseases such as type 2 diabetes and atherosclerosis. Insufficient sleep is not only associated with increased risk of atherosclerosis, but it is also associated with increased risk of mortality due to a cardiovascular event. Here, we hypothesized that sleep fragmentation would result in accelerated atherogenesis and development of complex atherosclerotic plaques comprised of large necrotic cores and reduced collagen content.

METHODS: Eight-ten-week-old female Apoe$^{-/-}$ mice were randomly assigned to a sleep fragmentation (SF) group or an activity control (AC) group. Chambers equipped with a mechanical bar were used to fragment sleep. Since mice are nocturnal, the SF group had the mechanical sweeper moving every 2 minutes during the light period. To account for the forced activity of stepping over the motorized bar, mice were housed in cages with the motorized sweeper moving across the cage every 2 minutes during the dark period, this group was assigned as the activity control (AC) group. Female Apoe$^{-/-}$ mice were fed a high fat diet (HFD) and were sleep fragmented for 12 weeks. Following 12 weeks of HFD feeding and SF, aortas, carotid arteries, and hearts were collected to examine immune cell infiltration and atherosclerotic lesion formation and stability (en face, qPCR, FACS). Blood biochemistry was assed (ELISA) and immune profiles of the blood, spleen, lymph nodes, carotid arteries, and bone marrow were analyzed by flow cytometry

RESULTS: Following 12 weeks of SF, HFD-fed female Apoe$^{-/-}$ mice showed almost a two-fold increase in aortic plaque formation compared AC mice without significantly changed circulating cholesterol or body weight compared to AC Apoe$^{-/-}$ control mice. When compared to control AC Apoe$^{-/-}$ mice, sleep fragmented Apoe$^{-/-}$ mice exhibited peripheral monocytosis and neutrophilia because of heightened hematopoiesis in the bone marrow. More specifically, SF mice had increased total number of circulating blood inflammatory Ly6C^{Hi} monocytes with a heightened presence of CD68^{+} macrophages in the carotid arteries and aorta. Importantly, aortic plaques from SF Apoe$^{-/-}$ mice had an increased percentage of necrotic core formation with decreased collagen content when compared to AC Apoe$^{-/-}$ controls. Furthermore, SF resulted in a shift in the composition and distribution of collagen fibers present in the aortic plaques of female Apoe$^{-/-}$ mice, with SF Apoe$^{-/-}$ mice having more thin collagen fibers and fewer thick collagen fibers.

CONCLUSION: Our data suggests that sleep fragmentation induces elevated hematopoiesis resulting in monocytosis, neutrophilia, and alters the immune composition of the aortas of atherosclerosis-prone Apoe$^{-/-}$ mice, which results in an increase in accelerated atherosclerotic plaque burden and decreased collagen content. Together these results suggest that sleep fragmentation accelerates the development of atherosclerosis and induces rupture prone, vulnerable atherosclerotic plaques in female Apoe mice.

Abstract Title: Widespread E-cigarette Use Among Cigarette Smoker Sample Unrelated to Gender or Race

Investigators: Tori Murray[1], Karen Soohoo[1], Paul T. Harrell, PhD[1],
Department: [1]Eastern Virginia Medical School.

Abstract

Significance: Electronic cigarette ("e-cigarette") use continues to rise among cigarette smokers. Prior research indicates Whites and Males were significantly more likely to use e-cigarettes. Contemporary, regional trends in use patterns can be informative in understanding potential public health impact.

Methods: Recruitment took place from April, 2019 to March, 2020. Advertisements in Eastern Virginia sought cigarette smokers to participate in a paid research study. Respondents to a screening survey (N=248, M age= 35.4, SD = 9.5, 61% Male, 52% White, 36% Black, 12% Other) on average smoked 16.2 (SD=8.7) cigarettes per day. A majority (50.4%) reported they drink alcohol, over three-quarters (76.2%) reported lifetime marijuana use, and a few (4.0%) reported past-month illegal non-marijuana drug use. The majority (69%) had used an e-cigarette in their lifetime. However, only 14.5% (n=36) had used in the last week. Univariate and multivariate forward stepwise logistic regression models ($p<.05$) investigated age, gender, race, and substance use as predictors of lifetime, past-month, and past-week use of e-cigarettes.

Results: Lifetime e-cigarette use was quite similar across gender (Male lifetime use: 71% vs. Female: 66%; past-month: 37% vs. 35%; past-week: 22% vs. 21%) and race (White lifetime use: 68% vs. Black: 69% vs. Other: 72%; past-month: 33% vs. 38% vs. 41%; past-week: 20% vs. 24% vs. 23%) In univariate and multivariate models, only age (Odds Ratio: 0.96, 95% Confidence Interval: 0.93-0.98; Adjusted OR: 0.96, 95% CI: 0.93-0.98) and use of alcoholic beverages (OR: 1.96, 1.13-3.39; AOR: 1.87, 1.06-3.31) predicted lifetime use of e-cigarettes. Similarly, only age and marijuana use predicted past-month use of e-cigarettes. No variables examined significantly correlated with past-week use of e-cigarettes.

Conclusions: E-cigarette use appears to be more widespread among cigarette smokers in this contemporary sample, lacking previous divergences related to gender and race. Further research is needed to replicate this shift and, if validated with larger samples and in other geographical areas, investigate the potential public health impact.

FUNDING: Academic Institution

Abstract Title: The Role of ACE2 in CoVID-19-Induced Myocardial Injury

Investigators: Sarah O'Berry, Eva Forgacs, PhD
Department: EVMS Physiological Sciences

Abstract

INTRODUCTION: Coronavirus Disease 2019 (COVID-19) is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It commonly causes dyspnea, cough, fever, and myalgia, similar to Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). All of these diseases use Angiotensin-Converting Enzyme 2 (ACE2) for viral entry and increase inflammatory cytokines, resulting in pulmonary inflammation and fibrosis. ACE2, a negative regulator of the renin-angiotensin system (RAS), cleaves angiotensin II to form angiotensin 1-7, counteracting the vasoconstrictive effects of angiotensin II. It is highly expressed in cardiomyocytes to protect against heart failure. Following the binding of SARS-CoV-2 to ACE2, the receptor is internalized and downregulated, causing an accumulation of angiotensin II and unopposed inflammation and fibrosis. Therefore, high expression of ACE2 in cardiomyocytes may be responsible for the cardiovascular effects of COVID-19. The goal of this review is to summarize current knowledge on how SARS-CoV-2 affects the cardiovascular system, specifically focusing on the role of ACE2 in myocardial injury due to COVID-19 infection, which may guide future research and clinical practice.

MAIN BODY: It is known that COVID-19 patients with pre-existing comorbidities such as cardiovascular disease, hypertension, and diabetes experience more severe symptoms. However, COVID-19 can manifest with cardiovascular symptoms such as arrhythmia, heart failure, acute coronary syndrome, thromboembolism, and cardiogenic shock, even without pre-existing comorbidities. Patients with severe COVID-19 disease have elevated troponin compared to milder cases, suggesting that the disease causes some degree of myocardial injury. There are several proposed mechanisms by which myocardial injury occurs in COVID-19 patients. Elevated proinflammatory cytokines have been found in many patients, indicating that cytokine storm may cause systemic inflammation and multiorgan damage. In addition, hypoxemia secondary to pulmonary fibrosis may cause ischemic myocardial damage, and endothelial instability may lead to coronary plaque rupture, resulting in acute coronary syndrome or myocardial infarction. Another possible mechanism of injury is related to the renin-angiotensin system. ACE2 has been shown to be protective in heart tissue, as *ACE2* knockout mice exhibit inflammation, ventricular dysfunction, and respiratory distress. This may explain the inflammation, fibrosis, endothelial instability, and multiorgan damage resulting from ACE2 downregulation when SARS-CoV-2 binds. Therefore, focusing on the RAS pathway, such as recombinant ACE2, ACE inhibitors, and angiotensin receptor blockers (ARBs) are promising treatment options. These treatments counteract the damaging effects of decreased ACE2 and increased angiotensin II on the cardiovascular system.

CONCLUSIONS: Here we summarized the effects of COVID-19 on the cardiovascular system, specifically focusing on the role of RAS and ACE2 in this disease. While worsened by comorbidities, cardiovascular effects have been found in patients with no pre-existing cardiovascular disease, demonstrating that the virus directly causes myocardial injury. This injury may be due to systemic inflammation triggered by cytokine storm, ischemic injury secondary to hypoxemia, or endothelial instability and thromboembolism. All of these pathological effects can be caused by downregulation of ACE2 by SARS-CoV-2 and the subsequent accumulation of angiotensin II. Understanding how the RAS system is implicated in COVID-19 may greatly facilitate development of treatment options, such as recombinant ACE2, ACE inhibitors, and ARBs. Further research is needed to determine the degree of cardiovascular effects directly caused by SARS-CoV-2 infection versus exacerbation of pre-existing conditions. Future studies are also needed to investigate the long-term effects of COVID-19 in recovered patients.

Abstract Title: Implementation of a Standardized Radiology Education in the Pediatric Residency Curriculum

Investigator(s): Daniel O'Neal, Jessica O'Neal, Susan Samreth, Michele Retrouvey, Sanaz Devlin
Department(s): Pediatrics, Radiology

Abstract

Introduction: An integral part of residency is lecture based education. Currently the EVMS Pediatric Residency receives two lectures a day that encompass a wide range of important topics. One such of these topics is pediatric radiology. Imaging is integral to the diagnosis and treatment of patients and it is important for providers to learn how to comfortably order and preliminarily interpret imaging in an emergent setting. Traditionally, the pediatric residents would receive a lecture from one of the Pediatric Radiology Attendings every month or so. There was no set curriculum for these lectures and the style and content varied significantly. Due to this, several pediatric residents suggested that the radiology lectures may benefit from a new approach. The purpose of this quality improvement project is to develop and implement a standardized curriculum of radiology topics for the EVMS Pediatric Residency.

Methods: The implementation of the curriculum was designed to involve three parts, a pre-curriculum evaluation, a standardized lecture series, and a post curriculum evaluation. The pre-curriculum evaluation involved a short anonymous survey sent out to the pediatric residency. The questions gauged their interest in revamping the radiology curriculum, their confidence in interpreting and ordering various types of studies, and what radiology topics they were most interested in coving. This data was used to created 8 standardized lectures. These lectures were scheduled for once per month and were given by a pediatric radiology attending. The first part of each lecture went through example images of the topic. The second part consisted of 10-20 interactive unknown cases where members of the audience attempted to make the correct diagnosis utilizing Poll Everywhere. As part of the first lecture, a pre-test was administered. A post test and anonymous post survey were administered after the curriculum to determine the impact of the lecture series on the residency. Unfortunately, only 5 of the lectures were completed due to the COVID-19 Pandemic. A post curriculum survey was still administered prior to the end of the academic year in order to gauge the impact of the incomplete curriculum.

Results: Both pre and post survey questions were structured as 5 point Likert scale ranging from negative (1) to positive (5). The effect of the curriculum on the survey questions was analyzed using a two-sided Mann-Whitney test with a $p<0.05$ considered as statistically significant. A total of 42 residents completed the pre survey and 23 completed the post survey. The questions analyzed where "How important are imaging studies to your ability to practice medicine?", How comfortable are you in interpreting radiographs?", "How comfortable do you feel ordering imaging studies?", and "Do you feel that you receive adequate training to order the optimal studies for your patients?". No statistical difference was found between the pre and post curriculum survey answers with p values of 0.98, 0.60, 0.45, and 0.84 respectively. The post survey did show that 100% of the participants felt it was at least somewhat important to continue the pediatric radiology standardized curriculum with 73.9% viewing it as very important.

Conclusion: No statistical difference was seen in the responses of the pre and post survey questions. Many factors likely influenced these findings, including the program being abbreviated and that the significantly less people filled out the post survey compared to the pre (23 vs 42). It had been discussed whether to administer the final lectures virtually, but it was determined this would not be ideal given the lectures interactive aspects. The response rates of the post survey may have been limited due to the timing of administration at the end of the academic year well after the last lecture was given. Statistical analysis was also limited due to the anonymous nature of the surveys. On a positive note, all post survey participants felt it was at least somewhat important to continue the curriculum with the majority viewing it as very important. We hope to relaunch the curriculum in it's full form with pre and post tests this academic year once in person conferences resume, as well as utilize non-anonymous surveys for improved statistical analysis.

Abstract Title: Systematic review and comparative analysis of disease-modifying effect of drugs in experimental epilepsy.

Investigators: Heather Ots, Taylor Anderson, William Sherrerd-Smith, John DelBianco, Gordana Rasic, Anthony Chuprin, Zeehan Toor, Alberto E. Musto
Department: Department of Pathology and Anatomy

Abstract

Introduction: Epilepsy affects approximately 50 million people worldwide causing significant medical, financial, and sociologic concerns for affected patients and their families. To date, treatment of epilepsy is primarily symptomatic management because few effective preventative or disease-modifying interventions exist. However, recent research has identified neurobiological mechanisms of epileptogenesis, which provides new pharmacologic targets to investigate. The current data remains scattered across multiple small-scale studies without comparative evidence for which interventions are most effective. Therefore, this systematic review of anti-epileptogenesis research aimed to compile data to compare and identify the most potent drugs for epilepsy prevention.

Methods: Freely available, full-text articles indexed on PubMed were screened and analyzed. The keyword used in the PubMed search was "epileptogenesis," and the search was restricted to a publication period from 2007 through 2020. Studies with animal models of epileptogenesis and explicitly detailed experimental procedures were included in the systematic review. In total 2,004 articles were screened and thirty-three were selected and grouped by the following variables: seizure frequency, seizure severity, recurrent seizures, seizure duration and mossy fiber sprouting. Values obtained in each study were converted to units of percent of its respective control (100%) and reported in ascending order.

Results: Many interventions showed statistically significant reduction in percent difference from the mean in individual variables, but WIN55,212-2, Aspirin, and Rapamycin stood out as effective across multiple categories. Stark discrepancies in current epileptogenesis models significantly complicate inter-study comparison of potential anti-epileptogenic interventions.

Conclusion: Rapamycin; WIN 55,212-2; and Aspirin showed potent anti-epileptogenic modulation across multiple variables. We believe they warrant further study both individually and synergistically. Additionally, our review highlights the need for consistent methodology in epilepsy research. Inconsistent experimental designs hindered comparison between studies, which slows the collective progression towards appropriate treatments for epilepsy. If the research community can optimize and standardize parameters such as administration schedule, sampling time, and animal models, more robust meta-analysis and collaborative research would follow.

Abstract Title: A case series of subchorionic hemorrhages and their sonographic appearance

Investigator(s): Anthony Pang, Garrison Glavich, MD, Tyler Klause, MD, Emily Glavich, MD, Sarah Shaves, MD
Department(s): EVMS Radiology

Abstract

INTRODUCTION
Subchorionic hemorrhage is the most common vaginal bleed between weeks 10-20 of gestation, estimated to compose 11% of cases, but may be as high as 39.5%. It is defined by bleeding that separates the embryonic chorionic membrane from the uterus. Patients with recurrent pregnancy loss, multiparity and known uterine malformations in particular are at risk. (1, 2)

There is conflicting data regarding its clinical implications but one retrospective cohort study of 451 patients with subchorionic hemorrhage did not demonstrate an independent association between subchorionic hemorrhage before 14 weeks gestation and pregnancy loss before 20 weeks gestation in singleton pregnancies. (3) Other studies have linked the condition to elevated risks of hypertensive disorders, abruption, preterm delivery, small for gestational age neonates, a low 5-min APGAR score and a twofold risk of pregnancy loss. In addition, persistent symptomatic hematomas may result in abortion or premature labor. (4) While the implications of subchorionic hemorrhage continue to be elucidated, it is important to hone the diagnostic understanding of the condition, most notably in ultrasonography.

CLINICAL FINDINGS
We present a case series on subchorionic hemorrhages and their sonographic appearance. We examined the sonographic imaging findings of four patients that presented to the emergency department with vaginal bleeding. All patients were in the first trimester of pregnancy with viable pregnancy confirmed on ultrasound imaging. All four patients were found to have a hypoechoic collection between the gestational sac and the uterus with varying size ranging from large to less than a centimeter consistent with subchorionic hemorrhage. These examples serve to illustration the appearance of this important imaging finding in pregnant women endorsing vaginal bleeding.

CONCLUSION
Ultrasonographic evaluation may demonstrate elevation of the chorionic membrane on the side of the uterus opposite the placenta with extension towards the placental margin. Thick septations or tubular membranous structures may also be visualized. The diagnosis can be frequently missed due to the wide spectrum of its echogenicity which may camouflage the condition with surrounding anatomy. When anechoic, subchorionic hemorrhage may be mistaken for amniotic fluid; when isoechoic it can be mistaken for the myometrium and when hyperechoic for the placenta. (5)

Timing is the main determinant of echogenicity in this scenario. Blood initially appears anechoic and increases in echogenicity as it organizes. Over a few weeks, the fluid collection returns to an anechoic appearance. There is limited data correlating ultrasonographic findings to clinical outcomes but a number of studies have described the major contributing factor to pregnancy outcomes as the size of the hematoma. In general, those with smaller hematomas tend to have more favorable outcomes. The exact volume measurement separating smaller hematomas from larger ones is up for debate, but multiple studies have cited numbers between 45-60mL. (6)

Abstract Title: The appearance of free silicone secondary to breast prosthesis rupture on ultrasound

Investigator(s): Kevin Parsons, Garrison Glavich, MD, Tyler Klause, MD, John Plemmons, MD
Department(s): EVMS Radiology, Eastern Virginia Medical School, Norfolk, VA

Abstract

INTRODUCTION

Silicone has been used in prosthesis since the 1960s and have been widely used for breast augmentation and reconstruction (1). One of the complications of these implants is rupture which allows for leaking of silicone into surrounding tissue.

Once a silicon implant ruptures, it will start a granulomatous foreign body reaction known as a siliconomas (1). Siliconomas are granulomatous nodules formed as a reaction to liquid silicones found within, the body either due to direct injection of silicone or rupture of silicone containing implants (2). Disregarding direct silicone injections ruptures of silicone implants is a common occurrence with an overall incidence rate of 5.3 ruptures/100 implants per year (3). This rate increases with implant age and with older versions of implants (3). A minimum of 15% of modern implants can be expected to rupture within 10 years of implantation (3).

CLINICAL FINDINGS

We present a series of cases of siliconomas and their associated ultrasound imaging to help educate other physicians as well as present an uncommon finding on ultrasound imaging. We researched 3 patients who had findings of silicone prosthesis rupture with corresponding mammography or CXR imaging and compared the aforementioned imaging modalities to the sonographic findings as a way to illustrate typical findings for this not commonly seen etiology. We feel this is important due to the fact that many patients will get breast prosthesis secondary to mastectomy due to breast cancer which makes knowing the imaging findings for free silicone from malignant etiologies all the more important.

CONCLUSION

While unlikely to cause significant damage in and of themselves siliconomas present diagnostic difficulties for physicians as it can mimic carcinoma or recurrence on certain imaging modalities (1). The exact pathogenesis of siliconomas is unknown but it is believed T-cell activation is involved, possibly triggered by infectious processes, adulterants added to silicone to enhance fibroplasia, or denaturing host proteins (4). Siliconomas like many other granulomatous diseases are associated with elevated TNF-4.

Abstract Title: Utilization of collateral vasculature to navigate variant anatomy for treatment

Investigator(s): Kevin Parsons, Veer Gariwala, MD, Daniel O'Neal, MD, Christopher Dobzyniak, MD
Department(s): EVMS Radiology, Eastern Virginia Medical School, Norfolk, VA

Abstract

Introduction

Interventional radiology and its application to oncology treatment has a long history with the first application of hepatic artery embolization for treating liver tumors being done in 1974 by Dr. Doyon in Paris, France[1]. Overtime the subspecialty of interventional oncology has developed multiple new treatment modalities including thermo/cryoablation, radiofrequency ablation, microwave ablation, chemoembolization and radioembolization. Transarterial chemoembolization (TACE) and yttrium 90 (^{90}Y) radioembolization have become common procedures for patients with hepatocellular carcinoma (HCC)[2,3]. TACE is considered first-line therapy for patients with intermediate-stage (BCLC-B class) HCC and ^{90}Y allows for more accurate administration of radiation to treat tumors[2].

The liver, unlikely most organs, exists with a dual blood supply from the portal vein and hepatic artery[4]. With the majority, 75%, of the blood flow being through the portal vein. Primary HCC nodules alter this blood flow through angiogenesis via the synthesis of angiogenic factors such as vascular endothelial growth factor A (VEGF), cyclooxygenase-2 (COX-2), and basic fibroblast growth factor (bFGF)[5]. Metastatic liver tumors >3mm in size derive 80-100% of their blood supply from the hepatic arterial supply rather than portal hepatic[6]. This allows for unique therapeutic treatments using TACE and ^{90}Y.

Clinical Findings

Here we will present a case of TACE in a known HCC patient with prior ^{90}Y treatment. In a normal TACE the arterial pathway is go from the aorta into the celiac trunk to the common hepatic artery to the proper hepatic artery and then finally into either the left or right hepatic artery. Initial celiac angiography should new significant stenosis of the proper and common hepatic artery, necessitating a work around to gain access to the tumoral blood supply. This was done by entering and performing angiography to test for collateral tumor blood supply via the left gastric artery and then proceeding further into the right gastric artery and performing further angiography and finally passing completely through both gastric arteries to arrive at the proper hepatic artery thus bypassing the stenotic common hepatic segment. From here the procedure continued as normal with the eventual chemoembolization of the tumoral arterial blood supply.

Conclusion

During the procedure our patient demonstrated new variant vascular anatomy that impacted the treatment strategy. The new stenosis of the common and proper hepatic arteries was likely due to ^{90}Y induced atrophy from the patient's prior treatment. Even though the common arterial pathway was compromised, the patients HCC was still receiving arterial blood supply. The knowledge of common collateral pathways within the abdominal vasculature allowed us to readily locate and traverse the new dominant arterial blood supply of the liver and successfully perform TACE. This demonstrates the importance of vascular anatomy knowledge for interventional radiologists but also the benefits of adaptability and creative solutions at the time of treatment.

Abstract Title: The sonographic appearance of triple negative breast cancer

Investigator(s): Nakul Patel, Garrison Glavich, MD, Tyler Klause, MD, John Plemmons, MD
Department(s): EVMS Radiology, Eastern Virginia Medical School, Norfolk, VA

Abstract

INTRODUCTION
Globally, breast cancer is the 2nd most diagnosed cancer following lung cancer, and the most commonly occurring cancer in women, with an annual incidence of 2.1 million per year. In 2017, the US incidence of female breast cancer was approximately 250,000. Based on data ranging from 2015-2017, it is estimated that approximately 12.9 percent of women will be diagnosed at some point in their lifetime.

Breast cancer is also the 2nd most common cause of cancer death in the US, after lung cancer. The mortality rate for breast cancer has declined since the 1970s, due to improved screening and strides in adjuvant therapies. Currently, the average 5-year survival rate of female breast cancer is 90%. “Triple negatives” describe a subset of breast cancers that do not express estrogen, progesterone, or human epidermal growth factor receptors. These types of breast cancer are of clinical importance due to their different treatment profiles as well worse prognosis.

CLINICAL FINDINGS
We present the ultrasound findings of 6 patients with pathologically proven triple negative breast cancer to illustrate the typical appearance of this important malignancy as well as to demonstrate the subtle differences that can sometimes be present between lesions that are pathologically the same.

CONCLUSION
Triple negative breast cancer compromise less than 20% (some estimates state the true figure is between 10%-15%) of all breast cancer diagnoses. Triple negative cancers have higher tumor grades on initial diagnosis, as well as increased mortality rates as they do not respond to hormone receptor targeted treatments. Patients with triple-negative breast cancer have an increased likelihood of distant recurrence and of death compared with women with other types of cancer, and the difference persists after controlling for established prognostic factors.

The standard guideline for breast cancer screening from the American Association of Family physicians recommends that all women receive biennial mammograms beginning at age 50 and extending until age 74. Screening beginning at age 40 has been shown to have a 60% increased false positive rate and shows minimal effects on mortality. Mammography is the widely used screening tool, but Ultrasound can be used as a fast-acting test in a symptomatic patient as well as an investigative tool.

Abstract Title: Imaging findings of Potts disease and disseminated osseous mycobacterium tuberculosis infection.

Investigator(s): Nakul Patel, Garrison Glavich, MD, Tyler Klause, MD, Rick Lussier, MD, Sarah Shaves, MD FACR

Department(s): Radiology

Abstract

INTRODUCTION: We report an unusual case of a 19 year old male presenting with chest pain, back pain, and unintentional weight loss found to have disseminated osseous tuberculosis infection without pulmonary manifestation.

In 2017, 6.4 million cases of Tuberculosis were reported globally- of those cases, approximately 14% were extrapulmonary, and of the extrapulmonary cases, skeletal tuberculosis comprised 9.8% of cases. In the same year, the United States reported 9088 cases of Tuberculosis, with 20.7% of those cases being extrapulmonary, and of those cases, only 9.2% were musculoskeletal Tuberculosis.

CLINICAL FINDINGS: A 19 year old male presented with 3-4 weeks of lower back pain, 1 week of chest pain and unintentional weight loss of approximately 25 pounds over the prior year. Computed tomography angiography of the chest was performed and revealed that the patient had a destructive soft tissue mass at the T10 vertebral body as well as left hilar lymphadenopathy and pelvic bone and rib lesions.

Testing with QuantiFERON-TB Gold was positive, strongly predictive of true infection, and bone marrow biopsy cultures grew pan sensitive Mycobacterium tuberculosis. MRI of the thoracic spine revealed multiple lesions, the largest at T10. After the patient's work up revealed multifocal infection, he was started on RIPE therapy (rifampin, isoniazid, pyrazinamide and ethambutol) for 6 months.

Towards the end of the treatment period, re-imaging showed extensive healing at the sites of previous lesions and patient was asymptomatic.

CONCLUSION: Mycobacterium tuberculosis is a gram-positive, acid-fast bacillus that is primarily known for causing pulmonary Tuberculosis, an infectious disease of the lungs where alveolar macrophages are able to phagocytose bacterial particles, but unable to destroy them due to inhibition from bacterial virulence mechanisms.

Tuberculosis is generally considered a pulmonary disease, but during primary infection M. tuberculosis may seed the bone or synovial tissue. When M. tuberculosis seeds the spine and causes spondylitis, it is referred to as Pott's Disease. Spinal Tuberculosis has been found in Egyptian mummies from over 5000 years ago, making it one of the oldest diseases known to man. Pott's Disease is characterized by local inflammation and tissue destruction that extends into the intervertebral disc space and may eventually cause vertebral narrowing and collapse.

Clinically, patients will experience pain in the affected region and symptoms may progress to muscle spasm or rigidity. Musculoskeletal Tuberculosis is diagnosed by culture and microscopy of infected material after CT guided biopsy. For the diagnosis of spinal Tuberculosis, imaging with MRI has a greater sensitivity than X-Ray and greater specificity than CT, but biopsy is gold standard for definitive diagnosis. Treatment of musculoskeletal Tuberculosis revolves around the same microbial agents used to treat pulmonary Tuberculosis, in our case RIPE therapy (rifampin, isoniazid, pyrazinamide and ethambutol) for duration of 6 months.

Abstract Title: Is Ovarian Angiogenesis Directly Regulated by LH and Local Oxygen Concentration?

Investigator(s): Andrew C. Pearson[1], and Diane Duffy, PhD.[1]
Department(s): 1. Physiological Sciences, EVMS

Abstract

INTRODUCTION: Angiogenesis is the process by which new blood vessels form from existing vessels. An early step in angiogenesis is the migration of vascular endothelial cells away from their current vessel, along with proliferation of endothelial cells to form the new capillary. This process is essential for successful ovulation and occurs in the ovulatory follicle in response to the luteinizing hormone (LH) surge. Recent data suggest that the concentration of oxygen in the environment into which new blood vessels are growing during ovulatory angiogenesis is likely closer to 5%, rather than the ~21% traditionally used in cell culture systems. It is currently unknown whether the hypoxic environment of the ovulatory follicle promotes angiogenesis. Current investigations of ovulatory angiogenesis have focused on the role of locally-produced angiogenic factors, such as VEGFA, to stimulate new capillary growth. The ability for LH or human chorionic gonadotropin (hCG, a more stable ligand of LH receptors) to directly affect ovarian microvascular endothelial cells has not been studied to this point.

METHODS: Monkey ovarian microvascular endothelial cells **(mOMECs)** are enriched from cynomolgus macaque follicle aspirates via CD31 bead selection, yielding >95% endothelial cell population. mOMECs maintained their endothelial phenotype up to at least 16 passages. All experiments were performed on mOMECs between passages four and nine. Treatment groups for all experiments were control media or 20IU/ml hCG in control media then incubation at 37C, 5% CO2, and either 21% (high) or 5% (low) O2. To quantify **proliferation**, mOMECs (n=3 lines) were grown on 8-well chamber slides and the media was changed at about 60% confluence to treatment conditions. After 24 hours of treatment, cells were then fixed, and immunocytochemical detection of Ki67 was performed to detect proliferating cells. Slides were imaged, and the percentage of Ki67+ cells was determined. To quantify **migration**, mOMECs (n=3 lines) were grown on 8 μm pore size PET translucent 6-well plate inserts. Treatment media was added to the lower media beneath the cells, and control media was added on top of the cells. After 24 hours of treatment, cells which migrated through the insert were H&E stained, imaged, and counted. Endothelial cell **sprouting** was quantified by coating Cytodex 3 microcarrier beads with mOMECs (n=2 lines), suspending cell-coated beads in a thrombin/fibrinogen clot, and adding treatment media. Images of individual beads were taken at 24 & 48 hours. For each image, the number of endothelial sprouts/bead and the length of each sprout was determined.

RESULTS: A statistically significant difference in migration was observed between control and hCG treatment in high O2, but not low O2. Measurement of proliferation demonstrated a trend towards significance between control and hCG treatment. Endothelial sprouting assay is currently underway. Measurement of migration in mOMECs yielded no statistically significant change between low and high oxygen concentrations, with no trend toward significance. However, a trend toward significance was observed in proliferation between low and high oxygen concentrations. We believe increasing the number of mOMEC lines studied will achieve a significant increase in proliferation in low O2 relative to high O2. Endothelial sprouting assay is currently underway.

CONCLUSION: These data indicate that LH/hCG has the potential to directly induce angiogenesis in mOMECs. Additionally, these data include evidence that hypoxia may drive ovulatory angiogenesis. Increasing the number of mOMEC lines studied may yield more conclusive results.

Abstract Title: Triage of Isolated Gunshot Wounds to the Extremities is Improved with Use of Hemodynamic Criteria Over Anatomic Criteria

Investigator(s): Craig A. Sadler, MD[1]; Saivarshith Peddireddy, MS[2]; Jay N. Collins, MD[1]
Department(s): 1. EVMS Department of Surgery, 2. EVMS

Abstract

INTRODUCTION: Over-triage of patients sustaining gunshot wounds is commonplace. Currently, a system assigning patients with injuries proximal to the elbow or knee with the highest trauma designation results in many high alert patients being discharged home from the trauma bay for inconsequential injuries. Cost of mobilizing of significantly more staff and resources. This analysis sought to identify changes to trauma screening that may potentially optimize resource deployment for trauma team activations. Our current alert system determines level of activation for penetrating trauma by anatomic boundaries. Extremities: Proximal to elbow or knee → "Alpha" Alert does not include physiologic or neurologic findings. Observation that current system results in high number of patients with trivial injuries receiving highest alert designation. Many discharged home from trauma bay alert system can be thought of as a screening test for patients at highest risk of death and requiring highest level of care. What is the statistical profile of our current screening test? How can we improve screening of gunshot wound injuries?

METHODS: Retrospective review of patients with gunshot wounds between 1/1/2016-12/31/2018. Patients were excluded if: Age <18 or >89 and underwent workup by ED staff prior to trauma team consultation. Injuries were categorized to the head, chest, abdomen, extremities, or multiple zones. Disposition from ED and hemodynamic measures were collected. A statistical profile of the alert screening system was calculated. Hypothetical scenarios where anatomic and/or hemodynamic screening criteria were changed was performed.

RESULTS: 806 alerted adult trauma patients met criteria, 642 "Alpha" alerts, 164 "Bravo" alerts, Overall trauma bay mortality was 8%, Overall mortality was 14%. Current anatomic boundary extremity screening system has High sensitivity (91%) and Low specificity (30%). 229 Alpha alert patients had isolated extremity injuries: 2 deaths in the trauma bay, 9 requiring ICU admission, 44 requiring immediate operative intervention and 161 not requiring admission. Hypothetical analyses performed-Isolated extremity injuries as Bravo alerts; given lower trauma designation without factoring hemodynamics. Current boundaries AND using hemodynamic criteria to downgrade alert level. Hemodynamic derangements alone to upgrade patients to higher trauma designation HR >100, SBP <90, or Shock Index >0.7.

CONCLUSION: Trauma alert criteria act as screening tests for the acute care needs of the injured patients. Heavy consequence to patient if false negative; test needs to have high sensitivity. Not insignificant cost to mobilizing resources for false positives; specificity cannot be overlooked. Changing alert criteria to focus on hemodynamics may be superior to criteria that consider anatomic boundaries in the extremity.

Abstract Title: Ultrasound characterization of hyperechoic lesions of the breast with pathologic correlation

Investigator(s): Thomas Pender, Garrison Glavich, MD, Tyler Klause, MD, John Plemmons, MD
Department(s): EVMS Radiology, Eastern Virginia Medical School, Norfolk, VA

Abstract

INTRODUCTION

Breast ultrasound is an important primary and adjunct diagnostic tool in the evaluation of breast masses, whether used in lieu of mammography in women under the age of 30, or in conjunction with mammography in difficult to characterize lesions in women over 30. Hyperechoic masses on breast ultrasound are a relatively uncommon finding, with only 0.6-5.6% of breast masses being reported as echogenic. (1-4)

While hyperechoic masses are more commonly found to be benign, anywhere from 0.6-4.9% have previously been found to be malignant, and samples of only malignant lesions have shown roughly 0.4% of these masses to be hyperechoic. (3,5) Overall, the incidence of hyperechoic breast masses is quite low, but their clinical impact can be significant. Therefore the utility of characterizing these masses based on ultrasound and their corresponding pathology cannot be understated.

CLINICAL FINDINGS

We present a case series of hyperechoic lesions of the breast characterized on ultrasound with pathological correlation. Hyperechoic lesions of the breast are not as commonly encountered as other lesions in the breast. We examined 7 patients found to have hyperechoic lesions with their unique sonographic characteristics as well as pathological correlation of the lesions post biopsy. This serves to illustrate and educate other medical professionals on the varied pathologies that can present with this sonographic appearance.

CONCLUSION

Hyperechoic masses on breast ultrasound can represent benign and malignant pathologies. Though benign pathologies are more common, the implications of these malignant pathologies make extensive evaluation necessary in the event of a hyperechoic mass. Certain features have been found to have high predictive value of malignancy in ultrasound masses, and these features are applicable to hyperechoic breast masses as well. The three most prominent characteristics predictive of malignancy on ultrasound include irregular shape, microlobulated or spiculated margins, and width-to-anterior-posterior dimension ratio of 1.4 or less. (2,6)

Recent studies also stress the importance of describing the echogenicity of these masses as homogenous or heterogeneous, as the latter is more likely to be malignant. (7) However, even with these predictive factors and descriptions, ultimate management of these masses falls upon the American College of Radiology Breast Imaging Reporting and Data System criteria (BI-RADS), at which point the decision of whether or not to biopsy the mass comes down to physician assessment.

Abstract Title: Structural Characterization of a Cardiac Troponin C Mutation Associated with Altered Calcium Sensitivity and Hypertrophic Cardiomyopathy

Investigator(s): Ian Pepper, Cristina Risi, Howard D. White, Vitold E. Galkin
Department(s): Physiological Sciences

Abstract

INTRODUCTION: The cyclical formation and dissociation of cross-bridges between myosin-containing thick filaments and actin-containing thin filaments comprises the molecular basis of cardiac muscle contraction. The troponin (Tn)-tropomyosin (Tm) protein complex, present at regular intervals along the thin filament, exerts regulatory control over crossbridge dynamics. Binding of intracellular calcium (Ca^{2+}) ions to the core subunit of troponin (TnC) permits the azimuthal rotation of the Tm around the thin filament. This conformational change of Tm exposes the previously restricted myosin-binding sites on actin; thus, Ca^{2+} binding by TnC serves as a fundamental prerequisite for actomyosin interaction and cardiac muscle contraction. Higher calcium levels increase the probability that Tn will exist in its "open" calcium-bound conformation, which provides more available surface area for it to bind the inhibitory subunit (TnI) and prevent its interaction with actin. This TnC-TnI interaction that occurs upon calcium binding releases actin's restraint on Tm and permits its azimuthal rotation (Yamada et al 2020). Previous work from our lab has revealed a calcium-mediated equilibrium of Tm structural states. In this model, the "blocked" and "closed" states which restrain actomyosin interactions are most prevalent in low calcium conditions, whereas higher Ca^{2+} shifts the equilibrium towards a greater proportion of Tm in the "open" state that permits actomyosin crossbridges (Risi et al 2017).

Given the critical importance of calcium binding for the proper regulation of cardiac muscle contraction, it is logical that Tn mutations have been detected in human patients with hypertrophic cardiomyopathy (HCM). Hearts affected by HCM generally possess increased ventricular wall thickness, excess contractility during systole, and impaired relaxation during diastole. One particular mutation associated with HCM is the substitution of an alanine to valine at residue 8 (A8V) of human cardiac TnC. Isolated cardiomyocytes and transgenic mice with this mutation display increased calcium sensitivity, enhanced systolic function, and impaired diastolic function in agreement with the general HCM phenotype (Martins et al 2015). The calcium sensitization occurs as a consequence of increased TnI binding affinity of TnC-A8V compared to wild-type (WT) TnC. Since A8V mutation of TnC leads to a greater proportion of TnI interacting with TnC vs. actin, a lower calcium threshold is required to produce half-maximal tension in cardiomyocytes with the mutation (Zot et al 2016). In this study, we aim to characterize the effect of cardiac TnC A8V mutation on the calcium-mediated equilibrium and TnI-TnC interaction using state-of-the-art cryo-electron microscopy (EM) techniques.

METHODS: We acquired high-resolution cryo-EM images of murine cardiac thin filaments from both WT and A8V-mutant organisms using a Titan Krios microscope equipped with K3 direct detector. Filaments were imaged under conditions of intermediate calcium (pCa 5.8). The images were imported into the Relion software package for single-particle analysis, and filaments were manually selected for further processing. The chosen filaments were subdivided into helical segments and subjected to 3D classifications in order to filter particles with optimal Tn complex position and occupancy. Selected subsets of particles were further refined to obtain high-resolution electron density maps.

RESULTS: Three-dimensional reconstruction of filaments from mice with A8V mutation at pCa 5.8 reveals structural alterations to the troponin complex near the junction between TnC and TnI. 3D reference-based sorting of the particles indicates that the A8V mutation shifts the ratio of particles considered to exist in "calcium-bound" vs. "calcium-free" conformations at an intermediate calcium level.

CONCLUSION: Our structural characterization of the TnC A8V mutation reveals that it changes the Ca^{2+}-mediated equilibrium of structural states along the thin filament, as well as the physical interaction between TnI and TnC which determines tropomyosin's freedom of movement around the actin filament. This information will help to better understand the molecular basis of HCM caused by the A8V mutation.

Abstract Title: Effect of 2016 CDC Guidelines for Prescribing Opioids for Chronic Pain on Prescription Patterns in Inpatient Palliative Care

Investigator(s): Tram Phung, B.S.;[1] Sarah Alnaif. B.S;[1] Ying Li, M.D;[3] Qi Lin, M.D.;[3] Jiangtao Luo, Ph.D.;[4] Ismail El Moudden, Ph.D.;[4] Hongyun "Tracy" Fu, Ph.D.[2]

Department(s): 1) EVMS School of Medicine, 2) EVMS Department of Pediatrics, 3) Sentara Healthcare Medical Group, 4) EVMS-Sentara Health Care Analytics and Delivery Science Institute

Abstract

Background: Since the release of the CDC "Guideline for Prescribing Opioids for Chronic Pain" in March 2016, legislations regarding opioid prescription limits have been subsequently enacted in most states to combat the devastating opioid crisis in the U.S. Although the restrictions do not apply to patients in palliative care, much concern has been raised that pressure of the 2016 guideline and subsequent legislations may result in unintended changes in opioid prescribing for those receiving palliative care, undergoing pain management during active cancer treatment, and getting end of life care. The result could be undertreated pain and decreased quality of life for these patients.

Methods: This retrospective study which involves a secondary analysis of existing EPIC data from patients (N=20,536) who have used in-patient palliative care and who were prescribed opioids during in-patient care and/or at discharge in six major Sentara hospitals between January 1st, 2014 and May 30, 2019. We examine the patterns (e.g. type, length, dose, prescriber) of opioid prescriptions have changed before and after the 2016 CDC Guideline for Prescribing Opioids and factors associated with the changes, using multivariable regression analyses and difference in difference test.

Results: The analysis included a total of 217,525 opioid medications prescribed for pain management in patient care during the 24 months before the 2016 Guideline (between January 1 2014 and December 31, 2015; and a total of 303,816 opioid medications prescribed during the 41 months (between January 1, 2016 and May 31, 2019) after the 2016 Guideline. The most commonly prescribed opioids were fentanyl, hydromorphone, and morphine, which comprised almost half of prescriptions of the total prescription issued. Data analysis is currently underway.

Conclusions: Findings from the preliminary analysis indicated that the types of opioid prescribed and specialty of prescribers have changed over time before and after the issue of the 2016 CDC Guideline for Prescribing Opioids. There was a reduction in the number of prescriptions over time, and the differences varied across types of health care providers. Findings supported there was an unintended consequence of the 2016 Guideline for in-patient palliative care settings in Hampton Roads, Virginia.

Abstract Title: Intranasal administration of AntiCD40L reduces seizure severity

Investigators: Esther Pototskiy, Andrew Ojeda, Katya Vinokuroff and Kendall Howard Alberto E. Musto
Departments:
Biomedical Sciences, Old Dominion University
Department of Pathology and Anatomy, Eastern Virginia Medical School
Department of Neurology, Eastern Virginia Medical School

Abstract

INTRODUCTION
NeuroInflammation mediates initiation and maintenance of seizures by inducing neuronal hyper-excitability, interneuron damage, and aberrant post-synaptic formation.
CD40L, a small protein belonging to the TNF superfamily that interacts with the CD40 receptor protein, transduces molecular signaling that mediates neurite organization during brain development. Previously, our laboratory showed that CD40 deficiency downregulates seizure severity, increases seizure latency, and reduces seizure frequency in an experimental model of acute seizures. Therefore, the goal of this research was to determine if blocking CD40L mediates seizures.

METHODS
Adult male mice C57BL/6 were used in this study. To evaluate seizure susceptibility successive 10mg/kg, intraperitoneal (i.p.) doses of pentylenetetrazole (PTZ) given at 5 min up to 6 doses, and to test seizure severity PTZ (75mg/kg, i.p.) was given as single doses. Anti-CD40 (BioXCell InVivoMAb anti-mouse CD40L (CD154, 10ug/5ul) or vehicle were administered intranasal two hours before seizure induction with pentylenetetrazole (PTZ). Seizures severity was evaluated using Racine's score, including the latency to elicit seizure after PTZ. Then brain samples were collected to evaluate the activation of CD40 and neuronal damage using immunohistology from the hippocampus and neocortex. An additional group of mice was evaluated for neural oscillation at different time points after administration of antiCD40L using a chronically implanted silicon probe in the hippocampus.

RESULTS
During seizure susceptibility paradigm, antiCD40L administration (n=6) reduced seizure severity after the first(p=002), third (p=02) and fourth (p=0.01) dose of PTZ compared to vehicle (n=6). In addition, mice treated with antiCD40L showed increased latency to develop severe seizures (p=0.04). After PTZ 75mg/kg, antiCD40L treated mice (n=9) had reduced seizure severity (p=0.03) and increased latency (p=0.01) compared to vehicle (n=9). AntiCD40L administration limited expression of CD40 and attenuated neuronal damage after PTZ 75mg/kg. Also, AntiCD40L administration limited power of gamma oscillations.

CONCLUSION
These preliminary findings indicate that the up-regulation of CD40L-CD40 could mediate epileptogenesis by influencing inflammatory mechanisms that involve and propagate seizure-induced neuronal damage. These observations pave the way for understanding the role of chemokines and cytokines during the development of epilepsy, especially after brain injuries.

Abstract Title: An Atypical Case of Cutaneous Neurofibroma: Dendritic Cell Neurofibroma with Pseudorosettes

Investigator(s): Vanessa L Ramos, MS; Alice Roberts, MD
Department(s): Dermatology

Abstract

INTRODUCTION: Dendritic cell neurofibroma with pseudorosettes (DCNP) is a benign peripheral nerve sheath tumor found in the skin. It has unique histopathology characterized by two types of cells organized into a psuedorosette pattern. To date, there have been less than 40 cases reported. It was originally described in 2001 by Michal et al who proposed it to be a rare form of cutaneous neurofibroma. In this report, we describe a typical case in order to enlighten people about this entity.

CLINICAL FINDINGS: A 56-year-old Caucasian female presented to the office for a total body skin exam. She had a past medical history significant for recurrent skin cancer and was concerned about a lesion on her trunk. It was unknown how long the lesion had been present, and the patient reported it "catching on clothing." She denied any other associated symptoms such as pain, itching, or drainage. On physical exam, the tumor appeared as a 1.5 cm flesh-colored, soft, pedunculated nodule on the right flank. A shave biopsy was performed with a differential diagnosis suspicious for nevus vs neurofibroma. Histopathology showed tumor nodules with a pseudorosette arrangement. Type I cells were small, darkly colored lymphocytic-like cells with irregularly shaped nuclei and inconspicuous cytoplasm. Type II cells were larger, pale appearing cells with vesicular nuclei, copious eosinophilic cytoplasm, and dendritic extensions. Type I cells concentrically surrounded type II cells to form the distinctive pseudorosette. The diagnosis was confirmed by immunohistochemistry (IHC). Both type I and type II cells stained positively for S100 and CD57 suggesting a dendritic lineage. EMA IHC highlighted the capsule (perineum) surrounding the tumor nodules and CD34 identified fibroblasts in the stroma. Due to the tumors benign clinical course, no additional treatment was indicated.

CONCLUSION: Clinicians should be aware of DCNP's distinctive histopathology and the importance of using immunohistochemistry to correctly differentiate it from similar-appearing tumors.

Abstract Title: The Effects of Economic Disparity on Online Engagement Among Students

Investigator(s): Gracielle Resurreccion, BS, Emily R. Gordon, MPH, Dr. Andrew Plunk, PhD
Department(s): Pediatrics Community and Health Research

Abstract

INTRODUCTION: Amidst the outbreak of SARS-CoV-2 early 2020 in the United States, many educational systems were forced to move online in order to contain the spread of the novel virus and promote the safety and wellbeing of students. Doing so affected educational extracurricular activities. Students who experience economic disparity may lack access to certain technology in order to participate in such activities online. This study focuses on students living in low-income housing and their experiences with participating in the Eastern Virginia Medical School (EVMS) Youth Engagement Program (YEP).

METHODS: Students living in Norfolk low-income housing were enrolled and mentored by 2 EVMS faculty staff, 3 EVMS students, and 3 Old Dominion University (ODU) pre-med students during the Summer 2020 sessions. This study compares experiences from the Summer 2019 sessions to Summer 2020 sessions (in-person versus online, respectively). Stipends were given to the students who participated in the 2019 and 2020 sessions. Communication with the students' caregivers was consistent in order to remind and confirm participation as well as address any concerns. Mentors also communicated with the students regularly on a weekly basis outside of the sessions to maintain relationships.

RESULTS: There was decreased engagement amongst students in the Summer 2020 sessions compared to the 2019 sessions. 14 students were enrolled in the 2020 sessions which was less than the enrollment of the 2019 sessions which were 20 students. No new students were recruited for the 2020 sessions and instead focused on maintaining relationships with previous cohorts. The percentage of attendance in 2020 dropped to 64% compared to 2019's sessions (70%). The decrease in attendance amongst the students could be due to barriers. Such barriers included connectivity issues due to multiple people in the household and lack of access to proper technology. The program was able to provide students with transportation and accommodations needed for the activities in 2019. In 2020, students were responsible for attending on time and providing their own devices. Four of the students in the 2020 sessions had shared a household device (i.e. laptop or desktop) with their families. Others were lent laptops (or other mobile device) from their schools but were unable to access the video conference platform which resulted in using their smart phones. Students also felt their responsibilities at home were prioritized, which decreased their engagement with the program. Barriers regarding household responsibilities could be living in a single-parent household, unemployment of a parent or guardian, or caring for siblings and/or extended family. Although no new students were recruited, relationship building between the mentors and students remained consistent and was maintained from the sessions of Summer 2019 (as indicated by the small percentage drop of attendance). Students were able to initiate insightful and interactive dialogue regarding the educational topics over time.

CONCLUSION: Students experiencing economic disparity often lacked access to personal laptops and stable wi-fi which led them to use their smart phones or not attend. Some students expressed preference for the use of smart phones although a laptop was readily accessible. In addition, the students felt it was harder to participate in some of the interactive online activities when done on their smart phones. Students were unable to experience hands-on STEM related activities and field trips unlike in the Summer of 2019. Lastly, the students felt that although the transition and setting of the meetings were unconventional, their experiences with the lessons and relationship building were enriching. It is important to consider barriers caused by economic disparity, particularly those in low-income neighborhoods, in order to properly accommodate to students in their academic and extracurricular endeavors.

Abstract Title: An investigation into the effect of a virulence factor-targeted immuno-fusion protein on complement-mediated opsonization of methicillin-resistant *Staphylococcus aureus*.

Investigator(s): Megan A. G. Sage, M.S.[1], Y Tran, M.S.[2], Keith Wycoff, Ph.D.[2], Julia A. Sharp, Ph.D.[1]
Department(s):
[1] Department of Microbiology and Molecular Cell Biology, EVMS - Norfolk, VA
[2] Planet Biotechnology, Inc. - Hayward, CA

Abstract

INTRODUCTION: *Staphylococcus aureus* causes a plethora of severe pathologies resulting in significant morbidity and mortality worldwide. *S. aureus* pathogenesis relies heavily upon host-immune evasion including surface proteins Protein A, which binds IgG Fc, and SdrE, which binds complement regulator Factor H (FH). Previously, we have shown that *S. aureus* lab strain Reynolds binds FH-Fc, a fusion protein (FP) containing IgG Fc and a region of FH known to interact with SdrE (CCP18-20), significantly more than an Fc-containing control protein. We hypothesize that this binding preference also occurs in clinically relevant strains, i.e., community associated (CA), that FH-Fc competes with FH present in normal human serum (NHS), and that FH-Fc increases complement-mediated opsonization of *S. aureus*.

METHODS: The binding and functional effect of FP was assessed using mid-log phase "R7," a CA-MRSA strain. R7 bacteria were incubated with FH-Fc, Fc-control proteins (DPP4-Fc, DAF-Fc, or FH(6-7)-Fc) or FH-control proteins (Variant 1 or Variant 2) for 1h at 37C with manual mixing every 10 minutes.

Bound FP was extracted with 2% SDS at 95 C for 5 minutes and quantified using immuno-dot blot assay and confirmed with anti-FH Western blot. To determine the extent to which FPs compete with serum FH for R7 binding, bacteria were incubated with NHS and fluorescently labeled FP for 1h at 37 C with manual agitation every ten minutes. Bound FP on intact bacteria was detected using the SpectraMax iD3 plate reader at 408 nm excitation and 452 nm emission spectra, and quantified using a standard curve of fluorescent FP. To examine the effect of FP on the binding of serum FH, R7 were incubated with NHS ±FP for 1h at 37C with manual agitation; serum FH was extracted from the bacterial surface using 2% SDS at 95 C for 5 minutes and quantified using FH ELISA, probing with monoclonal mouse anti-human FH CCP1, and confirmed by anti-FH Western blot. To determine the effect of FPs on complement-mediated opsonization of R7, bacteria were incubated with NHS ±FP for 30 minutes at 37 C with manual agitation every ten minutes. Opsonizing C3-fragments were extracted using 25 mM methylamine at 37 C for 1 hour. The ratio of deposited C3b to iC3b was determined using anti-C3 Western blot and optical densitometry of the' band for C3b and the 1 and 2 bands for iC3b. Total C3-fragment deposition was quantified using C3 ELISA, probing with chicken anti-human C3.

RESULTS: CA-MRSA strain R7 bound significantly more FH-Fc than control proteins, with binding occurring in a dose-dependent manner for all FPs tested. The binding of FH-Fc competitively inhibited the recruitment of serum FH, with an inverse correlation of FP to serum FH binding observed. Total C3-fragment deposition was increased in the presence of FH-Fc, but decreased with Variants 1 and 2, whereas the ratio of deposited C3b to iC3b was decreased with FH-Fc but increased with Variants 1 and 2, with Variant 2 having the greatest effect overall.

CONCLUSION: The preference of R7 for FH-Fc confirms that the interaction with SdrE is quantitatively significant, while the competition of FH-Fc with serum FH confirms that recombinant FH(18-20) binds with similar affinity to that of serum FH, supporting its viability as a potential therapeutic. The increase in complement activation seen in C3-fragment deposition indicates that the binding of FP in competition with NHS is functionally significant. Future experiments will investigate the impact of FH-Fc binding on complement activation through the generation of anaphylatoxin C5a and on phagocytosis.

Abstract Title: Evaluation of Peer-led Evidence-Based Medicine Instruction in the Pre-Clerkship Medical Curriculum: Analysis from Two Successive Cohorts

Investigator(s): Mark Schmitt[1], Bryce Aidukaitis[1], Nicole Feng[1], Stephen Johnson[1], Sudarshan Mohan[1], Michel Rogers-Johnson[2], Anca Dobrian[3], April Pace[4]
Department(s): [1] EVMS MD c/o 2022, [2] EVMS Office of Assessment, [3] EVMS Department of Physiological Sciences, [4] EVMS Library

Abstract

INTRODUCTION: Peer-led teaching is an understudied approach for medical school education. To the best of our knowledge, no study of peer-led EBM instruction at a United States medical education institution has been published. EBM was not systematically covered in the CareForward curriculum and the USMLE Step 1 performance of our students in this domain was slightly under the reported national average. **The goal** of the peer-led approach was to increase the effectiveness of instruction and to engage students in the learning of this self-perceived challenging topic. We capitalized on the student members of the EBM Club at EVMS. Four students whom were part of the EBM club since the beginning of their pre-clerkship education volunteered to serve as peer-instructors for each of the two cohorts. Prior to instruction, they worked with an EBM faculty expert for 18 months to master EBM-related concepts and applications. The classes of MD2021 and MD2022 received peer-led instruction in the context of large and small group problem solving sessions during the Multi-Systems Disease (MSD) module. Although direct causation cannot be claimed, performance on the EBM and biostatistics topics of USMLE Step1 was substantially improved for the MD2021 cohort exposed to peer-led instruction; USMLE Step 1 from MD2022 is currently being collected. **The aim** of this project was to determine student feedback and satisfaction with the EBM peer-led instruction in two consecutive student cohorts.

METHODS: An anonymous 11-item survey was administered in 2019 and 2020 to gather the students' perceptions of EBM peer-led instruction after completion of the three problem solving sessions. The survey was formatted as a 5 point Likert scale questionnaire. Demographics data including age, race and gender were also collected. The data was expressed as percent of students that responded by "agree" or "strongly agree" to each of the questions. A ranking was generated based on such data.

RESULTS: A total of 87 responders (60% response rate) from the MD class of 2021 and 77 (52% response rate) from the MD class of 2022 completed the survey. The four students that led the sessions were excluded from the responder's pool for each year. Over 70% of students agreed or strongly agreed on 8 out of 11 survey questions for the MD 2021 class and 10 out of 11 questions for the MD 2022 class. The highest rated question for both cohorts was "The material covered was Step 1 relevant" with 94.2% of students in 2021 cohort responding "agree" or "strongly agree" and 98.7% in the 2022 cohort. Examples of other top-ranked questions were "The goals of the sessions were clearly communicated" (87.3% for 2021, and 88.3% for 2022), "The peers leading the sessions were well prepared and effective" (86% for 2021 and 96.1% for 2022), and "My level of understanding of EBM was improved after these sessions" (77% for 2021, and 88.3% for 2022). The bottom ranking question for each cohort was "I would like to see this peer-led model applied to other disciplines" with 35.6% responding with "agree" or "strongly agree" in the 2021 cohort and 63.6% in the 2022 cohort. Overall, the results of both surveys showed that students perceived the peer-led EBM instruction sessions as a generally positive experience that was beneficial to their Step 1 preparation. Qualitative data from planned focus group interviews will allow for further exploration into student perspectives.

CONCLUSIONS: Surveys are an important component of a mixed-method approach aimed to evaluate students' experiences, attitudes and performance as a result of EBM peer-led instruction. Additional data includes competency quizzes, exam items measuring EBM concepts, and qualitative data from focus groups. This multi-faceted approach will lead to strategies for improvement and validation of this innovative peer-led instructional activity. Scholarship based on last year's cohort has been disseminated through a conference proceeding[1] and an accepted peer-reviewed publication[2].

Abstract Title: An Infographic Highlighting the Incidence, Risk Factors and Treatment Disparities of CKD and ESRD within the Hispanic Population in the US

Investigator(s): Robert Seby, Dr. Vishal Kumar, Dr. Amina Farooq, Christopher Gallo, Dr. Yechiel Mor, Dr. Vatakencherry

Department(s): Society of Interventional Radiology

Abstract

INTRODUCTION: Each year the Medical Student Council's Diversity and Inclusion Committee for the Society of Interventional Radiology creates infographics to shed light on a major disease affecting minority populations within the US and the multiple ways that interventional radiology (IR) can be used for treatment. The main questions that spurred the creation of this infographic are what disease disproportionately affects Hispanics and what are the ways that IR can be used to treat this medical condition? Through an exhaustive literature research, it was determined that chronic kidney disease (CKD) and end stage renal disease (ESRD) disproportionately affected numerous Hispanic individuals in the US and that IR played a significant role in hemodialysis used to treat ESRD. The hope is that the knowledge presented in this infographic will help to shed light on the importance of eliminating this health disparity for this incredible community.

METHODS: There was a detailed literature review to solve this research question. Specifically, the literature review was broken down into subsections titled Definitions of CKD and ESRD, Epidemiology and Disparities of CKD/ESRD, Risk Factors for CKD, Signs and Symptoms, ESRD Treatment Options, ESRD Treatment Disparities, and Future Improvements. Each subsection contained 3 or four bullet points listing concise information that could be included in the infographic. The literature review was done using the CDC, PubMed database as well as UpToDate where we used the following search queries: chronic diseases affecting Hispanics, risk factors for CKD, signs and symptoms of CKD/ESRD, incidence of CKD in Hispanics, incidence of ESRD in Hispanics, arteriovenous fistula use in hemodialysis for Hispanics, surgical graft use in hemodialysis for Hispanics, indwelling catheter use in hemodialysis for Hispanics, CKD/ESRD disparities in Hispanics, and kidney transplant inequities for Hispanics. The population comparison was done between Hispanics and non-Hispanic whites. The infographic itself was first formed as a template in PowerPoint and then later professionally made using Fiverr.

RESULTS: It was found that within the US, Hispanic individuals have a 1.5 times greater risk of developing ESRD compared to non-Hispanic whites. Additionally, it was found that Hispanic individuals are twice as likely to develop Type 2 diabetes, a major risk factor for CKD, compared to non-Hispanic whites. The identified treatment options for ESRD are dialysis and kidney transplant. The dialysis treatment options were further broken down to include both peritoneal dialysis and hemodialysis and there were three ways to establish hemodialysis, those being via indwelling catheters (less preferred), via surgical grafts, and via arteriovenous fistulas (AVF, recommended). Within this, there were several treatment disparities identified. 72% of Hispanics are placed on indwelling catheters when initiating hemodialysis compared to 66% for non-Hispanic whites. Furthermore, when adjusting for age and sex, Hispanic patients are 60% less likely to receive a live donor kidney transplant compared to non-Hispanic whites. During the literature review there was a perplexing observation that showed that while the incidence rates of CKD were similar between Hispanics and non-Hispanic whites, Hispanics were at a much greater risk at developing ESRD compared to non-Hispanic whites. This was found to be because Hispanics were 6 times more likely to have delayed referral to a hospital nephrologist and because they were 1.5x more likely to have late initiation of dialysis compared to non-Hispanic whites.

CONCLUSION: The main conclusions were that ESRD is a severe medical complication that disproportionately affects the Hispanic population in the US and that Hispanic patients are less likely to receive recommended treatment options compared to non-Hispanic whites. It is the hope of all the researchers involved in this infographic that on-time referrals to a hospital nephrologist, greater emphasis on health education regarding risk factors, increased screening for CKD, and the development of healthier lifestyle choices will help in eliminating this health disparity within the Hispanic population in the US.

Abstract Title: Adult B cell acute lymphoblastic leukemia with PTHrP mediated hypercalcemia: A case report

Investigator(s): Sharma KD, Arora I, Tahhan SG
Department(s):EVMS Internal Medicine

Abstract

Introduction: Acute B-cell lymphoblastic leukemia (ALL) is mostly seen in children and adolescents. ALL is very rare in adults, with a prevalence of 1 in 100,000 in the general adult population. An important mechanism resulting in hypercalcemia in childhood ALL is due to secretion of the parathyroid hormone-related peptide (PTHrP), whose mechanism of action is similar to that of parathyroid hormone.

This is a rare case of an adult patient diagnosed with acute B-cell lymphoblastic leukemia who was found to have PTHrP-mediated hypercalcemia.

Clinical Findings: A 75-year-old Japanese male with a past medical history of type 2 diabetes mellitus, hypertension, gout, vitamin D deficiency presented with generalized malaise, weakness, loss of appetite, and a 20-pound weight loss over the last 4 months. The patient had also noted an increased frequency of urination.

Initial workup included labs significant for platelets of 53,000(N=140 - 440 K/uL), BUN of 44 mg/dL(N=6 - 22 mg/dL), creatinine of 4 mg/dL(N=0.8 - 1.6 mg/dL), and ionized calcium of 8 mg/dL(N=4.4 - 5.4 mg/dL). Due to hypercalcemia and polyuria, the intact parathyroid hormone was obtained and was down to 8 pg/ml(N=15 - 65 pg/mL). PTHrP was found to be 4.1 pmol/ml(N=<2.0), Vitamin D 25 was 151.4 ng/ml(N=32.0 - 100.0 ng/mL), and 1,25 dihydroxy Vitamin D was 81.3 pg/ml(N=19.9 - 79.3 pg/mL).

The patient was initially given IV at NS 200cc/hr but bisphosphonates were deferred due to elevated creatinine. He was started on calcitonin 300 units twice a day for 3 days, and then received a one-time dose of zoledronic acid 4mg IV after day 3 of calcitonin with gradual resolution of his hypercalcemia. He subsequently underwent a bone marrow biopsy which showed hypercellular marrow with more than 95% B lymphoblasts expressing CD10, CD19, CD20, CD34, and TDT. BCR-ABL gene was positive. A diagnosis of acute B-cell lymphoblastic leukemia was made, and the patient was started on induction chemotherapy using a modified Linker regimen.

Conclusion: Hypercalcemia due to PTHrP, even though most commonly seen with squamous cell carcinoma, can also be found in ALL and some patients with non-hodgkin's lymphoma. PTHrP has been hypothesized to be produced directly by lymphoblasts in patients diagnosed with ALL, leading to hypercalcemia as a paraneoplastic syndrome. PTHrP functions by altering renal tubular calcium and phosphate transport, as well as by increasing renal cyclic adenosine monophosphate and 1,25-dihydroxy vitamin D production. It also stimulates osteoclasts which then increase bone resorption. Adverse effects due to hypercalcemia include polyuria, confusion, and cardiac arrhythmias. Rapid hydration, calcitonin, and bisphosphonates remain a cornerstone in the treatment of hypercalcemia.

Abstract Title: A comparison of two ventilation strategies for airway stenosis surgery: intraoperative hemodynamics.

Investigator(s). Shaan Sharma, Pranav Baderdinni, Sarah Deperrior MPH,Jacob Benedict M.D.,John T. Sinacori M.D., Benjamin J. Rubinstein M.D

Department(s): Department of Otolaryngology-Head and Neck Surgery

Abstract

INTRODUCTION: Laryngotracheal stenosis (LTS) causes an extra thoracic restriction in pulmonary ventilation that can be life threatening. Patients with severe LTS benefit from surgical widening of the airway via scar excision, steroid injection, and balloon dilation. There are various options for ventilation management during an operation on the upper airway. Two ventilation techniques are used at this institution - jet ventilation and intermittent apnea. In jet ventilation, short bursts of oxygen are supplied through a small transtracheal or transglottic catheter with low frequency. Intermittent apnea entails ventilation via an endotracheal with intermittent removal and operation during brief periods of apnea. Jet ventilation carries a risk of barotrauma and can be difficult in patients with limited chest compliance. A paradigm shift for ventilation management occurred at this institution which offers a unique opportunity to compare intraoperative hemodynamics across and between patients. Hemodynamic data has been used as a key indicator of the health of the patient during the procedure with implications for postoperative complications. The preferred ventilatory technique is of interest to the surgical community, but to our knowledge these techniques have not been compared against one another previously.

METHODS: A retrospective chart review was conducted identifying adult patients undergoing airway dilation surgery at a tertiary care institution. 20 adult patients are included in this preliminary analysis. Inclusion criteria include complete electronic anesthesia record, minimum of two endoscopic airway surgeries and type of procedure performed. For each patient procedure, the number of minutes with spO2 less than 92% was calculated, as was the proportion of total minutes with spO2 less than 92%. In order to assess whether the proportion of time under 92% spO2 differed by ventilation technique (intermittent apnea vs. jet ventilation), Wilcoxon rank sum test was used. Other data collected are End-tidal CO2, HR, Systolic/Diastolic BP, and MAP.

RESULTS: Out of 107 total procedures, 99 had complete data and were used in analysis. Intermittent apnea was the most common ventilation technique, used in 72% of patients. Jet ventilation, or jet ventilation converted to intermittent apnea, was used in 18% of patients. Patients spent a mean of about 2 minutes under 92% spO2, accounting for about 4% total time. Proportion of total time under 92% spO2 did not differ significantly by ventilation technique.

CONCLUSION: The current data suggests that there is no significant difference in hypoxemia during intermittent apnea and jet ventilation techniques. The hypoxemia threshold is passed 4% of the total time in surgery. This finding may represent the surgeon and anesthesiologists' tolerance for hypoxemia at this institution. Oxygen saturation during surgery is an important hemodynamic variable to observe, since it can lead to hypoxemia which may lead to tissue damage. Further analysis will provide a full hemodynamic profile interpreting End-tidal CO2, HR, Systolic/Diastolic BP, and MAP. This preliminary data suggests that both techniques appear equally efficacious with respect to maintenance of oxygen saturation.

Abstract Title: Mandated Training for Health Care Providers in Identifying Child Sex Trafficking Victims

Investigator(s): Rohini Siva Srinivas and Dr. Alexandra Leader
Department(s): MD 2023

Abstract

INTRODUCTION:
In the United States, there are 244,000 to 325,000 minors at risk for sexual exploitation and an estimated 199,000 cases of sexual abuse every year as reported in 2001. It is difficult to estimate the total number of child sex trafficking victims, but according to the National Human Trafficking statistics, there has been a 25% increase in human trafficking cases from 2017 to 2018 and of those, 1 in 7 were most likely minors. Recent studies demonstrate that despite the many barriers to accessing health care, victims of human trafficking still encounter and seek care from health care professionals.

METHODS:
Medline (Ovid), Google Scholar and 6 databases from ProQuest were searched to identify studies published about training medical providers on identification of sex trafficking victims.

RESULTS:
Evidence from 21 studies points to the need for training health care providers, especially nurses, emergency department providers, and obstetrics/gynecologists, to identify sex trafficking victims. 28% to 92.5% of trafficked persons utilized health care services while being trafficked. The majority of health care professionals acknowledged lack of experience identifying red flags of human trafficking and lack of understanding on how to care for this vulnerable population.

CONCLUSION:
The studies evaluated in this literature review demonstrate that training health care providers significantly improved their knowledge of human trafficking and suggest that training is an imperative step to ensure appropriate referral steps can be taken to provide services for trafficked persons, particularly minors. Mandated training for health care providers on recognizing sex trafficking victims as well as creating policy on data collection of human trafficking issues would be beneficial in combatting this major human rights violation.

Abstract Title: Obstructive Sleep Apnea Syndrome in Children with Severe Persistent Asthma

Investigator(s): Jarrett Slater, MS4, Carlos Sendon, MD, J. F. Chocano, MD
Department(s): Eastern Virginia Medical School, Children's Hospital of the King's Daughters – Department of Pediatrics, Division of Pediatric Pulmonology

Abstract

INTRODUCTION
Asthma and obstructive sleep apnea syndrome (OSAS) in children frequently coexist, but the reasons are not fully elucidated. The common co-morbidities possibly link asthma with OSAS. This study aims to determine the clinical characteristics of obstructive sleep apnea syndrome in severe persistent pediatric asthma.

METHODS
This is a retrospective review of 145 pediatric patients classified as having severe persistent asthma based on NHBLI guidelines. Out of these patients, 25 were found to have had a polysomnography (PSG) performed for evaluation of sleep apnea. Severity of OSA was classified using the Apnea-Hypopnea index (AHI). An AHI of 1-5 events/hr was classified as mild OSAS, an AHI of 5-10 events/hr as moderate, and an AHI of >10 events/hr as severe. Patient demographics and commonly associated co-morbidities such as obesity, allergic rhinitis, gastro-esophageal reflux (GERD) were collected. Therapeutic interventions used to treat OSAS were also evaluated.

RESULTS
Twenty four of 145 patients with severe persistent asthma presented with OSAS (17%). Mild OSAS was found in 19 patients (79%) and moderate OSAS in 5 patients (21%). Fourteen patients (58%) were male and 20 patients (83%) were African American. Medical intervention was used in 11 patients (46%) and a surgical approach was used in 13 patients (54%). The most common pharmacologic agents used were Montelukast in 19 patients (79%) and Fluticasone nasal spray in 15 patients (63%). The co-morbidities found included chronic rhinitis in 24 patients (100%), obesity in 18 patients (75%), eczema in 12 patients (50%), GERD in 9 patients (38%), Chiari malformation in 1 patient (4%), eosinophilic esophagitis in 1 patient (4%) and laryngo-malacia in 1 patient (4%).

CONCLUSIONS
The prevalence of OSAS in this study was significantly high especially if we compare it with the prevalence in the general pediatric population. OSAS was more prevalent among African American patients, concurrent with the literature. OSAS severity was mild to moderate, despite our expectation of more patients in the severe range. The surgical approach was the preferred method to treat OSAS, including the mild cases. Chronic rhinitis and obesity were highly associated as co-morbidities. Future consideration is needed to evaluate if the treatment of OSAS improves the control of asthma symptoms.

Abstract Title: Analyzing the Effectiveness of Goal Setting with Student Objective Cards Among Third Year Medical Students.

Investigators: Christopher Sommer, MS; Rachel Holmes, BA; Carmen Ingram-Thorpe, MS Ed, MPH; Bruce Britton, MD; Justin Tondt, MD

Department: Department of Family and Community Medicine, Eastern Virginia Medical School

Abstract

Introduction: The Liaison Committee on Medical Education's (LCME) clearly defines the educational and institutional objectives for medical school accreditation. Within these standards, cultivation of lifelong learning skills and continuous evaluation are of the utmost importance. In 2018, EVMS addressed these concerns by implementing a Family Medicine Student Objective "Blue" Card to better track student activities, determine students' professional goals, and improve feedback throughout the clerkship. The aim of this quality improvement study was to inspect the personal goals set by students at the pre- and mid-clerkship checkpoints in order to better understand perceived curricular needs for future classes and evaluate the utility of feedback provided to students.

Methods: A retrospective review of the EVMS MD Class of 2021's pre- and mid-clerkship goals from July 2019 to March 2020 was conducted. These goals were independently coded, and students who completed the objective cards within this timeframe were recruited by purposive sampling via email for interviewing about their experience. Student volunteers were then virtually interviewed by two medical students using Blackboard Collaborate in groups following a semi-structured guide. These interviews were recorded, transcribed, and de-identified. Transcripts were independently coded, transcribed, and analyzed using constant comparative analysis to identify emergent themes.

Results: A total of 17 students were interviewed in focus groups of four to six. Four themes were determined across these student focus groups: The majority of students expressed that the objective cards provided a helpful organizational infrastructure for their clerkship. Students also expressed that the objective cards presented an opportunity to seek feedback and be more involved with patient care. The majority of students also expressed a desire for more authentic and meaningful goals. Many students described perceived barriers for implementing and completing student objective cards.

Conclusion: Students experiences with the objective cards varied widely, with all students sharing both positive and negative aspects. Faculty may consider additional SMART goal-planning training to help students construct more genuine and purposeful goals. Faculty may also consider limiting the total number of goals on the objective card to ensure this is a time-efficient practice.

Abstract Title: Mesenteric Ectopic Pregnancy with Tubo-ovarian Abscess

Investigator(s): Sam Son, Eunice Wu, Veer Gariwala MD, Christopher O'Neil MD
Department(s): Radiology

Abstract

Introduction:
An ectopic pregnancy is the implantation of a fertilized ovum in a location other than the main cavity of the uterus. Ectopic pregnancies are reported in approximately 1-2% of pregnancies, and while 95% of ectopic pregnancies are in fallopian tubes, only 3% are in ovarian, cervical, or abdominal sites. An undiscovered ectopic pregnancy can lead to several serious complications including sepsis, DIC, and death.

Clinical Findings:
We present a case of a 38-year-old female with acute onset of severe lower abdominal pain, sepsis, chills, and diarrhea who was evaluated with CT of the abdomen and pelvis with IV contrast only. The imaging revealed a likely second trimester age fetal skeleton with a partially collapsed calvarium within the peritoneal cavity and an abnormal complex cystic lesion in the right adnexal area. The abnormal fluid collection was later identified as a tubo-ovarian abscess secondary to the mesenteric ectopic.

Conclusion:
Ectopic pregnancy is always a differential diagnosis for many young females who present with lower abdominal pain. Given the considerable morbidity and mortality that is associated with ectopic's which are discovered late, our case report shows an example of a very rare ectopic outside of the usual expected locations for ectopic's along with the significant complication of a tubo-ovarian abscess.

Abstract Title: Booster Seat Messaging: A Mixed Methods Analysis of Parent Perceptions

Investigator(s): Springer, Charles, MD Candidate; Edwards, Ann, MS; Gordon, Emily, MPH; Dobyns, Taylor, MD Candidate; England, Kelli, PhD
Department(s): Department of Pediatrics, Eastern Virginia Medical School

Abstract

INTRODUCTION: Motor vehicle crashes remain a leading cause of death and injury for children and teens (CDC, 2019). Among 4- to 8-year olds, booster seats reduce the risk of injury by 45% compared to seat belts (Arbogast et al., 2009; Durbin et al., 2018), yet only half (52%) of 6- to 7-year-olds in the USA travel in a booster seat or child restraint (Li & Pickrell, 2018). Virginia State Law requires that all children age 7 and younger be properly secured in a child safety seat, regardless of heigh and weight. The American Academy of Pediatrics (AAP), however, recommends that children should remain in a car safety seat until the lap and shoulder seat belts fit properly, usually by the time the child reaches a height of 4 feet 9 inches. Noncompliance with these safety recommendations has a multifactorial etiology, involving lack of knowledge, low perceptions of risk, unsafe norms, poor recognition of restraint system effectiveness, flawed understanding of crash forces, and numerous other potential factors (Will et al., 2012). In order to gain insight into parental needs and preferences regarding booster seat messaging, we conducted both virtual focus groups and an online survey with parents/guardians of young children. Participants watched a publicly available, 4-minute video, "Boost 'em in the Back Seat," and a condensed, 30-second version of the same video. Our goal was to seek parental feedback, understand what they valued in the videos, and learn how to improve the video's usage. We hope to better understand parental perceptions of booster seat usage, barriers to compliance with recommended booster seat safety guidelines, and ultimately produce further resources that both educate and motivate parents to adhere to proper booster seat laws and recommendations.

METHODS: Our team prepared relevant questions designed to gauge parental perceptions of booster seat messaging, and incorporated them into both a template for virtual focus group dialogues and a secure, Qualtrics online survey. We recruited 20 parents for participation in 4 focus groups held via BlueJeans Video Conferencing, and we collected 30 parental responses from a mixed-methodology online survey. All participants were parents/guardians, aged 18-60, with a child under age 13 in their primary care, living in Southeastern Virginia. Participants received a $40 gift card (focus group) or a $15 gift card (survey). Recordings from the virtual focus groups then were transcribed, and all data currently is being analyzed using NVivo software for qualitative data. All data collected is confidential.

RESULTS: We coded qualitative data to organize major themes and to analyze preliminary information, and next we will use subthemes to analyze the parental responses in greater detail. Parents found the 4-minute video to be emotionally impactful, resonant, and memorable, and gave varying suggestions for how to best condense its content, character dialogue, and messages to best resonate with a larger audience. Through our analysis thus far, we have found that parents do have a general awareness that booster seat laws exist, though they often are not aware of the details of the Virginia State Law or recommendations from the AAP. After reasoning behind the guidelines was explained, parents were generally supportive of the detailed law and recommendation, and they expressed interest in improving their own children's booster seat safety. Although there was a general support for laws and official recommendations for proper child passenger safety, there are numerous barriers to adherence with these guidelines, especially lack of education as to why booster seats are safer than normal seats, and the availability of confusing, sometimes contradictory online resources of low quality. Selecting the ideal booster seat was rated as a difficult task, and parents often were unsure how to properly install their seats.

CONCLUSION: Child passenger safety in motor vehicles is an area of utmost importance, and there remains significant work to be done in educating and motivating the general public on child safety laws and recommendations. The feedback for "Boost 'em in the Backseat" allows us to better understand what matters most to parents, and will help in promoting the same video, as well as other vehicle safety content. Our next steps include further collection and analysis of data, and increasing the education of parents in the greater community through social media campaigns and the creation of targeted communications. Our results will allow for a better understanding of the challenges of child passenger safety, and yield more concise, effective advertisements and resources promoting booster seat safety.

Abstract Title: Otolaryngologic Manifestations of Chronic Recurrent Multifocal Osteomyelitis

Investigator(s): Jason Toy BS[1], Emily Wikner MD[1], William Owen MD[2], Thomas Gallagher DO[3]
Department(s): [1]Department of Otolaryngology, Eastern Virginia Medical School, [2]Division of Hematology and Oncology, Children's Hospital of The King's Daughters, [3]Department of Otolaryngology, Children's Hospital of The King's Daughters

Abstract

INTRODUCTION: The objective of this case report is to discuss the presentation, diagnosis, and treatment of a case of chronic recurrent multifocal osteomyelitis (CRMO). CRMO is a rare disease characterized by non-infectious inflammation of bone without an exact known pathogenesis.

CLINICAL FINDINGS: A 10-year-old female presented with a history of left sided facial pain and subtle swelling over the left maxilla. Initial laboratory tests showed elevated C-reactive protein and erythrocyte sedimentation rate. Imaging results revealed lytic process of the left maxilla extending into the zygoma, sphenoid, lateral pterygoid plate, and clivus without evidence of soft tissue mass. Biopsy of the left maxilla was most consistent with infectious osteomyelitis, indicating antibiotic treatment. Four months later the patient presented with right wrist pain, prompting imaging that revealed a lesion of the right distal radius. Subsequent biopsy of the right radius identified a similar fibro-osseous lesion to that of the left maxilla, suggesting a diagnosis of CRMO. Patient then began non-steroidal anti-inflammatory drug therapy resulting in significant improvement in pain and limitations on follow-up.

CONCLUSION: The diagnosis of CRMO is one of exclusion and is challenging due to the lack of specific findings on laboratory tests, imaging, and biopsy. Common differential diagnoses include those of infectious or neoplastic etiologies. CRMO primarily presents as insidious bone pain of the extremities, vertebrae, pelvis, and clavicle. Involvement of the mandible is relatively rare and lesions of the skull or facial bones, as seen in the case, are exceptionally infrequent. The prognosis of CRMO varies both in terms of severity and reoccurrence frequency.

Abstract Title: Adapting an ongoing Youth LifeSkills curriculum for remote delivery during the COVID-19 pandemic

Investigators: Ryan Truitte, Emily Gordon, MPH, Andrew Plunk PhD
Department: EVMS Pediatrics, Eastern Virginia Medical School

Abstratct

INTRODUCTION
In the wake of the Coronavirus Disease 2019 (COVID-19) pandemic there have been unprecedented interruptions to daily life. Young adults have been particularly affected by the cancellation of school and extracurricular activities as well as opportunities for educational and prevention programs, such as those aimed at substance use prevention, increasing health literacy, enhancing communication skills, and relationship building/maintenance. Efficacy of the evidence-based Botvin LifeSkills program in an in-person, classroom setting is well described for high-school-age students. Implementation of these programs over virtual space, as required by the COVID-19 pandemic, is not yet fully established. The Youth Engagement Program (YEP), part of the Division of Community Health and Research at Eastern Virginia Medical School, set out to utilize existing relationships with high school aged students to adapt a summer LifeSkills program for an online forum in compliance with physical distancing requirements.

METHODS
A team of mentors (3 EVMS faculty members, 2 medical students and 3 undergraduate students from a local college) collaborated to adapt the existing ten week summer program from in-person delivery to an online video conference format. The summer program consisted of ten weekly 1.5 hour long virtual sessions which were held on the Zoom video conferencing platform. The Botvin LifeSkills ® Training high school curriculum was used as a framework. Each session was a mix of mentor lead topic exploration and open-ended conversations. Conversations were intentionally kept open-ended to allow teens to explore the presence and impact of each weekly topic on their own experiences. Outside of weekly meetings, mentors were assigned mentees from the students to individually contact to ensure consistent communication was maintained throughout the summer. Students were recruited from the previous 2 YEP cohorts (N=13, 9 females, 4 males).

RESULTS
The modified, online Botvin LifeSkills training curriculum provided unique experience for both students and peer mentors. Throughout the ten week summer program teen attendance was recorded (average attendance = 9 students per session). As students became more comfortable with the format and norms of the online forum participation and quality of discussion improved. Responsiveness to peer mentor discussions of LifeSkills topics was consistently positive. Discussions focusing on decision making for health, risk-taking, managing stress, and family communication were of particular impact owing to the ongoing COVID-19 pandemic and quarantine. Students shared relevant personal anecdotes related to their experiences in these areas prompting further conversation.

CONCLUSION
An online-based LifeSkills curriculum provides a medium for group discussions to take place in accommodation of physical distancing requirements brought on by the COVID-19 pandemic. Planning and implementing the changes to the youth program was necessary to continue to build relationships with youth in the Norfolk community as well as to provide an outlet for these students during a difficult period. Future assessments for evaluation of programmatic impacts on teen self-efficacy and other outcomes are being prepared as the program transitions into the new school year with physical distancing requirements continuing for the foreseeable future.

Abstract Title: Unmet needs for long acting reversible contraceptives in Virginia mothers who experienced unintended pregnancy – results from 2016 – 2018 PRAMS data

Investigator(s): Lauren Truwit, Katherine Hawkes, Amy C. Paulson, Kenesha Smith, Hongyun Fu
Department(s): Pediatric Community Health and Research

Abstract

INTRODUCTION
Nearly half of pregnancies in the United States are unintended, leading to a range of adverse maternal and child health (MCH) outcomes. Although Long Acting Reversible Contraceptives (LARC) are the most effective method of birth control, they are not widely used in the U.S. This study examined patterns of contraception before conception and postpartum among mothers with unintended pregnancy, using 2016-2018 Virginia Pregnancy Risk Assessment Monitoring System (VA-PRAMS) data.

METHODS
The VA-PRAMS collected information about mothers' experiences before, during and after recent pregnancies. This analysis included a subsample of 1,124 mothers who recently experienced unintended pregnancies. Multivariable logistic regression was used to examine factors related to types of method used before conception and postpartum, using STATA15 to adjust for sampling weights.

RESULTS
Before conception, 44% of mothers reported using a contraceptive method, including 29% condoms, 23% rhythm/withdrawal, 17% pills/shots, and 4% LARC. Being unmarried (AOR:1.69; 95% CI:1.24-2.31) and receiving Medicaid (AOR:1.41; 95% CI:1.03-1.94) were associated with increased odds of using withdraw/rhythm. Mothers who were nonwhite (AOR:1.89; 95% CI: 1.32-2.72) and teens (AOR: 3.34, 95% CI:1.55-7.20) had high odds of using condoms.
At postpartum, 21% of mothers reported using rhythm/withdrawal, 24% condoms, 27% pills/shots, 20% LARC, and 11% sterilization. Being under 31-year-old (AOR: 1.30; 95% CI: 1.03-1.90) and having insurance coverage (AOR: 1.69; 95% CI: 1.12-2.50) was related to higher odds of postpartum LARC use.

CONCLUSION
Findings highlight the need to promote postpartum LARC in Virginia, particularly among older, uninsured and minority mothers to reduce unintended pregnancy and improve MCH outcomes.

Abstract Title: PTSD, Anxiety, and Depression Among Resettled Refugees: An Evaluation of the Refugee Health Screener Questionnaire by Refugee Status in Hampton Roads, Virginia

Investigator(s): Jordan Tyrrell[1], Lydia Cleveland[1], Ibrahim Maroof[2], Brynn Sheehan[3], Elizabeth Lindsay[1], Aaliyah Joseph[1], Alexandra Leader[1]

Department(s): [1]EVMS Global Health, [2]Commonwealth Catholic Charities, [3]Healthcare Analytics and Delivery Science Institute (HADSI)

Abstract

INTRODUCTION

Since 2002, approximately 21,000 refugees and Special Immigrant Visa (SIV) holders have resettled in Virginia. These communities are unified by shared traumatic experiences, often presenting as emotional distress. This study's aim was to analyze the Refugee Health Screener-15 (RHS-15) questionnaire data to identify patterns in mental health risk between refugees and SIV holders in the Hampton Roads region of Virginia.

METHODS

The RHS-15 is a 15-question screening tool that assesses refugees for emotional distress. The first 14 questions assess a range of symptoms and an individual's ability to cope, measured using a four-point Likert scale. The final question asks individuals to rate their level of distress on a thermometer from 0-10. RHS-15 data from 497 refugees (%) and SIV holders (%) who resettled from May 2013 to June 2018 were collected and analyzed. The RHS-15 was divided into three subscales for PTSD, anxiety, and depression to test for differences in symptom presentation between refugees and SIV holders.

RESULTS

The results indicated that SIV holders are at 1.65 higher odds of screening positive on the RHS-15 and exhibit significantly greater anxiety symptoms compared to refugees, $z = 2.028$, $p = 0.042$, [95% CI 1.02-2.69]. However, no significant differences were found in PTSD or depression symptoms between refugees and SIV holders. Additionally, when comparing the frequency of reported symptomology, depression symptoms were reported more often than both PTSD, $p < 0.001$, [95% CI 0.275-0.432], and anxiety symptoms, $p < 0.001$, [95% CI 0.294-0.440]. This trend was consistent for both SIV holders and refugees.

CONCLUSION

This study identified SIV status as a significant predictor of a positive RHS-15 screen and higher anxiety levels compared to refugees. Reports of depression symptoms were also significantly higher than both PTSD and anxiety symptoms, and this trend was consistent across both SIV holders and refugees. Findings from the current study may inform the resettlement process and development of mental health programs for SIV holders and refugees. Further research should be conducted on the psychometric properties of these RHS-15 subscales and to include other regions of Virginia.

Abstract Title: Ionotropic Receptor-dependent cool cells control the transition of temperature preference in Drosophila larvae

Investigator(s): Jordan Tyrrell[1,2], Jackson Wilbourne[2], Alisa Omelchenko[2], Jin Yoon[2], Lina Ni[2]
Department(s): [1]EVMS School of Medicine, [2]Virginia Tech School of Neuroscience

Abstract

INTRODUCTION: Temperature sensation is vital for animals to avoid extreme temperatures and to seek optimal temperatures to survive, mate, and reproduce. Therefore, it is crucial to understand molecular and cellular mechanisms of temperature sensation, which may provide molecular targets to prevent host-seeking behaviors in disease vectors. Temperature sensation is distinctively regulated through the developmental stages, at least in ***Drosophila*** larvae. In this study, we focus on low-temperature sensing systems and investigate whether and how low-temperature sensing pathways contribute to the transition of temperature preference in ***Drosophila*** larvae. While early-stage ***Drosophila*** larvae pursue a warm temperature (24°C), late-stage larvae seek a significantly lower temperature (18 – 20°C) when they stop foraging and prepare for metamorphosis. Our findings establish a mechanism underlying the transition of temperature preference in *Drosophila* larvae.

METHODS: To prepare synchronized larvae for assays, 72 hours after egg laying (AEL) coincided with the initiation of third instar (early-stage), while 120 hours AEL was a mix of wandering-stage and foraging-stage larvae near the end of third instar (late-stage). Thermotactic behavior assays utilized a temperature gradient from 13 – 31°C. Functional blockage of dorsal organ cool cells (DOCCs) utilized the synaptic neurotransmitter blocker, tetanus toxin light chain (TNT). Optogenetic assays utilized the red light-shifted channelrhodopsin, CsChrimson. Cool activation was determined by calcium imaging using the genetically encode calcium indicator GCaMP6m. Cool receptor expression levels were determined with immunostaining.

RESULTS: Here, we show that early-stage larvae (early third instar), in which DOCCs were functionally blocked, concentrate in a cooler temperature region (18 – 20°C) than ***wildtype*** (24°C). In contrast, blockage of DOCCs did not affect the temperature preference for late-stage larvae (late third instar), suggesting that DOCCs are dispensable for cool avoidance at the late third instar. Red light-mediated activation of DOCCs drove strong light avoidance for both early- and late-stage larvae, suggesting that the neural circuit downstream of DOCCs remains intact at the late third instar. Furthermore, DOCCs of late-stage larvae exhibited significantly reduced responses to cooling than DOCCs of early-stage larvae when exposed to similar temperature stimuli. At the late larval stage, expression of the DOCC cool receptor proteins Ionotropic Receptor (IR) 21a, IR93a, and IR25a were significantly decreased compared to the early larval stage, demonstrating that DOCCs express a lower level of IR21a, IR93a, and IR25a in the late third instar resulting in a decrease of cool sensitivity in DOCCs. IR21a-, IR93a-, and IR25a-deficient mutants all pursued a cooler temperature (18 – 20°C) at the early larval stage compared to ***wildtype*** (24°C), while the same mutants exhibited a similar temperature preference as ***wildtype*** at the late larval stage. Mutant-specific rescues restored the ***wildtype*** phenotype for all three IR mutants at the early larval stage, suggesting that IR21a, IR93a, and IR25a are required to avoid cool temperatures at the early, but not the late third instar. Importantly, late-stage larvae that overexpressed IR21a, IR93a, and IR25a in DOCCs exhibited similar warm preference to that of ***wildtype*** early-stage larvae.

CONCLUSION: Taken together, these data suggest that IR21a, IR93a, and IR25a in DOCCs navigate early-stage larvae to a warm temperature and the reduction of these IRs directs animals to move towards a cooler temperature during the late larval stage. Reduced expression of cool receptors leads to decreased cool sensitivity of DOCCs, which, in turn, limits the ability of late third-instar larvae to avoid cool temperatures. Thus, our findings identify a novel mechanism underlying the transition of temperature preference in *Drosophila* larvae.

Abstract Title: Attenuation of renal failure by Vitamin C in LPS induced acute kidney injury (AKI)

Investigators: Trevor Uhl, Austin Mullaly, Dr. Siddhartha Ghosh
Department: Department of IM/Division of Nephrology, Virginia Commonwealth University

Abstract:

Introduction: Lipopolysaccharide (LPS) has been frequently used as a model for septic acute kidney injury (AKI). Elevation of hypoxia inducible factor (HIF1α) aggravates AKIs such as ischemic reperfusion injury, gentamicin induced AKI etc. However, in septic AKI, HIF1α elevation aggravates kidney injury. Our long-term goal is to see if decreasing the HIFα levels can alleviate septic AKI.

Methods: Mice were injected with 10 mg/kg LPS (500µl) to induce septic AKI and control animals received 500 µl saline. A third group received LPS and 200 mg/kg ip ascorbic acid. The mice were culled 12 hours after LPS administration and blood was collected to measure serum creatinine and serum urea. Kidneys were homogenized and cytosolic and nuclear extracts were separated by PAGE gel electrophoresis gel and proteins were transferred to PVDF membrane. Immunoblots were carried out using HIF1βantibodies.

Results: Serum creatinine and serum urea are biomarkers of kidney injury. In our preliminary study we show that compared to controls, LPS administered mice had significant increase in serum urea and serum creatinine ($p<0.001$). Ascorbic acid treatment significantly reduced both the renal biomarkers suggesting that ascorbic acid can alleviate septic AKI in LPS treated mice. We also determined HIF1α levels in the kidney and there was almost 11-fold increase in HIF1α levels in the kidney cytosol and 6-fold increase the kidney nucleus of LPS injected mice.

Conclusion: Vitamin C (ascorbic acid) is known to inhibit transcription of HIF1α. Based on our findings with LPS induced septic AKI and reduction of injury in Vitamin C therapy, our long-term goal is to see if inhibition of HIF1α by Vitamin C can protect renal function in septic AKI.

Abstract Title: Changes in liver macrophage subtypes following sleep fragmentation in a mouse model of NASH

Investigator(s): Manasa Vallabhaneni, Sezgi Arpag-McIntosh, Anca Dobrian
Department(s): EVMS Department of Physiology

Abstract

INTRODUCTION: Liver macrophages (LMΦ) are a dynamic and diverse population that changes in response to various pathologies. NASH is a chronic inflammatory condition characterized by fibrosis and with high risk of progression to hepatocellular carcinoma. Sleep dysregulation is known to impact on metabolism, immunity and inflammation. The goal of our study was to determine the effect of short term sleep fragmentation (SF) on inflammatory milieu in the liver in a mouse model of NASH. DIAMOND (diet-induced animal model for NASH disease) mice closely recapitulate progression of human liver disease. The initial stages of fatty liver and steatohepatitis lead to hepatocyte injury and death. This damage leads to a persistent, unresolved inflammatory response that contributes to progression to advanced fibrosis and cirrhosis. We characterized the LMΦ spatial and phenotypic profile at different points in the disease progression. We used F4/80 and galectin-3 markers to differentiate between macrophages of different phenotypes. Recent studies showed that F4/80+ Gal-3-+ MΦ have a pro-fibrotic phenotype, while F4/80+Gal-3- MΦ are more pro-inflammatory. By analyzing LMΦ functional phenotypes and, in conjunction with fibrotic changes, we can determine pathways potentially affected by SF that lead to progression of NASH.

METHODS: The DIAMOND mice are a stable isogenic cross between C57Bl/6J and 129SI/Sylm strains. When fed a 40% high fat diet and 4% fructose water, starting at 8 weeks of age, mice develop progressively fatty liver and NASH. The history of disease and the histopathological findings closely resemble human NASH progression. We examined 3 time points in the disease development, after 18, 26 and 40 weeks of diet that correspond to steatohepatitis and early fibrosis, advanced fibrosis and, bridging fibrosis and occasional hepatocellular carcinoma, respectively. Male mice at each of the 3 time points were randomly assigned to either a 2-week SF protocol (daily for 6hrs, every 2 min), or controls (n=5-6/group). FFPE liver sections were co-stained with F4/80 and Gal-3 primary antibodies and the nuclei were stained with DAPI. For each mouse, 12 images were acquired from 4 sections collected from separate liver lobes (3images/slide). The number of cells that expressed Gal-3, F4/80 or co-expressed the two markers were counted using Image J software. LMΦ that surrounded lipid droplets (lipid crown-like structures, LCS) were counted separately from the isolated parenchymal LMΦ. Data was analyzed using t-test between SF and control groups and null hypothesis was rejected for a p-value<0.05.

RESULTS: SF had the greatest impact on number and phenotype of LMΦ in younger mice (18 weeks on diet) in early stages of fibrotic changes and steatohepatitis. The total number of MΦ was double in SF mice ($p<0.01$) and the percent of MΦ associated with LCS was increased 4-fold in SF mice compared to age matched controls ($p<0.01$). The difference was significant in MΦ that only expressed Gal-3. These cells are likely pro-fibrotic Kupfer cells or newly recruited monocyte/ MΦ. Also, the number of LCS-associated MΦ that co-expressed F4/80 and Gal-3 was significantly increased in SF mice ($p<0.05$). Collectively, these results suggest increased MΦ recruitment in liver and polarization of resident Kupfer MΦ towards a pro-fibrotic phenotype. Indeed, increased fibrosis was also found in livers of SF mice after 18 weeks of diet (please see poster by Fisher,R. et al). Similar phenotypic changes were also found in the 26 week mice after SF. In addition, the number of LCS-associated MΦ that expressed F4/80 but not Gal-3 were increased by ~60% ($p<0.05$) compared to age-matched controls. These MΦ were reportedly more pro-inflammatory in atherosclerotic plaques. No significant changes in MΦ numbers or phenotype were found in mice with advanced disease (week 40) in response to SF.

CONCLUSION: Our study contributes to understanding the changes in LMΦ after SF and will help identify targetable pathways to reduce chronic inflammation and fibrosis. Importantly, SF induces significant changes in numbers and phenotype of LMΦ in early disease stages, which underscores the utility of a therapeutic approach targeted towards reduction of immune infiltration early in the disease progression in individuals with dysfunctional sleep.

Abstract Title: Mentorship in translational neurosciences research. A personalized educational approach

Investigator(s): Musto, A.E[1,3], Vinokuroff, K[2]. Pototskiy, E[2]. Howard, K[3]. Major, K.[3], Sharma, D[3].
Department(s):
1. EVMS, Department of Neurology
2. Old Dominion University, Department of Biological Sciences
3. EVMS, Department of Pathology and Anatomy

Abstract

PURPOSE
Scientific training in medical and scientific education could contribute to improve current scientific research and enabling better health outcomes, all while enabling mentees to develop better understanding of the scientific field thereby enhancing their own undergraduate and graduate experience enabling them for better job and education opportunities in the future. This mentorship experience helps bridge the theoretical and practical aspects of the neuroscience field by enabling students to combine critical scientific thinking, problem solving, and to get hands-on experience with practical scientific research techniques. This approach allows for the students to contribute to projects in substantial ways with a focus on translational neuroscience research which would equip them with a better understanding of the nervous system, pathologies associated, scientific method, differential diagnosis, laboratory techniques, biomarkers, and to introduce them to novel therapeutic targets.

METHODS:
Medical and undergraduate students self-selected themselves and submitted their resumes and a scientific research justification. An initial interview meeting was conducted understanding their motivation and expectations, followed by a working plan. All students performed a systematic review, formulated a question, created a hypothesis, and develop an experimental approach to test in the laboratory in the area of neuroinflammation, epilepsy or glioblastoma multiforme. After institutional approval to conduct research, students interacted with laboratory personnel and received feedback about their progress. Assessments were based on: i) successful identification of scientific premises, description of the experimental designs, summary of results and alternative methods, impact of disease, presentation of results in of abstract, poster or manuscript; ii) laboratory techniques, presentation and writing skills, professionalism, and teamwork; iii) feedback was conducted before, during, and after to evaluate this mentorship as a learning experience.

RESULTS:
A total of 42 students (3 undergraduate, and 39 graduate), which represent of 9 % of the medical student's population per year, requested voluntarily to participate in this experience. They showed more availability during the second semester working in presence or online; 100% of the student completed a literature review; 35% of the students obtained certifications which allowed them to work with at least 2 or more laboratory techniques. 54% of students were able to be named as coauthors in scientific manuscripts, and 88% of the students were able to coauthor a presentation of poster. One student also received an award for his project in this mentorship program from EVMS.

CONCLUSION:
This optional educational activity contributed to improve the research environment at EVMS and has been associated with greater satisfaction from the students with their training as well as greater opportunities for scientific publication. This mentorship program has also proved to be effective in helping students cultivate scientific skills which help them in furthering their educational journeys.

Abstract Title: Inpatient Dermatology Consultations for Suspected Skin Cancer

Investigator(s): Scott M. Whitlock MD[1], Arjun Saini MD[2], Katie A. O'Connell MS[1], Thomas Michael Pender MS[1], Abby S. Van Voorhees, MD[1]
Department(s): [1]EVMS Dermatology, [2]EVMS Internal Medicine

Abstract

INTRODUCTION
Skin cancer, including nonmelanoma skin cancer, is the most common type of cancer in the United States. It causes significant morbidity, and depending on the subtype, risk of metastasis and mortality. Dermatologists are sometimes consulted in the inpatient setting to evaluate a skin lesion concerning for malignancy. This provides an opportunity to identify and treat skin cancer, often in patients who may not have sought outpatient dermatologic care.

METHODS
We conducted a retrospective review of inpatient dermatology referrals at Sentara Norfolk General Hospital. We identified all patients with an inpatient dermatology consult for suspected skin cancer or "skin lesion" between 07/01/13-07/01/19. We collected patients' sex, age at time of consult, race, specialty of referring provider, lesion location, maximum diameter of diameter, whether a biopsy was performed, inpatient vs outpatient setting for biopsy, clinical diagnosis, histopathologic diagnosis, and subsequent treatment.

RESULTS
38 total patients were referred, with 47 total lesions, of which the majority were on the head and neck (66%). 20 of the 38 patients were found to have at least one pathology-confirmed cutaneous malignancy (23 total tumors). Of these, 10 were basal cell carcinoma, 11 squamous cell carcinoma, 1 malignant melanoma, and 1 anaplastic T-cell lymphoma. Of note, 17 of the 23 tumors were ≥2.0 cm in diameter at the time of biopsy (74%). Subsequently performed treatments for these patients included wide local excision (3), Mohs micrographic surgery (5), radiation (3), topical fluorouracil (1), electrodessication and curettage (4), and chemotherapy/immunotherapy (2). Patients in this population had been admitted to the hospital for a variety of reasons, most unrelated to their cutaneous malignancy.

CONCLUSION
This study highlights the opportunity in the inpatient population to identify skin cancer, in particular high-risk tumors, which might otherwise be unaddressed. Hospital-based physicians should be alert for opportunities to identify and address suspicious skin lesions in the inpatient setting, even in patients admitted for unrelated reasons.

Abstract Title: Ultrasound findings in cases of male infertility

Investigators: Abigail Winz, MD, Lauren Jutras, MD and Sarah Shaves, MD, FACR
Department: EVMS Department of Radiology, Eastern Virginia Medical School

Abstract

INTRODUCTION:
Approximately 50% of cases of infertility involve the male partner. In addition to history, physical exam and laboratory studies, imaging can play a key role in the evaluation of male infertility. Ultrasound is the preferred modality for scrotal imaging as it is noninvasive, lacks ionizing radiation, and is cost effective. A number of testicular and post-testicular causes of infertility can be evaluated with ultrasound, and examples of these were identified from Picture Archiving and Communication System (PACS) imaging studies from scrotal ultrasounds and transrectal ultrasounds (TRUS) at a large hospital system.

METHODS:
We reviewed causes of male infertility that may be seen at ultrasound imaging. Then, using Montage's mPower software, we used keywords to locate images representing examples of male causes of infertility. Testicular and post-testicular pathologies were searched using keywords including varicocele, intratesticular varicocele, testicular atrophy, torsion, orchitis and epididymo-orchitis, testicular microlithiasis, tubular ectasia, testicular infarct, cryptorchidism, prostatic utricle, and testicular cancer.

RESULTS
Review of the male causes of infertility visible at ultrasound included testicular and post-testicular causes. They were able to be classified as obstructive or post-obstructive. More examples of scrotal pathologies were able to be found from scrotal ultrasounds than from TRUS as these studies were most commonly performed as guidance for TRUS biopsy. De-identified images were used to demonstrate the various conditions.

CONCLUSION
Ultrasound findings can demonstrate causes of male factor infertility from a variety of conditions, both obstructive and non-obstructive. Examples of these ultrasound findings are demonstrated with studies from PACS system from a large hospital system.

Abstract Title: Gastric Gist with Co-Occurrence of Pancreatic Neuroendocrine Tumor

Investigator(s): Eunice Wu, Sam Son, Veer Gariwala MD, Christopher O'Neil MD
Department(s): Radiology

Abstract

Introduction:
Mesenchymal tumors make up only about 1% of primary GI tumors, with Gastrointestinal Stromal Tumors (GIST) being the most common nonepithelial GI neoplasms. They are derived from the interstitial cells of Cajal, and occur predominantly in older individuals, with a mean age of diagnosis of 64 years. Pancreatic neuroendocrine tumors are a type of islet cell tumor with several different varieties and have an incidence of 0.001% in the general population.

Clinical Findings:
In this report we discuss the case of a 39-year-old female who presented with migratory lower back and abdominal pain with some radiation into her chest. Initial examination and lab work had been negative when a CT abdomen/pelvis with IV contrast was done which demonstrated heterogeneous masses at the greater curvature of the stomach as well as at the pancreatic head. Biopsies were done of both masses with pathology confirming the stomach mass to be a GIST and the pancreatic mass to be of neuroendocrine origin. The patient underwent a partial gastrectomy with gastrojejunostomy, partial pancreatectomy, splenectomy, and a cholecystectomy and is currently symptom free.

Conclusion:
Both GIST and pancreatic neuroendocrine tumors are very rare within the general population and co-occurrence of both within a patient is extremely rare with almost no cases documented within the literature. This case report aims to add further evidence of a synchronous GIST with pancreatic neuroendocrine tumor without a known underlying genetic syndrome.

Abstract Title: An Institutional Study of Gastrointestinal Bleeding in Mechanical Support

Investigators: Alexander P. McNally, MS, Colten A. Yahn, BS, Nicholas L Bandy, MD, Michael Martyak, MD, FACS, David A Baran, FACC, FSCAI, John Herre, MD, FACP, FACC, Rebecca C Britt, MD, FACS, Jay Collins, MD, FACS

Department: Department of General Surgery, Sentara Advanced Heart Failure Center, Healthcare Analysis and Delivery Science Institute (HADSI), Eastern Virginia Medical School

Abstract

Introduction Mechanical circulatory support has proven as lifesaving therapy in patients with complex medical diagnoses. However, mechanical support therapy requires combination anticoagulation which may increase the risk of adverse bleeding, including recurrent gastrointestinal bleeding (GIB). This study will review the incidence of suspected GIB, associated risk factors, types of procedures and interventions, and complication rate in this cohort of patients at one institution.

Methods All patients at our institution under durable and non-durable mechanical support were retrospectively reviewed for GIB. Patient demographics, etiology of heart failure, co-morbidities, and coagulation status were documented. Consult records were reviewed to determine GIB etiology, location, rate, and type of procedure performed in evaluation and complication rates.

Results A total of 427 patients were reviewed, with 116 patients (27.2%) accounting for 218 episodes of suspected GIB during our study period. Durable support patients experienced 96.7% of recorded bleeds. A mean length of time from reception of mechanical support to initial GIB consult was 193.6 days. Higher rates of GIB were recorded among patients with pre-existing comorbidities of hypertension (182; 83.9%) and diabetes mellitus (146; 67.3%). A previous GIB was recorded in 55.2% of cases. Confirmed bleed location was determined as upper in 123 cases (57.5%), lower in 78 cases (36.4%) and both in 13 cases (6.1%). The most common etiology of bleed included angiodysplasia/vascular malformation (35.8%) and unknown (29.4%), followed by peptic ulcer (7.8%), diverticular disease (7.3%), and colonic polyps (4.6%). Endoscopic procedure and intervention were performed in 90.4% of consults, including 143 esophagogastroduodenoscopies (EGD), 72 push small bowel endoscopies (SBE), and 78 colonoscopies. Surgical and endovascular intervention accounted for 4% of total procedures. An average of 1.7 procedures was performed per patient admission. Management through blood transfusion was performed in 81.2% of cases. The overall complication rate was 34.8%. The most frequent complication was chronic GIB (89.4%), followed by post-intervention shock (5.3%), vasopressor support 24 hours post-procedure (2.6%), and pre-intervention shock (2.6%).

Conclusions Gastrointestinal bleeding is a complication in patients under mechanical circulatory support. Development of this disorder is multifactorial and presents with many etiologies. Confirmed diagnosis of this disorder requires multiple procedural interventions and overall incidence carries the risk of further medical complications. Development of further studies to evaluate diagnosis technique and best management practice for this disorder is important for long-term outcomes in this patient population.

Abstract Title: Congenital l5 hemivertebra presenting as abdominal pain

Investigator(s): Kei-Lwun Yee, Muhammad Sherani, Veer Gariwala MD, Christopher O'Neil MD
Department(s): Radiology

Abstract

Introduction:
Hemivertebra is a type of congenital vertebral malformation in which half of the involved vertebra fail to form. It is generally detected in the neonatal period and early interventions prevent lasting complications and promote good prognosis. When the diagnosis is not made early on it leads to abnormal spinal curvatures such as kyphosis, lordosis, or scoliosis.

Clinical Findings:
In this report, we showcase a previously healthy 33-year-old female presenting with abdominal and back pain who had negative labs and was found to have a partially formed right sided L5 hemivertebra with partial fusion to the L4 and S1 vertebra. The patient was also found to have lumbar scoliosis and degenerative change secondary to the L5 hemivertebra.

Conclusion:
There is a paucity of literature on the topic of complications arising in the adult population secondary to congenital hemivertebra. This case report aims to shed further light on this presentation and show the extent that undiagnosed congenital spinal abnormalities can present in the adult population.

Abstract Title: Painful scrotal dermatitis secondary to topical 5-fluorouracil

Investigator(s): Julie Z. Yi, BS[1]; Richard S. Himes, PA-C[1]; Abby S. Van Voorhees, MD[1]; Phillip H. McKee, MD[2]; Alice A. Roberts, MD, PhD[1]

Department(s): [1]Department of Dermatology, Eastern Virginia Medical School; [2]Retired from Brigham and Women's Hospital, Boston, MA.

Abstract

INTRODUCTION

5-Fluorouracil (5-FU) is a pyrimidine analog that disrupts DNA and RNA synthesis. Topical 5-FU is commonly prescribed to treat actinic keratoses, while systemic 5-FU is used as a chemotherapy agent. The most frequent adverse effects of topical 5-FU cream occur locally and include burning, erythema, photosensitivity, and erosions at the site of application. We report an unusual case in which a patient had been applying topical 5-FU cream to his chest and subsequently developed a scrotal dermatitis.

CLINICAL FINDINGS

A 70-year-old man presented to the clinic for a rash on his groin. The symptoms started eight days after he began using topical fluorouracil 5% cream twice daily to treat actinic keratoses on his chest. Since then, he has experienced rapidly worsening scrotal erythema and pain accompanied by itching and burning. He reported having difficulty sitting in a chair and sleeping through the night due to exquisite scrotal tenderness. Histopathology showed an interface dermatitis with a sparce superficial lymphocytic infiltrate in the dermis and admixed neutrophils and eosinophils. These histologic findings were consistent with an interface drug reaction. Symptoms improved 3 weeks after discontinuation of topical 5-FU and treatment with topical and systemic steroids.

CONCLUSION

To our knowledge, five cases of scrotal dermatitis associated with topical 5-FU have been reported in the literature. In these instances, inadvertent contact with the scrotum after using the topical drug was suspected. An unusual aspect of our case is the histologic pattern of interface change, which is not classically seen in contact dermatitis. The remarkable permeability of scrotal skin makes the scrotum especially susceptible to a variety of toxic and irritant agents. Patient education and an emphasis on careful hand washing after application of topical 5-FU is important in preventing adverse reactions in areas of increased sensitivity.

Abstract Title: A slow-growing papule on the shin: pleomorphic hyalinizing angiectatic tumor

Investigator(s): Julie Z. Yi, BS[1]; Clinton W. Enos, MD[1]; Edward M. Prodanovic, MD[1]; Alice A. Roberts, MD, PhD[1]

Department(s): [1]Department of Dermatology, Eastern Virginia Medical School

Abstract

INTRODUCTION

Pleomorphic hyalinizing angiectatic tumor (PHAT) is a rare, locally aggressive soft tissue tumor that tends to occur subcutaneously in the lower extremities. Since its initial description by Smith et al in 1996, approximately 165 cases have been reported in the English literature. PHAT is histologically characterized by a proliferation of spindled and pleomorphic tumor cells and clusters of ectatic, hyalinized blood vessels.

CLINICAL FINDINGS

We report a case of a 75-year-old man who presented with a slowly enlarging mass on his lower leg. His past medical history included actinic keratoses, basal cell carcinoma of the eyelid, and angiodysplasia of the colon. Physical examination revealed a firm, well-circumscribed, reddish papule 8 mm in diameter on the lateral right shin. Microscopically, there was a spindle cell proliferation centered in the dermis with numerous thin-walled, ectatic blood vessels surrounded by prominent amorphous eosinophilic material. Immunohistochemistry demonstrated focal CD68 and Factor XIIIa positivity and was negative for CD34, S100, desmin, actin, pancytokeratin, and vascular markers.

CONCLUSION

This case displays some of the classic findings associated with PHAT but also demonstrates its variability in presentation. While PHAT most commonly occurs in subcutaneous tissue, it can be intramuscular or centered within the dermis. In addition, while PHAT is usually CD34 positive, a portion of these tumors are CD34 negative. PHAT is known to have a high rate of local recurrence and display locally aggressive behavior. In some cases, PHAT has also been reported to progress to a high-grade myxoid sarcoma. Wide local excision is the recommended treatment and decreases risk for recurrence.

Abstract Title: AI-powered data curation tool significantly expedites COVID-19 literature reviews

Investigator(s): Justin T. Zaremba, Jan Bremer, Maikel Boot, Lucas Byron, Paul Mooney, Byron Wallace, Jamie Geraghty, Nicole Crofton, Jose Morey, Tayab Waseem

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Abstract

INTRODUCTION

The COVID-19 pandemic illustrated the rapid pace that scientific literature can be produced, which demonstrated the need to utilize automated extraction tools to streamline and expedite data curation for literature reviews. These tools are often used to create tables for data extraction, but the utility of such AI-produced tables has not been assessed to determine if it worthwhile to create such tools. At the suggestion of our journal editor partners, we saw it pertinent to determine the utility these of types of tools to determine if they warrant future resource allocation. Here we report the utility of AI-powered literature review tool for researchers

METHODS

To determine the utility of an AI-powered literature review tool, we conducted a study with 50 researchers writing 83 literature reviews. The institutions were provided with pre-made information tables for their research questions. Half of the participants at each institute used the AI-powered tool, while the other half performed traditional literature reviews to serve as controls. Each literature review was evaluated for speed, completeness, accuracy, and advantages provided by summary tables. A 2-page structured survey questionnaire was used to evaluate the gain of such a tool from the perspective of the researchers.

RESULTS

Supporting literature reviews with premade information tables significantly reduced the time spent searching for papers by 52% ($p < 0.001$), extracting useful information from the papers by 35% ($p = 0.001$) and the time of the full literature review by 25% ($p = 0.02$). All researchers reported that it helped them put their review together faster and 94% thought these would have yielded a more comprehensive study.

CONCLUSION

Using tables of extracted data (such as automated systems might produce) was shown to significantly decrease the time to obtain relevant research papers to write reviews. This shows the potential supportive function of machine learning and the need for accurate automated knowledge extraction tools in writing literature reviews.


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