



GW RESEARCH DAYS

— WEDNESDAY, APRIL 11, 2018

HEALTH & MEDICINE RESEARCH DAY

THE GEORGE WASHINGTON UNIVERSITY

WASHINGTON, DC



GW RESEARCH DAYS

2018

HEALTH & MEDICINE RESEARCH DAY

WEDNESDAY, APRIL 11, 2018

MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

8:00-11:30 a.m. Registration and Poster Setup
(Grand and Continental Ballrooms)

LISNER AUDITORIUM

730 21ST STREET, NW

8:00-8:50 a.m. Continental Breakfast

9:00-9:05 a.m. Welcome to Research Days 2018
Jeffrey S. Akman, MD
Vice President for Health Affairs and Dean
School of Medicine and Health Sciences

9:05-9:10 a.m. Introduction of Keynote Address
Robert H. Miller, PhD
Senior Associate Dean for Research
School of Medicine and Health Sciences

9:10-10:00 a.m. Keynote Address
Mary Woolley
President
Research!America
"Your Role in Changing Hearts and Minds for Science"

10:00-10:20 a.m. Coffee Break

10:30-11:30 a.m. William Beaumont Research Awards
Nicole Casasanta and Sarit Toltzis
"Relationship of Hereditary Cancer Syndromes to
Oncotype DX Recurrence Score"

Dara Baker
"The Role of DFMO in Helicobacter Pylori Infection:
Modulation of ROS Response"

Christina Pugliese
"Etiology and Management of Hospitalized and
Outpatient Diarrhea Among Children Less than 5 Years
Old in Lambarene, Gabon"

Speck Endowed Prize

Laura Tiedemann
"Neonatal Intensive Care Management During Laser
Treatment of Retinopathy of Prematurity"

MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

12:30-3:00 p.m. Poster Presentations and Judging
(Grand and Continental Ballrooms)

3:00-3:30 p.m. Poster Removal
(Grand and Continental Ballrooms)

3:30-4:15 p.m. Awards Ceremony and Oral Presentations
(Includes 5-minute presentations by winners of oral
competition awards) (MC Amphitheater)

MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

950 NEW HAMPSHIRE AVENUE, NW,
1ST FLOOR CONVENING CENTER

Refreshments Provided

4:30-4:35 p.m. Welcome and Introduction of Keynote Address
Lynn R. Goldman, MD, MS, MPH
Michael and Lori Milken Dean
Professor of Environmental and Occupational Health
Milken Institute School of Public Health

4:35-5:15 p.m. Keynote Address
Thomas A. LaVeist, PhD
Professor and Chair, Department of Health Policy
and Management
Milken Institute School of Public Health

"Where Research Questions Come From"

5:15-5:30 p.m. Poster Award Winners Announced
Melissa J. Perry, ScD, MHS
Professor of Environmental and Occupational Health
Interim Associate Dean for Research
Milken Institute School of Public Health



GW RESEARCH DAYS

APRIL 11, 2018

3:30-4:15 p.m.

AWARDS CEREMONY

SCHOOL OF MEDICINE AND HEALTH SCIENCES, DONALD H. GLEW PRIZE

Moderator: **Katherine Chretien, MD**
*Assistant Dean for Student Affairs,
School of Medicine and Health
Sciences*

David Strum:
*"Pupillometric Assessment of Small Doses
of Opioid in a Pediatric Population"*

INSTITUTE FOR BIOMEDICAL SCIENCES

Moderator: **Alison Hall, PhD**
*Associate Dean for Workforce
Development and Professor,
School of Medicine and Health
Sciences*

Katherine Blackmore:
*"A Forebrain-Hypothalamic Circuit Mediates
Hepatic Steatosis"*

SCHOOL OF NURSING

Moderator: **Jeanne Geiger-Brown, PhD, RN,
FAAN**
*Professor and Associate Dean for
Research, School of Nursing*

Bertha Wojnarski:
*"Piloting CareStart and Rapid Diagnostic
Test (RDT) to Promote Glucose-6-
Phosphate Dehydrogenase (G6PD)
Screening in Malaria Endemic Community
in Cambodia"*

RESIDENT ORAL PRESENTATION

Moderator: **Jeffrey Berger, MD**
*Associate Dean for Graduate
Medical Education, School of
Medicine and Health Sciences*

Cheralyn Hendrix, MD, Surgery, PGY 3
*"Utilizing Handoff Checklists Enhances
Nurse-Physician Communication and May
Prevent On-Call Fatigue"*

GRADUATE MEDICAL EDUCATION RESEARCH COMPETITION WINNERS

Moderator: **Jeffrey Berger, MD**
*Associate Dean for Graduate
Medical Education, School of
Medicine and Health Sciences*

Case Report:
Dane Slentz, MD, Ophthalmology, PGY 4
*"Orbital Malignant Meningioma: A
Unique Presentation of a Rare Entity"*

Clinical Science (Tie):
Tammy Ju, MD, Surgery, Research
*"Neoadjuvant Radiation is Associated
with Fistula Formation Following
Pancreaticoduodenectomy"*
Ivy Haskins, MD, Surgery, PGY 5
*"Older Age Confers a Higher Risk of 30-
Day Morbidity and Mortality following
Laparoscopic Bariatric Surgery: An
Analysis of the Metabolic and Bariatric
Surgery Quality Improvement Program"*

Basic Science:

**Kathleen Knudson, MD, Neurosurgery,
PGY 6**
*"Surgical Implantation of a Cannula
with an Osmotic Pump into Pons for
Convection Enhanced Delivery of Agents
in DIPG Murine Models"*

Quality Improvement Project:

Cheralyn Hendrix, MD, Surgery, PGY 3
*"Utilizing Handoff Checklists Enhances
Nurse-Physician Communication and
May Prevent On-Call Fatigue"*

POSTER AWARD WINNERS ANNOUNCED

School of Medicine and Health Sciences
Institute for Biomedical Sciences
School of Nursing



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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Role of Neuropeptide Y (NPY), Its Y5/Y2R Receptors in Neuroblastoma Cell Migration

Neuroblastoma is a pediatric tumor that is known for its variable clinical presentation, ranging from spontaneous regression to aggressive disease and subsequent metastasis. It is the most common childhood cancer after leukemia and brain tumors. Neuroblastoma tumors originate from sympathetic precursors and are known to express the sympathetic neurotransmitter Neuropeptide Y (NPY). NPY acts through the Y1-Y5 receptors. Tumor cell proliferation, survival, migration and angiogenesis are effects known to be mediated via two specific NPY receptors, Y2R and Y5R. In neuroblastoma, Y2R is constitutively expressed and maintains cell proliferation, while the expression of Y5R is inducible as a survival factor after periods of cellular stress, such as chemotherapy. These findings led us to believe that NPY via its two receptors may play a role in Neuroblastoma dissemination and metastasis. Our goal was to further elucidate the involvement of NPY in Neuroblastoma cell migration. Using Transwell migration assay on SK-N-BE-2 Neuroblastoma cells, we found that NPY stimulated spontaneous migration, while Y5 and combined Y2/Y5R antagonism significantly decreased cell motility. On the other hand, in SK-N-AS Neuroblastoma cells, exogenous NPY did not stimulate migration, yet the basal cell motility was significantly decreased in the presence of the combined Y2R and Y5R antagonists. These data indicate that in SK-N-AS cells, the endogenous NPY released from tumor cells is sufficient to saturate its receptors and stimulate cell migration. Additionally, we used CHO-K1-Y2R-GFP and CHO-K1-Y5R-GFP transfected cells as a model to investigate changes in cell morphology and phenotype induced by individual NPY receptors. Immunohistochemistry showed giant cells and the increased presence of migratory cells in the Y5R transfected group. These cells also expressed multiple cell membrane extensions and filopodia, not present in CHO-K1 cells transfected with other NPY receptors or GFP alone. A strong co-localization of Y5R and F-Actin signal was detected within these Filopodia in addition to the leading edges and trailing ends of migratory cells, further supporting a role for Y5R in migration and cytoskeleton regulation. Further investigation is required to clarify the role of NPY in metastasis. Currently, there is ongoing work to develop NB cell lines with NPY and Y5R knockout using CRISPR/Cas9 technology, which will be used to elucidate the role of the NPY/Y5R pathway in this process. Moreover, additional studies are needed to understand the role of other NPY receptors and its signaling mediators, such as RhoA, in cytoskeletal regulation as it relates to metastasis in NB.

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BASIC BIOMEDICAL SCIENCES



INSTITUTE FOR BIOMEDICAL SCIENCES

Investigating the Role of Tyrosine Phosphorylation in HDAC1 Regulation

Dysregulation of histone deacetylase enzymes (HDACs) can affect the deacetylation of their histone and non-histone substrates, thereby influencing the regulation of gene transcription and the function of specific HDAC target proteins, further contributing to the development of various diseases. HDACs can be regulated by different post-translational modifications (PTMs), including phosphorylation. Several phosphorylated tyrosine (Tyr) residues on HDAC1 have been identified by high-throughput mass spectrometry studies and listed on PhosphoSite, a PTM database. Site-directed mutagenesis of the individual identified phosphorylated Tyr residues was performed to generate tyrosine-to-phenylalanine mutant plasmids that encode an HDAC1 protein that can no longer be phosphorylated at the site of interest. Through an analysis of several mutants, it was found that the expression of the HDAC1 Tyr-72 mutant protein was less compared to WT HDAC1. Additionally, HDAC1 protein expression could be rescued by reversing the mutation from phenylalanine back to tyrosine. Interestingly, the Tyr-72 residue in HDAC1 is evolutionarily conserved and is also conserved amongst the Class I HDACs, indicating that this residue may be of some functional significance. Additionally, HDAC1 downregulation or inhibition is associated with a reduction in cell proliferation and tumor growth. Therefore, elucidating the mechanism and effects of HDAC1 phosphorylation at Tyr-72 will be important not only for understanding the molecular basis of the regulation of HDAC1, but also for identifying a possible therapeutic target for diseases such as cancer.

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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Plug 'N Play: Induction of Biomimetic and Hierarchical Angiogenesis Under Stimulation with S1P

INTRODUCTION

The field of tissue engineering has long held the promise of eventual production of an “off-the-shelf” vascularized free flap as a means of true dermal replacement. Our current state of dermal replacement utilizes an acellular dermal matrix that, while promising and effective, is severely limited by the condition of the wound bed. A tissue engineered dermal replacement that includes an inherent vascular network would obviate this limitation. Our previous experiments have demonstrated reliable endothelial cell sprouting from a monolayer under stimulation by a gradient of S1P, VEGF, and FGF, and we have even demonstrated the self-assembly of endothelial cells within a collagen matrix. The task remains to anastomose this microsurgically relevant monolayer with the capillary-like self-assembled vessels. It is our hypothesis that the induction of such sprouts into a self-assembled endothelial cell network will anastomose to the network, thereby achieving hierarchical vascular organization that can be utilized in the ultimate production of tissue-engineered pre-vascularized free flaps.

METHODS

Invasivity assays were created by injecting Type 1 Collagen impregnated with 1 μ M S1P into well plates. A monolayer of GFP-tagged Human Umbilical Vein Endothelial Cells (HUVECs) were topically seeded, covered with Endothelial Cell media enhanced with VEGF and FGF, and cultured for 1, 3, and 5 Days. Self-assembled network assays were created by seeding a monolayer of GFP-tagged HUVECs as above, followed by injecting a second layer of collagen above the monolayer and coverage with growth factor enhanced media. After optimization, combination cultures were created by layering a collagen base layer, a YFP-Tagged HUVEC network second layer, an S1P impregnated collagen third layer, and a topically seeded GFP-Tagged HUVEC monolayer. All constructs were fixed and confocal imaged for analysis.

RESULTS

Invasivity assays demonstrated robust sprouting with an average of 46.89 ± 2.54 by Day 1, 131.4 ± 10.34 by Day 3, and 321.3 ± 39.31 by Day 5 per 0.6 mm^2 . Self-assembled network assays demonstrated biologically appropriate inter-capillary distance less than $50 \mu\text{m}$ by Day 5. Combination cultures demonstrated robust sprouting from both the network and monolayer and anastomosis as evidenced by YFP and GFP multi-fluorescent channels, however quantification of anastomoses are still in progress.

CONCLUSIONS

In this project we have successfully demonstrated the ability of endothelial cells to form a hierarchical vascular network that mimics that of normal human tissue in a way that is readily scalable and easily reproducible. Future iterations of this project will focus on a straight channel design and maintenance of the channel and network with flow.

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BASIC BIOMEDICAL SCIENCES



INSTITUTE FOR BIOMEDICAL SCIENCES

Post-Translational Regulation of Poly (A)-Specific Ribonuclease

Post-translational protein modifications (PTMs), such as acetylation, play an important role in mediating the function, expression, interactions, and localization of proteins. Thus, PTMs can regulate a variety of cellular processes such as cellular differentiation, signaling pathways, metabolism and even cancer development. Protein acetylation is a reversible process that is tightly regulated by lysine acetyltransferases (KATs) and lysine deacetylases (KDACs). Lysine acetylation of non-histone proteins has been reported to affect enzymatic activity, stability, and complex formation. However, the exact role of acetylation on non-histone substrates is protein-specific. Using PhosphositePlus, a mass spectrometry database, and a published dataset identifying acetylated lysine enriched substrates, revealed that Poly (A)-specific ribonuclease (PARN) may be post-translationally modified by acetylation. PARN is a 3' exoribonuclease: it can cleave nucleotides one-by-one from the 3' end of RNA. PARN's exoribonuclease activity plays an important role in RNA maturation and degradation. PARN has the highest substrate affinity for adenosines; therefore it is referred to as a deadenylase. Adenosine repeats (poly (A)) on the 3' end of RNA prevent mature transcripts from degradation by nucleases, especially during transport from the nucleus to the cytoplasm for translation. Thus, removal of poly (A) tails by deadenylase enzymes such as PARN promotes mRNA decay. Currently there are no reports confirming whether PARN can be acetylated and its functional importance. This study reveals that PARN is modified by acetylation and that acetylation plays a key role in mediating its enzymatic activity.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Can Presence of Extracapsular Extension in Malignant Cervical Lymph Nodes in Patients with Oropharyngeal Cancer be Predicted with Staging MRI?

INTRODUCTION

Extracapsular extension (ECE) of metastatic lymph nodes has been considered a high-risk feature for loco-regional recurrence and distant metastasis after surgical resection in patients with oropharyngeal cancer (OPC). Patients with ECE classically require a multimodal treatment approach involving surgery, chemotherapy (CT) and/or radiation therapy (RT). However, post-operative RT causes significant short- and long-term sequelae, increasing patients' morbidity and mortality. Traditionally, ECE has been determined based on histopathological analysis. A few publications have reported that certain MRI characteristics of lymph nodes can identify presence of ECE. The focus of this project is to calculate the accuracy of these previously published parameters and novel MRI characteristics of malignant lymph nodes in patients with OPC who were treated in part with selective neck dissection immediately after staging MRI.

METHOD

In this IRB approved retrospective study, 28 patients with stage III or IV OPC treated with trans-oral robotic-assisted surgery (TORS) or trans-oral laser microsurgery (TLM) and selective neck dissection (SND) at the George Washington University Hospital during the past 10 years (July 1, 2007 to July 1, 2017) were included. All those included in the study were imaged with a preoperative MRI examination and had pathology reports pertaining to neck dissection. The stored images on PACS were reviewed by an experienced Neuroradiologist and a Neuroradiology fellow for the: 1) presence of suspicious nodes (SN) 2) the size of the SN, 3) the size of the area of central necrosis within SN, and 4) contour/margin of SN. Pertinent clinical and pathologic data were extracted from an electronic medical record.

RESULTS

Eleven out of twenty-eight patients had pathologically proven ECE. Of the MRI features characterized, presence of necrosis > 1 cm in post-contrast MRI was the most sensitive in predicting presence of ECE (72%), but had low specificity (58%). The two Radiologists differed in their analyses in less than 5% of the MRI findings.

CONCLUSION

Of the MRI findings characterized in this study, presence of central necrosis > 1 cm in a SN was the most sensitive MRI marker for the presence of ECE in patients with OPC, but was not specific for ECE. Ultimately, the overall accuracy of these MR findings was modest. This study demonstrates the importance of MRI in detecting ECE but also shows the need for improved standardization and accuracy of imaging characteristics predictive of ECE.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Ex-vivo Evaluation of Cytotoxicity and Melanocyte Viability of Fitzpatrick V Skin After A-101 Hydrogen Peroxide Topical Solution 40% or Cryosurgery Treatment in Seborrheic Keratosis Lesions

Seborrheic keratosis (SK) is a common benign lesion that is cosmetically treated with cryosurgery. Despite the frequency with which patients pursue cosmetic removal, all patients are susceptible to some degree of scarring and pigmentary changes. African American patients are particularly vulnerable to post-treatment hypopigmentation, yet the armament of effective SK treatment options that address this concern is surprisingly limited. A-101 is a stabilized, high concentration (40%) hydrogen peroxide (H_2O_2) topical solution recently FDA approved as a SK therapy. This drug harnesses the oxidizing potential of supraphysiologic H_2O_2 to overwhelm the antioxidant defense systems of SK keratinocytes to induce cell death. To evaluate the toxicological effects of cryosurgery versus A-101 on African American skin, we treated ex-vivo human full thickness skin equivalents derived from Fitzpatrick V skin with either liquid nitrogen cryosurgery or A-101. Using TUNEL immunostaining and MTT assay, we found that cryosurgery-treated tissues showed greater epidermal damage, apoptosis and decreased cell viability, suggesting that A-101 is less destructive to skin surrounding SK lesions, an important finding relevant to post-treatment epidermal recovery. Cryosurgery also significantly decreased number of melanocytes and epidermal melanosomes when compared to A-101 as demonstrated by Fontana-Masson and s100 staining. Interestingly, H_2O_2 treated tissues exhibited increased melanosome dispersion without dermal pigmentary incontinence, suggesting that A-101 may play a proliferative role in human pigmentation regulation and protect against post-treatment hypopigmentation. These data suggest that A-101 may offer better cosmetic outcomes than conventional cryosurgery, a finding salient to African American patients who are more vulnerable to post-treatment pigment alterations.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Effect of Genetic Variation in GSTP1 and AXIN1 on Bone Mineral Density in Children and Young Adults

BACKGROUND

The Glutathione S-transferase P 1 (GSTP1) family of enzymes minimize oxidative cellular damage which adversely affect bone health. Studies have shown that variation at rs1695 in GSTP1 negatively impacts BMD. Another determinant in bone quality is the canonical-Wnt pathway in which the AXIN1 protein functions as a negative regulator. Previous studies have associated the rs9921222 variant of AXIN1 with lower total BMD/osteoporosis.

OBJECTIVE

To expand our understanding of the influence of rs1695 and rs9921222 on BMD.

METHODS

DNA samples from the Bone Health (African-American) cohort and a Caucasian sub-cohort of the Assessing Inherited Markers of Metabolic Syndrome in the Young (AIMMY) were utilized to measure total BMD without head z-score (adjusted for height) and total BMD, respectively. Illumina Multi-Ethnic Genotyping Array (MEGA) chip and Applied Biosystems Taqman allelic discrimination assays/Real-Time PCR were utilized for the Bone Health and AIMMY cohorts, respectively. ANCOVA models where genotype was the dependent variable, appropriate phenotype the independent variable, and age (for Bone Health) or age and height (for AIMMY) as covariates were utilized.

RESULTS

A statistically significant association between total BMD and rs1695 was observed in males of the AIMMY Caucasian cohort ($p=0.047$). No significant association between the homozygous GG variant of rs1695 and total BMD was found. No statistically significant genotype-phenotype associations between rs9921222 or rs1695 and total BMD were present in the Bone Health cohort using an additive genetic model. There was no reported association between total BMD and the rs1695 GG homozygote variant.

DISCUSSION

Significant differences in the association of genetic variants of rs1695 and BMD in both the AIMMY and Bone Health cohorts could be influenced by race/ethnicity—both of which have been significantly associated with bone quality/fracture risk. The significant association present in Caucasian males of the AIMMY cohort ($p=0.047$) but not in females ($p = 0.33$) underscores the important role of sexual dimorphism in determining musculoskeletal phenotypes. The presence of the rs1695 G allele variant in GSTP1 could indicate appreciable build-up of ROS in males and subsequently result in lower quality of bone.

Our work did not find a significant association with rs9921222 and total BMD or BMD z-score minus head. Conflicting results with previous studies could be attributed to the highly polygenic nature of BMD. It is plausible that rs9921222 may be inherited with other SNPs that are associated with lower BMD. The present study could not account for confounding SNPs that may have been inherited along with rs9921222.

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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Clinical Testing Solution to Disrupt the Industry

Many healthcare providers are increasingly reliant on laboratory outsourcing to reduce overhead costs and simplify their systems. Unfortunately, these third-party labs delay patient results and timely provision of care, while inconveniencing many patients. These frustrations and delays are coupled with an increasing reliance on laboratory testing for diagnoses. Physicians report that 80% of diagnoses are based on clinical testing and patients and providers are often stuck waiting, on average 3 days, for results before medical care can continue.

Hospitals are often the only healthcare institutions with in-house labs, which are inherently high cost and take extended time for results. Even well insured individuals are left paying out-of-pocket for clinical testing due to outrageous markups when testing is billed to insurance.

I aim to disrupt this paradigm by designing an on-demand, in-house clinical diagnostic solution. My goal is to design a technology capable of covering many commonly ordered lab tests in an easy-to-use, compact package.

My design efforts included performing bioinformatics research to catalog available technologies throughout several disciplines. After compiling technologies, I consulted local experts in biomedical engineering, electrical engineering, and immunology, then formulated a design for a new biosensor. The result is the Rapid Diagnostic Suite (RDS).

The RDS system is a bench-top testing instrument that will only require 100 microliters of sample to run a 7-test panel. Each panel will be contained in a pre-manufactured cartridge. Cartridges will combine tests that are often ordered together. RDS will employ its proprietary microfluidic immune-based design to deploy the sample and testing cartridge materials, measure reaction and produce results. Instrument controls will be calibrated daily with a control sample.

The RDS system will be available at pharmacies and other convenient medical clinics. Consumers who use these facilities will avoid high co-pays and co-insurances associated with third-party labs and avoid the outrageous markups charged by hospitals when lab services are billed to insurance. In this use scenario, the provider saves money, the customer pays less, and everyone receives results faster.

Small healthcare businesses will recover missed revenue by performing comprehensive testing in-house, reducing outsourced testing. Low testing cost will ensure a profitable business model with generous margins for the company, while leading to tremendous customer satisfaction from reduced out-of-pocket cost and wait-time.

My summer research culminated with the beginnings of a prototype design that will continue to be developed and tested within the next two years.

PRIMARY PRESENTER

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CHILDREN'S NATIONAL MEDICAL CENTER

IPSE, A Urogenital Parasite Derived Protein, Drives Urothelial Proliferation and Alleviates Chemotherapy-Induced Hemorrhagic Cystitis

INTRODUCTION AND OBJECTIVE

Chemotherapy-induced hemorrhagic cystitis can be a difficult-to-manage complication. We previously reported that a single dose of H-IPSE^{H06}, a *Schistosoma haematobium*-derived host immunomodulatory protein, is superior to three doses of Mesna in preventing ifosfamide-induced hemorrhagic cystitis. Herein, we expand upon this work in three directions: 1) characterization of H-IPSE^{H06}'s influence over urothelial proliferation; 2) elucidating the mechanism of IPSE's therapeutic effect through transcriptional profiling.

METHODS

Recombinant H-IPSE or an NLS mutant of IPSE (H-IPSE^{NLS}) was incubated with mouse and human urothelial cell lines, and proliferation and cell cycle status measured by flow cytometry using CFSE and propidium iodide, respectively. Cellular RNA were isolated and subjected to RNA-seq analysis. Mice were administered H-IPSE^{H06} or H-IPSE^{NLS}, challenged with ifosfamide, and their bladder RNA subjected to RNA-seq analysis.

RESULTS

H-IPSE^{H06} increased both mouse and human urothelial cell proliferation, and drove cells towards S-phase. These effects are NLS dependent, and are consistent with H-IPSE^{H06}'s ability to protect the urothelium following ifosfamide challenge. RNA-seq analysis revealed that several cell proliferation related pathways were differentially expressed between H-IPSE^{H06} vs vehicle-treated mice challenged with ifosfamide. Also, multiple muscle contraction-related pathways are differentially expressed between H-IPSE^{H06} vs H-IPSE^{NLS}-treated mice challenged with ifosfamide. These findings are consistent with H-IPSE^{H06}'s ability to prevent ifosfamide induced bladder dysfunction.

CONCLUSION

H-IPSE^{H06} continues to prove to be a promising prophylactic against chemotherapy-induced hemorrhagic cystitis. Our mechanistic studies on H-IPSE^{H06} suggest potential means by which to optimize this molecule's NLS-dependent therapeutic effects.

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BASIC BIOMEDICAL SCIENCES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Association of Recently Described RANK and OPG Polymorphisms and Measures of Bone Quality in Young Adults

BACKGROUND

Increased fracture susceptibility is correlated with suboptimal bone quality measures, which are thought to be highly influenced by genetic factors. Previous studies have determined that specific receptor activator of nuclear factor-kappaB (RANK), RANK ligand (RANKL), and osteoprotegerin (OPG) single nucleotide polymorphisms (SNPs) are associated with bone mineral density (BMD) and bone geometry parameters in older men. The RANK, RANKL, and OPG systems play a vital role in the regulation of osteoclasts and bone resorption. Further investigation into genetic variation within these genes is essential in order to identify those at risk for future fragility fractures.

OBJECTIVE

Our study sought to determine whether RANKL/RANK/OPG SNPs rs3018362, rs17665435, rs6567276, and rs10505348 influence bone quality measures in younger populations.

METHODS

The Assessing Inherited Markers of Metabolic Syndrome in the Young (AIMMY) study comprised healthy, young adults (18-35yrs) from the University of Calgary (UC) sub-cohort (n=209). The Bone Health study comprised healthy African-American children (5-9yrs, n=97). The Functional Single Nucleotide Polymorphism Associated with Human Muscle Size and Strength (FAMuSS) study comprised healthy, young adults (18-40yrs, n=891). The bone quality phenotypes analyzed included total body BMD in AIMMY and total BMD adjusted for height in the Bone Health study measured by dual energy x-ray absorptiometry (DEXA). Three SNPs for RANK (rs3018362, rs17665435, rs6567276) and one SNP for OPG (rs10505348) were genotyped in the AIMMY sub-cohort using ThermoFisher's Applied Biosystems Taqman SNP genotyping assays. Alleles were determined through allelic discrimination assays using real-time PCR (qPCR). SNPs were genotyped in the FAMuSS cohort using Illumina Multi-Ethnic Genotyping Array (MEGA). Hardy-Weinberg equilibrium was tested for the allelic frequency of each SNP and analysis of covariance (ANCOVA) was used to test for associations.

RESULTS AND DISCUSSION

Our results did not support those of previous studies and suggest that the SNPs rs3018362, rs17665435, rs6567276, and rs10505348 are not associated with BMD or other bone quality measures in young adults. The only association that approached significance was rs3018362 and height-adjusted BMD in males of the Bone Health cohort ($p=0.07$). We suspect that the lack of association in our study indicates that these SNPs may not play a role in the development of peak bone mass despite being important in determining bone quality in seniors. To further characterize the effect of RANKL/RANK/OPG variations on the multifactorial regulation of bone quality phenotypes, future studies should evaluate the relationship between these variants and bone phenotypes in cohorts of varying ages and ethnicities.

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Mechanism for Mitochondrial Import of a Cytomegalovirus Anti-Apoptotic Protein vMIA

BACKGROUND

Human cytomegalovirus (HCMV) infection is responsible for developmental defects in neonates, as well as severe illness in transplant patients, and immuno-deficient individuals. The HCMV UL37 exon 1 gene encodes an anti-apoptotic protein known as viral mitochondria-localized inhibitor of apoptosis (vMIA). vMIA prevents HCMV-infected cells from undergoing apoptosis, enhancing production of viral progeny. vMIA is synthesized in the ER and localizes to the outer mitochondrial membrane (OMM) through the mitochondria associated membranes (MAM), which is required for its antiapoptotic function.

Most mitochondrial proteins are synthesized in the cytosol and then imported into mitochondria through dedicated translocase machinery. However, the mechanism by which vMIA and other ER-synthesized host proteins are imported into mitochondria is not known. Understanding this machinery is required to design drugs that can facilitate apoptotic clearance of the HCMV infected cells and to treat diseases with defects in proper importation of endogenous mitochondrial targeted proteins.

OBJECTIVE

Here we investigated the role of the mitochondrial translocase complex in the import of an ER-synthesized, essential, human cytomegalovirus protein – vMIA, to the mitochondria.

METHODS

We utilized drug-based inhibitors and siRNA-mediated genetic knockdown together with confocal, superresolution and fluorescence lifetime microscopy as well as biochemical approaches to assess the interaction of mitochondrial translocase complex with vMIA and to test their requirement for mitochondrial import of vMIA.

RESULTS AND DISCUSSION

vMIA co-clusters with the Translocase of Outer Mitochondrial membrane (TOM) complex import receptor protein–Tom20 and the channel protein–Tom40. Both of these proteins physically interact with vMIA. Knockdown of Tom40 protein abundance does not prevent OMM import of vMIA. Similarly inhibition of the Translocase of Inner Mitochondrial membrane (TIM) protein Tim23 and depolarization of mitochondria, both of which prevent import of mitochondrial matrix proteins, do not affect inhibit mitochondrial import of vMIA. These results identify a mitochondrial import pathway for vMIA that is independent of the mitochondrial import channels TOM and TIM.

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PPARGC1A and IGF Polymorphisms Correlate with Greater Strength Performance in Healthy Young Adult Caucasian Cohorts

BACKGROUND

Recent studies show single nucleotide polymorphisms (SNPs) in *PPARGC1A* (coding for PGC-1 α) and *Insulin-like Growth Factor 1 (IGF-1)* genes correlate with greater power sport performance in professional athletes. In rs8192678 on the *PPARGC1A* gene, a substitution causes lower PGC-1 α expression and reduced performance. For IGF-1 rs7136446 polymorphism, GG homozygosity correlates with greater expression of IGF-1 and increased maximal force.

OBJECTIVE

The purpose of our study was to investigate whether rs8192678 or rs7136446 predict strength performance in young Caucasian adults who are not elite athletes.

METHODS

Different measurements of strength were obtained from two cohorts of young adult Caucasian individuals, *Functional Single Nucleotide Polymorphism Associated with Human Muscle Size and Strength (FAMuSS)* and a sub-cohort of the *Assessing Inherited Markers of Metabolic Syndrome in the Young (AIMMY)* University of Calgary cohort. *IGF-1* in *PPARGC1A* was not in Hardy Weinberg equilibrium, but the distribution of alleles was similar to a prior study of *IGF1* gene variants. Analysis of covariance (ANCOVA) models were utilized to analyze for genotype-phenotype associations.

RESULTS

Ser/Ser genotype females had a greater percentage change in 1-RM strength in the dominant (D) arm, but no statistical significance was found regarding baseline strength, percentage change in the non-dominant (ND) arm, or percentage change of isometric strength. In male participants, the Gly/Gly genotype was more beneficial to baseline 1-RM strength. Our study found no significant associations for variants of rs8192678 with VO₂ max.

DISCUSSION

We found male G/G individuals had a greater percent change in isometric strength than heterozygous individuals. Females with at least one G allele had a greater baseline isometric strength and VO₂ max. Our results support earlier findings of correlation with greater maximal force production³ and indicate a sexually dimorphic effect. Variation in rs8192678 and rs7136446 may help predict individual response to an exercise program, particularly in females.

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Identifying Cellular-Level Epigenetic Markers for the Prediction of Cognitive and Learning Deficits in a Fetal Alcohol Spectrum Disorders Model

BACKGROUND/RATIONALE

Although the physical manifestations of prenatal exposure to alcohol are often easy to identify, the more devastating effects on cognitive function and intellectual ability, however, are highly varied and thus difficult to predict. In order to aid physicians in early identification of potential deficits and the implementation of the appropriate therapies, we aim to identify biomarkers that are associated with infants who have an increased risk of Fetal Alcohol Spectrum Disorders (FASD), and of developing cognitive and learning disabilities later on in life.

METHODS

For FASD model, pregnant female mice received 4.0g/kg intraperitoneal EtOH or PBS injections at embryonic day (E) 12-14 with expected pup delivery at E18-20. Postnatal day 30 pups (n=10) subsequently underwent rotarod behavior tests over 2 days in order to quantify learning capabilities as measured by latency to fall over a period of 6 trials. One day following the completion of the rotarod test, cardiac puncture was performed for whole blood collection and buffy coat, containing peripheral mononuclear cells, was isolated using Ficoll-density gradient medium. T lymphocytes, B lymphocytes and monocyte populations were collected via fluorescence-activated cell sorting (FACS) and underwent RNA sequencing to identify variations in gene expression between the EtOH exposed and PBS groups.

RESULTS

Findings up to date indicate that prenatal exposure to alcohol negatively impacts learning abilities where 44% of the EtOH-exposed group are classified as poor learners (learning index <10) compared to 28% in the PBS-control group. RNA sequencing analysis of collected cellular populations is currently underway with the goal of identifying specific biomarkers that may be correlated to results encountered in our behavioral model.

CONCLUSION

The identification of potential biomarkers associated with cognitive and learning disabilities in our FASD mouse model may be useful in the development of future investigations that target markers specific to human patients with FASD.

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Implication of the Long Non-Coding RNA Crnde in Multiple Myeloma

Multiple myeloma (MM) is an incurable malignancy of antibody-secreting plasma cells, with a wide clinical and prognostic spectrum, even within groups bearing the same primary initiating cytogenetic event, for which the molecular mechanisms responsible remain poorly understood. Long non-coding RNAs (lncRNAs; broadly defined as non-coding RNAs of > 200 nt) have recently emerged as an important class of regulatory molecules and are increasingly implicated in tumorigenesis and cancer progression. However, currently their contribution to the progression and clinical variability of MM is largely unknown.

In order to identify lncRNAs potentially implicated in the etiology of MM, we have taken a data mining approach to compare the expression profile of lncRNAs between CD138+ plasmocytes from healthy individuals with those from MM patients. Patients were stratified according to the presence of the t(4;14) or t(11;14) translocations and a third group bearing neither of these cytogenetic events. This analysis revealed 110 lncRNAs that are differentially expressed in CD138+ plasma cells from newly diagnosed MM patients compared to control subjects. A candidate to emerge from this analysis is Colorectal Neoplasia Differentially Expressed (CRNDE), a lncRNA implicated in other hematological malignancies and diverse solid tumors, by promoting growth and inhibiting apoptosis potentially via a physical association with epigenetic modifying complexes (PRC2 and CoREST). Our findings suggest that CRNDE is involved in MM disease progression, causing progression from the pre-malignant MGUS to the smoldering myeloma stage and reaching highest levels in overt symptomatic myeloma. Further, survival analysis indicates that high CRNDE expression is associated with poor overall survival, in particular in high risk t(4;14)+ myeloma patients. To directly test the role of CRNDE in MM and to investigate downstream oncogenic pathways, we are using CRISPR/Cas9 to delete the major nuclear and cytoplasmic isoforms of CRNDE in MM cell lines.

Results indicate that the deletion of CRNDE exerts a dose-dependent repressive effect on myeloma cell growth, supporting its involvement in MM disease progression. CRISPR/Cas9 deletion is being carried out in both a t(4;14) and non t(4;14) context. We also investigated the effect of CRNDE deletions on the sensitivity of MM cells to therapeutic agents and the interaction of CRNDE with Polycomb group proteins.

Overall, our results suggest that CRNDE plays a role in MM disease progression and outcome. This work has the potential to translate into clinical benefit, notably by providing a useful biomarker of MM and novel therapeutic strategies based on lncRNAs.

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Early Oligodendrocyte Ablation Alters CNS Responses to Immune Mediated Demyelination in the Adult Mouse

Experimental autoimmune encephalomyelitis (EAE) is the most common experimental model for multiple sclerosis, an autoimmune mediated neurodegenerative disease characterized by oligodendrocyte (OL) apoptosis, demyelination, and inflammation within the central nervous system. OLs are responsible for myelination in the central nervous system and their ablation results in demyelination. Remyelination occurs relatively soon following early OL ablation due to the high number of oligodendrocyte progenitor cells (OPCs) in early life. OL ablation was achieved by injecting MPB-icP9 transgenic mice, which express an inducible form of caspase 9 (icP9) driven by a fragment of the MBP promoter, with Chemical Inducer of Dimerization (CID). To induce the primary insult CID was delivered via intra-peritoneal injection to transgenic mice at postnatal day 4 over a 2 week period. Following remyelination, the second insult was introduced via EAE induction at 10-11 weeks of age. Mice were sacrificed 2 weeks post EAE induction and spinal cords harvested and fixed with PFA for histological examination. Demyelinating lesions were observed as patches of disrupted solochrome staining in spinal cord section preparations. Preliminary results show no significant difference in focal area of demyelination in spinal cord sections treated with EAE alone versus EAE preceded by CID. Immunohistological staining show relative increases in NG2 (OPC marker), CD45 (immune cell marker), Iba1 (microglia marker), and CD23 (mast cell marker) in spinal cord sections exposed to double insult compared to EAE alone. These results suggest an increase in both OPCs and an increase in inflammation in CID+ EAE versus EAE induction alone. Further studies will include examination of OPC proliferation in CID+EAE vs EAE by immunohistological staining with Ki67 and PDGFR α markers.

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New Genetic Tool to Study Gene Function in Fatal African Sleeping Sickness Parasite

African trypanosomes are unicellular parasites that result in death if left untreated. Treatment of African trypanosomiasis relies on six effective drug treatments, which can be highly toxic and difficult to administer. While there are on-going studies to develop new drugs, resistance to existing drugs is a persistent threat. Trypanosomes are an early branching eukaryote with only limited homology to highly studied genomes; more than 60% of the *Trypanosoma brucei* genome remains annotated as hypothetical genes of unknown function. To better understand basic biology, pathogenesis, and resistance of this parasite, we need to uncover gene functions and regulations.

To accomplish this goal, we have developed a whole-genome gain-of-function library to apply in forward genetic screens and identify genes associated with a wide range of phenotypes. Gene expression regulation in Trypanosomes required that we build an ORF-based (PCR amplified) library, which was cloned into a Gateway library for introduction into the *Trypanosoma brucei* genome by transfection. Preliminary genetic screens demonstrated that we were able to successfully incorporate 90% of the intended gene products into the genome with greater than 10-fold coverage. However, we encountered two challenges: 1) individual transfections result in different sets of genes represented and 2) inconsistent gene expression among transfections.

Here, we have implemented steps for the overall normalization and consistent usage of our cloned over expression library. Primarily, we undertook a process to produce a cell line that will permit the consistent, highly inducible expression of our library among multiple transfections. In addition, we have streamlined our transfection method to focus on producing a consistent population of cells that all harbor the same subset of library genes with the desired level of coverage. To further normalize the variance, we made our library cell line and expanded it to create a large bank of library cells for future genetic screens. With these steps now completed, we have prepared next-generation sequencing libraries to fully assess the expression and consistency. With this forward genetic tool in hand, we will be able to conduct genetic screens to uncover pathways of drug resistance, pathogenesis, and other key biological features of this devastating human parasite.

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Gut Colonization with Methanogenic Archaea Lowers Blood TMAO Levels and Prevents Atherosclerosis in Apolipoprotein e^{-/-} Mice

BACKGROUND

Trimethylamine (TMA) N-oxide (TMAO), a gut-microbiota-derived metabolite, has been shown to enhance atherosclerosis in animal models and be associated with cardiovascular risks in clinical studies. Gut microbiota metabolizes dietary choline, phosphatidyl choline, and L-carnitine (abundant in red meat) to TMA, which is further converted by the liver to a proatherogenic compound, TMAO. Here, we investigate the *in vivo* efficacy of gut colonization by certain methanoarchaea to lower blood TMAO levels and reduce the TMAO-induced atherosclerosis.

METHODS

Regular C57BL/6 and the atherosclerotic-prone apolipoprotein e^{-/-} (Apoe^{-/-}) mice were transplanted with sham or selected representative gut and non-gut species of methanoarchaea and put on a high-choline and TMA diet. Gut microbiome, blood TMAO levels and atherosclerosis levels were examined.

RESULTS

We found that all five species of methanoarchaea colonized and reduced blood TMAO levels in mice fed a high-choline and TMA diet, although to varying degrees. Sustained high level colonization and low blood TMAO levels were obtained in Apoe^{-/-} mice, following repeated monthly transplantation with *Methanobrevibacter smithii*, the most predominant methanoarchaea in the human gut. Most importantly, gut colonization with *M. smithii* significantly reduced blood TMAO levels and suppressed the development of atherosclerosis.

CONCLUSIONS

Stable colonization of gut microbiota with certain methanoarchaea prevented the development of atherosclerosis. Our findings suggest that certain methanoarchaea could serve as targeted probiotics to lower the gut TMA levels and have a potential therapeutic utility for reducing the atherosclerosis burden.

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IPSE, A Parasite-Derived Host Immunomodulatory Protein, Is a Promising Therapeutic for Pediatric Bladder Pain

BACKGROUND

Pediatric bladder pain syndromes and associated dysfunctional voiding behavior cause a significant decline in the quality of life of patients and their families. Currently available treatments have limited efficacy. Therefore, novel therapeutic options are needed. We previously reported, in a bladder pain model of ifosfamide-induced hemorrhagic cystitis (HC), that systemic administration of Schistosomiasis haematobium derived protein H-IPSE^{H06} (IL-4 inducing principle from Schistosoma mansoni eggs), relieves carrageenan-induced inflammatory pain. Furthermore, H-IPSE^{H06} is superior to mesna in alleviating HC by binding IgE on basophils and inducing IL-4 expression, promoting urothelial proliferation and translocating to the nucleus to modulate gene expression.

OBJECTIVE

We speculate that local bladder injection of IPSE ortholog IPSE^{H03} (H-IPSE^{H03}) might have a more potent effect in treating HC with less potential side effects compared with systemic administration of IPSE^{H06}.

METHODS/DESIGN

C57BL/6 female mice underwent bladder wall injection of H-IPSE^{H03}, or H-IPSE mutant lacking the nuclear localization sequence (H-IPSE^{H03NLS}) followed by exposure to ifosfamide. Urinary frequency was assessed by urine spot assays. Elicited pain scores were recorded in a blinded fashion. Mouse bladders were harvested, and evaluated for microscopic and macroscopic edema and hemorrhage. Bladder tissue was subjected to histologic analysis.

RESULTS/DISCUSSION

HC mice that underwent bladder injection of H-IPSE^{H03} had decreased pain response compared to HC mice. Pain tolerance conferred by H-IPSE^{H03} was reversed by blockade of IL-4 or IPSE^{H03NLS}. H-IPSE^{H03} improved voiding dysfunction in HC mice. Bladder wet weight (BWW) and Gray's scoring was decreased in HC mice treated with H-IPSE^{H03} compared to controls.

H-IPSE^{H03} is a promising therapeutic for the treatment of bladder pain in a model of ifosfamide-induced cystitis by relieving HC-associated pain sensitivity. H-IPSE^{H03} decreases edema and hemorrhage in an IL-4 dependent fashion. H-IPSE^{H03} may be a novel candidate for a non-opioid analgesic and anti-inflammatory in disorders that cause bladder pain and inflammation.

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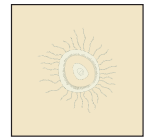
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Effect of Metformin on Jeko and Jurkat Cells

BACKGROUND

Metformin has long been presented to have an anti-glycemic effect and consequently is one of the most commonly prescribed drugs for diabetes, predominantly Type II Diabetes. It has been shown to exert its anti-glycemic effect by increasing insulin sensitivity as well as glucose uptake by peripheral tissues. However, the drug has potential for other uses. In addition to Metformin's established anti-diabetic effects, there has been substantial preclinical evidence put forth presenting it as a potential anti-cancer medication. Metformin has been associated with a reduced risk of developing certain types of cancer, via different molecular pathways, as well as an improvement in overall cancer survival rates in meta-analysis. Individuals with diabetes have been known to also have a higher risk for several types of cancers such as liver, pancreas, and breast.

METHODS

In order to determine what effect Metformin could have on a common cancer, such as lymphoma, at a cellular level we performed a 14 day experiment on the effect of 3 different doses of Metformin (0mM, 0.025mM, 0.25mM) on two different lymphoid cell lines, Jurkat and Jeko [Metformin at 0.025mM concentration is physiological]. Samples were collected on Day 3, 7, 10, and 14 and PCR targeted gene expression was subsequently conducted focusing on mitochondrial and apoptosis related genes (such as cytochrome oxidases (COX2 and 4), nuclear respiratory factor (NRF1), apoptosis gene (P53) and other mitochondrial genes such as PGC1A, SOD2, and TFAM) COX4, MT_CO2, NRF1, P53, PGC1A, SOD2, TFAM].

DISCUSSION

Jeko showed initial mitochondrial gene expression with Metformin. The suppression in mRNA gene expression appears to reverse by day 7. By Day 10 there is a uniform upregulation in mRNA expression and the effects stabilized by day 14. Therefore, we concluded that in Jeko cells, upon initial exposure to metformin, show a decrease in mitochondrial biogenesis and increased apoptosis. This initial suppression seems to be replaced by over-expression of mitochondrial genes over a period of time and effects stabilizes by day 10 of exposure. This phenomenon appears to be shown in both cell lines. Our Jurkat cells showed less consistent mRNA level changes. We plan to corroborate our gene expression findings with Sea-Horse cell respiration studies.

CONCLUSION

We believe that metformin initially causes cellular apoptosis, however subsequently the cells are able to escape that phenomenon by upregulating mitochondrial genes at physiological doses. In order for metformin to be an effective pro-apoptotic agent in a cancer scenarios, brief pulses of supra-physiological doses may be more effective.

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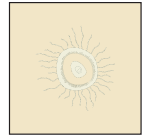
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Tumor Surveillance Using Liquid Biome in Pediatric High Grade Gliomas

Immunotherapy is currently being used to treat pediatric brain cancer, though its efficacy in treating patients with diffuse intrinsic pontine glioma (DIPG), the deadliest pediatric brain tumor, has not been evaluated. MRI is the gold standard for monitoring tumor response to therapy, but is limited by pseudoresponse and pseudoprogression: post-treatment, immune cells infiltrate the primary tumor causing transient tumor enlargement, which falsely resembles tumor progression on MRI. Thus, it is critical to develop more accurate approaches to monitor tumor response to immunotherapy. Here, we use a liquid biopsy platform we have already established to monitor tumor response to therapy, to assess whether this platform is sufficient to monitor response to immunotherapy. The most frequent driver mutation in DIPG is the conversion of lysine 27 to methionine in histone H3, encoded by H3 variants H3.3 (*H3F3A*) and H3.1 (*HIST1H3B/C*). Here, we report detection of *H3F3A* mutation allelic frequency (MAF) in circulating tumor DNA in plasma obtained from DIPG patients undergoing immunotherapy with Newcastle disease virus (NDV) vaccine. NDV selectively targets tumor cells and induces immunogenic cell death; we hypothesize that this treatment will decrease tumor burden, corresponding to lower levels of mutant H3F3A and HIST1H3B in plasma. We used our digital droplet PCR liquid biopsy platform to determine histone mutation status (H3.3, H3.1, H3 wild type) at time of diagnosis, and to monitor MAF through the course of treatment, in order to correlate MAF to tumor response. This platform allows for more sensitive, accurate monitoring of tumor response than conventional MRI.

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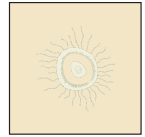
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Engineering the TGF β Receptor to Enhance the Therapeutic Potential of Natural Killer Cells as an Immunotherapy for Neuroblastoma

High-grade neuroblastomas (NB) have a poor prognosis, and there is a need to explore novel therapies. Natural killer (NK) cells rapidly lyse target cells without prior exposure, and serve as a promising source for adoptive cell therapy, however availability from adult donors is limited. Cord blood (CB) derived NK cells have promise as an ideal source for “off the shelf” therapy as they can be selected for optimally mismatched donors. However, CB NK cell efficacy is limited by the immunosuppressive microenvironment in solid tumors such as NB, where high levels of secreted TGF β actively impairs NK cell activity. To overcome this, we genetically-modified NK cells to express a modified TGF β receptor which contains an activation domain, and is thus able to engage with TGF β while potentially converting downstream signals to enhance NK cell function.

NK cells were isolated from umbilical cord donors, expanded, and transduced to express an engineered TGF β receptor: truncated TGF β RII external domain fused to the intracellular DAP12 motif. Cellular phenotype and proliferation was determined by flow cytometry, and cell function determined with in vitro cytotoxicity assays, cell signaling assays, and in vivo murine studies.

CB NK cells were transduced with a modified TGF β receptor (Trans-NKs; mean transduction 42.5 \pm 5.5%). Trans-NK had no variations in their expression of activating receptors NKG2D, NKp44, or NKp30 ($p > 0.05$) or proliferative capacity ($p > 0.05$) vs. non-transduced (NT) NK cells. Unlike NT NK cells, pre-treatment of trans-NKs with TGF β resulted in increased Erk1/2 phosphorylation, consistent with NK cell activation. NT NK cells exhibited dose-dependent cytotoxicity against K562 target cells (45.2 \pm 4.69% killing); however following pre-treatment with TGF β , NT NK cells had impaired cytotoxicity (34.6 \pm 4.58% killing). In contrast, trans-NKs exhibited dose-dependent cytotoxicity (40.2 \pm 4.42% killing), which was enhanced following exposure to TGF β (47.2 \pm 5.17% killing). In a xenograft model of human NB, administration of trans-NKs delayed tumor progression by >14 days.

We can successfully generate modified NK cells, which are phenotypically and functionally superior at eradicating NB in a TGF β -rich environment. This strategy provides preclinical evidence for the establishment of “off the shelf” gene-modified NK cells as a treatment for patients with NB and other malignancies that utilize TGF β secretion for immune evasion.

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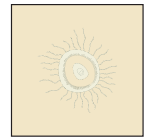
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CpG-Loaded Prussian Blue Nanoparticles as Photothermal Immunotherapy Agents for Cancer

Nanoparticle-based photothermal therapy (PTT) has been widely investigated in cancer therapy as a rapid and minimally invasive tumor ablation technique. An emerging area of interest is the effect of PTT on the immune system during tumor therapy, since PTT not only causes tumor cell death, but can also release tumor antigens and endogenous adjuvants under certain conditions. We describe biofunctionalized PBNPs as an enhanced “photothermal immunotherapy” wherein PBNP-based PTT is used for tumor ablation and in situ vaccine effects, complemented by adjuvant CpG-ODN biofunctionalization that increases antigen-processing and presentation. We believe PTT-elicited cell death combined with released antigens and added adjuvants will result in stronger/better engagement of an antitumor immune response. Building on our previously published studies, we assembled CpG on PBNPs using a layer-by-layer methodology. Nanoparticle characterization, therapeutic efficiency, and immune effects elicited by the therapy were tested in vitro using cell lines for both neuroblastoma and melanoma. Specifically, we looked at dendritic cell (DC) activation and T cell expansion after treatment with CpG-PBNPs and CpG-PBNP-based PTT. *In vivo* responses will be tested using syngeneic mouse models, wherein the mice will be intratumorally injected with CpG-PBNPs for PTT, and their tumor growth, survival, and immune responses will be studied. Our data suggests that CpG-PBNPs exhibit size, charge, and NIR spectrum stability over 7 days compared to naked PBNPs. Our CpG-PBNPs encapsulate CpG at a concentration of 40ug/mL, a concentration that is comparable to those used for current therapies. When CpG-PBNP was co-cultured with splenic DCs, there is an increased activation of DCs (measured by %CD40, CD80, CD86 expression levels) compared to DCs co-cultured with unmodified PBNPs and untreated controls. Further, the CpG-PBNP activated DCs increased proliferation of CD8+ T cells compared to controls. These findings demonstrate the potential of the modified PBNPs to overcome immune tolerance by increasing dendritic cell activation and T cell proliferation. In conclusion, we describe a “nano-immunotherapy” for treating cancers using CpG-PBNPs that leverages the ablative properties of PBNPs and the immunostimulatory properties of CpG. This combination treatment allows for a response that will lead to long-term survival and immune memory. Photothermal immunotherapy using CpG-PBNPs therefore have the potential of greatly improving the treatments and responses to cancer.

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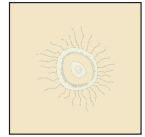
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PRAJA is Overexpressed in Glioblastoma and Contributes to Neural Precursor Development

PRAJA, a RING-H2 E3 ligase, is abundantly expressed in brain tissues such as the cerebellum and frontal cortex, amongst others, and more specifically in neural progenitor cells as well as in multiple cancers that include glioblastomas. However, the specific role that Praja plays in neural development and gliomas remains unclear. In this investigation, we performed bioinformatic analyses to examine Praja1 and Praja2 expression across 29 cancer types, and observed raised levels of Praja1 and Praja2 in gliomas with an inverse relationship between Praja1 and apoptotic genes and Praja substrates such as Smad3. We analyzed the role of Praja in the developing brain through loss of function studies, using morpholinos targeting Praja1 in embryonic zebrafish, and observed that Praja1 is expressed prominently in regions enriched with neural precursor cell subtypes. Antisense Praja morpholinos resulted in multiple embryonic defects including delayed neural development likely through increased apoptosis. Further studies revealed high levels of Cdk1 with loss of Praja1 in TGF- β or insulin treated cells, supporting the link between Praja1 and cell cycle regulation. In summary, these studies underscore Praja's role in mammalian brain development and Praja1 deregulation may lead to gliomas possibly through the regulation of cell cycle and/or apoptosis.

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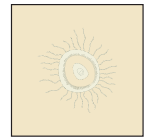
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Profiling of Urine Bacterial DNA to Identify an “Oncobiome” in a Mouse Model of Bladder Cancer

Although the bladder has traditionally been thought to be sterile, recent research has demonstrated that a variety of organisms colonize the bladder in health and disease states. The urine microbiome likely influences the onset and progression of bladder cancer, but precisely how is not known. Work by others has conversely shown that while chronic cystitis may be a risk factor for bladder cancer, bladder cancer patients with asymptomatic bacteriuria have a lower rate of tumor recurrence. We hypothesize that certain urine microbiome profiles may be linked to bladder cancer (the “oncobiome”). Our objective is to identify this oncobiome in a mouse model of bladder cancer. In a pilot study, a mouse given a dilute nitrosamine via the drinking water (0.1% n-butyl-n-(4-hydroxybutyl) nitrosamine, BBN), a bladder-specific carcinogen, had an altered bacterial community structure as compared to control mice. We then conducted a longitudinal study in which urine was collected from BBN-exposed and control mice over 5 months (n = 10, each group). At study conclusion, bladders were harvested and subjected to blinded pathological analysis. Bacterial DNA was isolated from the urine and oncobiome analysis was conducted by bacterial 16S rRNA V4 amplicon sequencing. A range of bladder pathologies were observed, including dysplasia, carcinoma *in situ*, and invasive cancer. Urine oncobiome analysis showed no differences between BBN and control groups at baseline, but greater diversity and relative abundances/deficiencies of certain species in the BBN mice as early as 1 month after beginning the study, although the profiles of both control and BBN-treated mice varied over time. While no bacterial group was consistently over- or under-represented in the BBN mice for the duration of the experiment, the Pasteurellaceae were over-abundant in multiple time points. Additional analyses and confirmatory experiments are currently underway. We will also test our central hypothesis in additional mouse models and by profiling human samples. Finally, we speculate that it may be possible to prevent or treat bladder cancer by manipulation of the bladder oncobiome.

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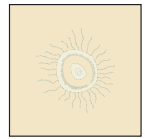
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SCHOOL OF NURSING

Variables Related to Colon Cancer Screening Rates Among Male Veterans

BACKGROUND/PROBLEM

Colorectal cancer (CRC) is the third most common cancer and the fourth leading cause of cancer deaths worldwide (Agency for Healthcare Research & Quality (AHRQ), 2013; Center for Disease Control & Prevention Colon Cancer (CDC), 2014).

CRC has been identified by the CDC as a preventable cancer. The CDC recommends colon cancer screening colonoscopy beginning at age 50 and every 10 years thereafter. The purpose of this study was to explore and compare differences in variables associated with the rate of CRC screening among male Veterans and age, race, income, educational level and marital status.

METHODS

An exploratory-comparative secondary data analysis design addressed study questions, using data from the 2014 Behavioral risk factor surveillance system (BRFSS). A Chi-Squared statistical analysis method was used to study the relationship between each independent variable and the dependent variable. An alpha level was set at 0.01 for all data analysis.

RESULTS

Data suggests a significant relationship exists between variables identified, showing an increased rate of Veterans receiving recommended CRC in specified time interval. Veterans were more likely than Non-Veterans to receive recommended CRC screening.

Among Veterans, people who were 65-74 years were more likely to have had CRC screening than people who were 50-64 years (74.2% vs 68.9%). Veterans who were white had a higher rate (70.1%) of meeting the CRC recommendations than Black Veterans (68.3%); Hispanic Veterans had the lowest rate of meeting CRC recommendations.

Higher income and higher educational level was related to higher rate of meeting CRC. Veterans who were married or living with a partner, also had a higher rate of meeting CRC recommendations.

CONCLUSIONS

There was a gap in the research studying male Veterans and how they choose to have a colonoscopy exam when influenced by identified variables. Further research, to include female Veterans is recommended. Providers in the VHA should provide targeted services to Veterans who have low social economic status to improve their CRC screening among all Veterans served.

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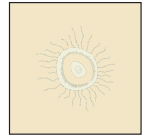
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INSTITUTE FOR BIOMEDICAL SCIENCES

Changes in the T-cell Immune Repertoire in AML Patients Developing Hypothyroidism During Anti-PD₁ Immune Checkpoint Therapy

Acute myeloid leukemias (AML) are a group of cancers of the myeloid line of blood cells that arise out of the bone marrow, progress rapidly, and interfere with the production of normal immune cells. Most AML patients who achieve a remission with standard cytotoxic chemotherapy will go on to relapse, after which there are very few treatment options. Immune checkpoint therapy is being explored as an immunotherapeutic option to treat AML relapse. Rationale for anti-PD₁ therapy, comes from preclinical data demonstrating increased PD-L₁ expression on tumor cells and that blocking the PD-₁ receptor on T-cells enhances T-cell function and tumor cell death. However, the PD-₁ checkpoint also has important immunoregulatory roles and is critical to maintaining peripheral tolerance.

Our group is currently testing the novel combination of the anti-PD₁ agent Pembrolizumab and the hypomethylating agent decitabine to treat relapsed/refractory AML (NCT02996474). Known side effects of immune checkpoint therapy do include immune-related adverse effects (irAEs), and on our trial, two patients developed hypothyroidism after 2 or 4 cycles of treatment. As recent studies have reported that as many as 20% of patients receiving Pembrolizumab will develop a thyroid-related immune condition, we are investigating the mechanism of this autoimmune irAE in our patients. Interestingly, HLA typing shows that these 2 patients shared 2 class I HLA alleles. These patients had low to no detectable anti-thyroid autoantibodies. From one of the patients, gDNA from blood, bone marrow, and positively selected CD8+ T-cells from bone marrow in longitudinal timepoints was extracted, and the CDR₃ region of the TCR β gene was sequenced to evaluate T-cell repertoire using the ImmunoSEQ platform from Adaptive Biotechnologies. Sequencing data revealed that the onset of hypothyroidism coincided with the expansion of several CD8+ T-cell clonotypes.

We are now collaborating with other groups at the NIH who have treated patients who also developed hypothyroidism during anti-PD1 immune checkpoint therapy. We are currently performing high resolution HLA typing on these patients to look for associations between class I HLA alleles and anti-PD1-induced hypothyroidism, as well TCR β sequencing to determine if there are shared T-cell clonotypes between these patients. Our work suggests that autoimmune events may be associated with detectable changes in T-cell clone frequencies, and that irAEs after anti-PD₁ therapy offer a model system for discerning a mechanism of action of this immunotherapy on CD8+ T-cells in relapsed/refractory acute myeloid leukemia and in other cancers.

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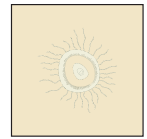
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Targeting p38 Isoforms to Control Growth, Survival, and Motility of Human Squamous Cell Carcinoma (SCC)

While cutaneous SCC is the second most common cancer worldwide, targeted treatment options are currently limited. p38 mitogen-activated protein kinases p38 α and p38 δ are overexpressed and/or activated in human skin SCCs, though the mechanisms by which they control skin carcinogenesis are poorly understood. We previously showed that keratinocyte p38 α or p38 δ loss significantly reduced squamous tumor growth in mouse models of skin carcinogenesis, identifying these kinases as potential targets for SCC treatment. To evaluate the requirement for p38 α and p38 δ function in growth, survival, and motility of human SCC cells, we inhibited both isoforms in SCC9 and SCC12 cell lines, derived from human head and neck and skin tumors, respectively, using a high potency p38 α /p38 δ co-inhibitor, Compound 62 (C62), or RNA interference (RNAi). p38 α /p38 δ co-inhibition induced apoptosis in both SCC9 and SCC12 cell lines, but not in normal human epidermal keratinocytes, via an "intrinsic", mitochondrion-dependent pathway, as shown by enhanced cleavage of poly(ADP)-ribose polymerase, a caspase 3 target. Upon p38 α /p38 δ co-inhibition, we noted decreased phosphorylation/activation levels of Erk1/2, a pathway implicated in promoting cancer cells proliferation and survival. Remarkably, while p38 α /p38 δ co-targeting increased apoptosis in an organotypic three dimensional (3D) co-culture model of SCC9 cells and stromal fibroblasts, it led to protection from apoptosis in SCC12 3D cultures relative to vehicle-treated controls. We found that the rates of scratch wound repair by SCC9 and SCC12 cells were significantly decreased not only by combined p38 α /p38 δ inhibition or RNAi-mediated knockdown, but also by selectively targeting, pharmacologically or genetically, of p38 α alone, indicating that p38 α is essential for SCC cell motility and invasion. Together, these data suggest that targeting both p38 α and p38 δ is a viable therapeutic strategy against SCC.

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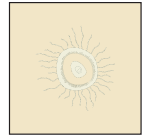
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INSTITUTE FOR BIOMEDICAL SCIENCES

Identification and Characterization of Pediatric Midline Glioma Specific Antigens: Wilms' Tumor in Diffuse Intrinsic Pontine Glioma

Pediatric high grade gliomas (HGGs), especially those associated with the pons, known as diffuse intrinsic pontine gliomas (DIPGs) are deadly pediatric brain cancer that makes up 10-15% of all central nervous system (CNS) tumors in children. Its anatomical location and infiltrative nature makes it one of the most challenging tumors to treat. Immunotherapy is a technique that is gaining more interest in CNS tumors. Identification of tumor associated antigens is one of many requirements in developing an effective immunotherapy. Wilms' tumor protein (WT1) has been ranked number 1 cancer immunotherapy target by National Cancer Institute. Many types of solid tumors have been shown to express WT1 and it is being examined as one of potential immunotherapeutic targets. Here we validated WT1 as a potential tumor associated antigen in pediatric diffuse midline gliomas using formalin fixed paraffin embedded (FFPE) tumor and intra-patient healthy specimens, fresh frozen post-mortem tissues and patient-derived DIPG primary cell lines. Our immunohistochemistry (IHC) staining of patient FFPE specimens showed strong WT1 immunoreactivity in tumor compared to adjacent normal tissue. Western blot of tumor tissues and cell lines were performed to further validate WT1 levels in the tumors versus adjacent normal tissues. Tumors showed cytoplasmic expression of WT1, confirmed by immunofluorescent (IF) staining. In addition, H3.1K27M subtype gliomas showed weak to absent WT1 immunoreactivity compared to strong to moderate in H3.3K27M subtypes. Western blots also validated the differential expression of the protein. Our study suggests that WT1 is a potential target protein for pediatric midline glioma immunotherapy.

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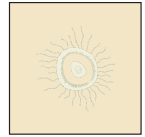
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SCHOOL OF MEDICINE AND HEALTH SCIENCES
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Manufacturing Antigen Specific T Cells for Tumor Immunotherapy

T cell therapies have been successfully used against certain malignancies—but broadening their application relies on generating specific cells against different targets. We therefore aim to develop a universal method for expanding T cells from any source against any antigen.

To evaluate different manufacturing methods we designed an optimization schema comparing four different protocols: (A) our current TAA-specific T cell protocol, (B) a TAA-specific protocol using naïve-T cells, (C) a TAA-specific protocol using memory T cells, and (D) a TAA-specific protocol using IL-18 during the initial priming step (a cytokine that has been shown to induce Interferon-gamma production in Th₁ cell populations).

Preliminary studies suggest that a protocol relying on naïve T cells (B) yields the highest fold expansion and the most specificity. T cells manufactured with this protocol from two healthy donors expanded at an average of 1705.11 fold \pm 436.94 and were specific for our tumor antigens of interest, as measured by Interferon- γ release on ELISPOT (458.75 \pm 154.50 spot forming cells (SFC)/1x10E5 cells plated for TAA vs 9.5 \pm 9.90 SFC/1x10E5 cells for human actin, a negative control). The final T cell product was predominantly of a terminal effector memory phenotype (CD45RO+CD62L-CCR7-); however, we plan to repeat our preliminary analysis with a comprehensive panel that includes looking for natural killer (NK) cells since IL-15, which is used heavily in our protocol, has been shown to drive NK cell differentiation and proliferation.

We have used this protocol (B) to successfully manufacture human papillomavirus (HPV) specific T cells. As a separate aim of this project, we optimized this manufacturing protocol for our Good Manufacturing Practices (GMP) facility by validating an alternate version of the protocol with changes relevant to the needs of the clinical manufacturing space. Such changes included slight alterations in cytokine concentrations and use of a GMP-compliant selection method for purifying the naïve cell population to be stimulated.

Future work will include completing the manufacture of the products we currently have in culture and increasing the number of donors. We will also continue to characterize these products with more comprehensive phenotyping and cytokine secretion assays.

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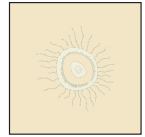
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

HDAC6 and DNMT Inhibition Affect Immunogenicity of Ovarian Cancer Cells: A Rationale for Combining Epigenetic and Immune Therapy in Ovarian Cancer

BACKGROUND

Therapies that activate the immune system to fight cancer have shown robust responses in most solid tumors. However, in ovarian cancer, most patients do not respond to these therapies alone. Inhibitors of epigenetic modifying enzymes increase immune signaling from cancer cells. Epigenetic modifiers DNA methyltransferase inhibitors (DNMTi) and selective histone deacetylase inhibitors (HDACi), such as HDAC6i, modulate immune-related pathways involved in anti-tumor immune responses. HDAC6i downregulates immunosuppressive ligands PD-L1 and PD-L2 by dephosphorylating pSTAT3 and upregulates tumor associated antigens (TAA) and antigen presentation machinery. Similarly, DNMTi activate anti-viral signaling via expression of Endogenous Retroviruses (ERVs) to trigger the type I interferon response. Our aim is to test if the combination of epigenetic modulators Nexturastat A (Next A), a selective HDAC6i, and 5-azacytidine (AZA), a DNMTi, can be safely used to increase an immune response in ovarian cancer. We hypothesize that these drugs will enhance tumor immunity alone and when combined with immune checkpoint blockades targeting PD-1.

RESULTS

HDAC enzymes are differentially expressed in A2780, HEY, Kuramochi, SKOV3, and TykNu human ovarian cancer cell lines. HDAC6 was expressed at lower levels in HEY and TykNu but at higher levels in SKOV3 and A2780. As previously reported, we believe this is due to the overexpression of the chromatin modifier ARID1A in SKOV3 and A2780. Upregulation of HDAC6 also correlated with a higher IC50 for Next A treatment in those cell lines. Immunoblots showed that PD-L1 protein, a marker of poor prognosis in ovarian cancer, decreased after treatment with Next A and even more in combination with AZA. qPCR demonstrates that combination therapy induce an additive type 1 interferon response and alters the expression of markers that modulate the tumor-immune reaction. DNMT1, the known target of AZA, was decreased after treatment with AZA and NextA, independently and in combination, a finding that has not been previously reported.

CONCLUSION

As shown previously, HDAC6 enzyme levels are higher in cell lines with ARID1A mutations. DNMT1 decreased after treatment with AZA, and surprisingly also after treatment with Next A. PD-L1 decreased after treatment with Next A and even more so when adding AZA. Thus, combining these epigenetic modifiers could lead to an additive effect on immune signaling through stimulation of antiviral signaling (DNMTi), which upregulates the immunosuppressive ligand PD-L1, which is then reduced by HDAC6 inhibition. We are testing this combination with anti-PD-1 in an immunocompetent mouse model of ovarian cancer.

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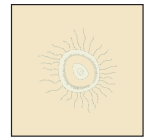
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Do You Know Where Your Patient's Cannabis Comes From? Dramatic Response to Integrative Treatment in Patient with Stage IV Colon Cancer

We present a 60 year old male with past medical history of hypercholesterolemia and nephrolithiasis, diagnosed with stage IV adenocarcinoma of the colon. The patient underwent routine surgical pathology exam and was found to have a primary tumor of 6.5 cm in the cecum (histologic grade: low, moderately differentiated) with extension into the serosal surface, greater than 6 positive regional nodes, and distant metastasis to the omentum. At that point the patient was given 3-6 months prognosis due to advanced metastatic colon cancer.

He initially presented to our clinic nine days status post partial right colon resection to discuss adjuvant chemotherapy vs. radiation vs. IV Vitamin C vs. IV Mistletoe. He was started on a low glycemic load, near ketogenic diet. In addition, he was started on methylated multivitamin, fish oil, OmegaAvail, N-Acetyl-Cysteine/Milk Thistle combination, probiotics and, and low-dose Naltrexone (LDN). He received 6 cycles of standard chemotherapy to shrink the tumor and weekly IV Vitamin C.

Patient also decided to seek out Medical Cannabis. While he was recommended to proceed through Washington DC legal route he opted out to obtain cannabis from another state due to lower cost and faster timing (average time from placing of recommendation to being able to obtain medical cannabis in DC is over 4 weeks).

Subsequently, the patient underwent exploratory laparotomy, during which minimal residual cancer was detected (1 mm microscopic focus at right colon resection site, 2 mm focus on greater omentum) and Biocept liquid biopsy tests were negative for circulating tumor cells (CTCs; defined as CD45-, DAPI+, CK+ or CK- cell).

This case represents an unusual response to a combination of chemotherapy and integrative approaches. Such "miracle cancer cures" are occasionally seen in integrative medicine practices and often generate lots of hype among cancer patient communities. Unfortunately, a clear understanding of how this result was achieved in this patient is not possible due to complex regimen.

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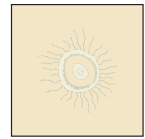
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Investigating a Novel Molecular Classification of Breast Cancer Based on the Tumor Proteome

BACKGROUND

Advancements in sequencing technologies have led to useful molecular classifications of breast cancer—specifically HER2, Basal-Like, Luminal-A, and Luminal-B classifications of the Prosigna PAM50 qPCR assay. These classifications allow a better prediction of disease outcome and have led to the development of more class-specific therapies. Towards a better understanding of the “proteo-genomic” relationship between somatic mutation and signaling in breast cancer, recent quantitative proteomic analyses suggest that breast-cancer may be subdivided into three, rather than four, distinct subgroups—Stromal, Luminal, and Basal. This opens the door for developing therapies based on the aberrant protein signaling of the tumor, especially for patients with significant stromal infiltrates, a phenotype that is strongly associated with poor clinical outcomes.

OBJECTIVE

A critical constraint to applying this proteomic classification to every breast cancer patient is the time and cost of whole proteome and analyses. We sought to identify an RNA signature similar to the PAM50 that predicts the newly classified proteomic subgroups based on differential RNA expression. Furthermore, we want to see if protein expression levels of the 50 genes in the PAM50 can be used to classify stromal subtype that emerged in the whole-proteome level.

METHODS

We began with RNA differential expression analysis of approximately 60,000 genes from 77 patients using The Cancer Genome Atlas (TCGA) database. We are now using k-means consensus clustering to explore the predictive value of the PAM50 protein expression in identifying the three groups identified in previous proteomics studies.

PRELIMINARY FINDINGS

We found that RNA differential expression could not stratify the patients into the proteomic subgroups, with the stromal group being the most heterogeneous patient population at the RNA level. This finding points to the vast amount of modification occurring between transcription and translation as well as the potential inaccuracy of classifications based on transcriptional clustering. We are in the process of conducting the consensus clustering.

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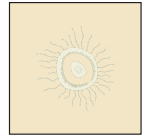
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INSTITUTE FOR BIOMEDICAL SCIENCES

BRCA1-Associated Protein 1 is a Tumor Suppressor in Pancreatic Cancer

BRCA1-associated protein 1 (BAP1) is a broadly expressed, nuclear-localized histone H2A lysine 119 (H2AK119ub) deubiquitinase that epigenetically regulates gene expression to regulate developmental decisions and cell cycle progression. BAP1 has also been identified as a player in DNA double-stranded break repair. Recent sequencing of cancer genomes revealed that loss of BAP1 occurs in a range of malignancies including uveal melanoma, mesothelioma, clear cell renal cell carcinoma, cholangiocarcinoma, and in sporadic cases of pancreatic cancer. Furthermore, germline mutations of BAP1 have been causatively linked to a familial tumor predisposition syndrome.

Meta-analysis of The Cancer Genome Atlas revealed that, although BAP1 is rarely mutated in pancreatic cancer, it is downregulated in about 15% of patients and this correlates with dismal prognosis. To study the role this epigenetic enzyme, I generated pancreas-specific Bap1 null mice in the context of Kras^{G12D}, the universal oncogenic driver of pancreatic cancer. I found that deletion of Bap1 induced genomic instability and compromised survival, even in heterozygotes. Gene expression and ChIP-seq analyses revealed that BAP1 loss resulted in an increase of transcriptionally repressive marks, including H2AK119ub and H3K27me3, and deregulated cell fate decisions and the response to DNA damage. Overall, our data suggest BAP1 functions as a tumor suppressor coupling epigenetic regulation and DNA repair pathways to restrict Kras-driven pancreatic cancer.

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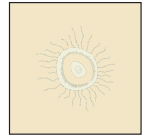
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TGF β Resistant Cord Blood Derived NK Cells As An “Off the Shelf” Immunotherapy for the Treatment of Medulloblastoma

Medulloblastoma (MB), the most common pediatric brain tumor, presents with a poor prognosis in a subset of patients with high risk disease. In these patients, current therapies are ineffective. Cord blood (CB) natural killer (NK) cells may be promising off the shelf effector cells for medulloblastoma immunotherapy because they recognize malignant cells without the need for a known target and are readily available from multiple banks. However, they are currently limited by immune suppressive cytokines such as Transforming Growth Factor β (TGF- β) in the MB tumor microenvironment.

To overcome the detrimental effects of TGF- β , we transduced CB-derived NK cells with a retrovirus expressing a dominant negative TGF- β receptor II (DNRII) (mean transduction efficiency of 39.54%, range 20.8 to 75.1%) and evaluated their ability to kill medulloblastoma in the presence of TGF- β .

Following manufacture using GMP compliant methodologies and transduction with DNRII, CB-derived DNRII-transduced NK cells expanded to clinically relevant numbers (mean 769 +/- 308 fold expansion) and retained both their killing ability (mean 21.16 +/- 8.26% for nontransduced NK cells at E:T of 5:1 vs 18.71 +/- 7.46% for transduced NK cells, n=5) and their secretion of IFN- γ upon activation. We observed that MB cell killing of CB-NK cells without DNRII expression was reduced (non-transduced cell killing at E:T 5:1 was reduced by 5% from 21.16 +/- 8.26% to 15.46 +/- 11.12% in TGF- β rich environment, n=5) while MB cell killing of CB-NK expressing DNRII was increased (mean 12.41 +/- 10.24% to 20.41 +/- 10.40% in TGF- β rich environment, n=4). More importantly they exhibit efficacy in vivo, migrating to the site of disease (mean 54.35 cells, n=2), and increasing survival in mice that were engrafted with a MB cell line ($p=0.0175$ vs untreated animals by Gehan-Breslow-Wilcoxon analysis, n=5 per group).

We have also begun looking at primary medulloblastoma samples, and show that these cells also secrete TGF- β .

In summary, CB NK cells expressing a DNRII have a functional advantage over unmodified NK cells in the presence of TGF-beta-secreting MB and may be an important therapeutic approach for patients with high risk disease.

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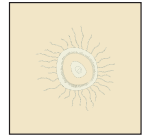
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Onyx Use in Extracranial Pathologies—A Retrospective Case Review

PURPOSE

Onyx is an embolic agent currently FDA approved for neurointerventional procedures such as in the treatment of aneurysms and arteriovenous malformations. Despite its limited indications, the agent's off-label use in the treatment of extracranial pathologies continues to increase. To date, there has not been a single-center study demonstrating a large number of cases demonstrating safe and effective peripheral embolization with Onyx.

MATERIALS

We performed a retrospective review of all cases that used Onyx between October 2010 and July 2016 at a single tertiary care academic university urban hospital. Institutional review board approval was appropriately obtained. Initial case selection was based on all of the procedures using Onyx. In our study, Onyx was used with the primary intention of providing definitive treatment; as a temporizing measure for future surgical resection; or for palliative symptomatic relief. Case selection was further scrutinized to exclude all cases involving the head, neck, or central nervous system.

RESULTS

49 patients were identified who underwent embolization with Onyx for extracranial pathologies. A total of 64 instances met our criteria. The incongruent number of cases compared to patients was secondary to multiple sessions for some patients. Such cases included: venous malformation, arteriovenous malformations, type 2 endoleaks, bronchobiliary fistula, and transgluteal rectal fistula. Technical success was achieved in 100% of cases. The clinical success rate was (98%). Among all 64 cases, only one complication had occurred with nontarget embolization of a renal pseudoaneurysm status post nephrectomy.

CONCLUSIONS

This study demonstrates the effectiveness of Onyx as an embolic agent that can be safely used beyond its limited FDA indication. Given the embolic agent's success in neurovascular pathologies, we were able to show a wide breadth and variety of extracranial uses.

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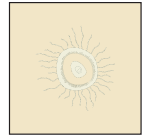
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Intracranial Targeting of Glioblastoma Multiforme with Cold Atmospheric Plasma

Glioblastoma multiforme (GBM) is a highly malignant aggressive neoplasm of the primary central nervous system characterized by rapid growth, extensive angiogenesis, and resistance to current therapies. The median survival is limited to 16-19 months after diagnosis. In this context, GBM treatment strategies remain largely palliative despite the advancement of multi-modal therapies. Thus, it is necessary to develop novel tools that can target proliferating tumor cells and enhance existing therapies. Conventional lasers in medical devices are based on the thermal interaction with tissues, which lead to necrosis and permanent tissue damage. In contrast, cold atmospheric plasma (CAP) has recently emerged as a novel therapeutic approach for targeting of cancerous tissue. Indeed, recent findings suggest that CAP jet interactions with tissue may allow for cell death without necrosis. However, studies to date have been limited primarily to subcutaneous implantation of tumors. While beneficial, this approach does not replicate the complex environment of the brain (i.e. GBM). Here, we developed a novel approach to target CAP to intracranial GBM tumors. This new device, termed μ CAP, consists of a Pyrex syringe through which CAP, employing helium gas, is supplied via the implanted endoscopic cannula. We first performed a set of experiments to test the influence of μ CAP on normal brain parenchyma. Female athymic Foxn1nu nude mice underwent intracranial μ CAP injection to the frontal lobe (15s total). Helium alone was administered as a control. Histological examination (Nissl staining) of the frontal lobe 7 days later revealed a similar number of apoptotic cells surrounding the injection site between μ CAP and control treated animals (9 ± 3 vs. 6 ± 1 apoptotic cells/ μm^2 , control vs. μ CAP, $n=2-3$, $p>0.05$). Similarly, no evidence of glia infiltration at the injection site was apparent. Next, nude mice underwent implantation of U87 glioblastoma cells (10^5 cells) into the frontal lobe and were simultaneously instrumented with a custom endoscopic cannula. Tumors were allowed to develop for 7 days and mice were then treated intracranially with μ CAP (15s total) or helium control. Using *in vivo* bioluminescence imaging (Figure), the tumor volume in control animals increased nearly 1000% over the course of a week, whereas μ CAP treated tumor volumes remained at baseline levels (day 7: 1035 ± 773 vs. 172 ± 107 radiance %baseline, control vs. μ CAP, $n=3$, $p>0.05$). These findings indicate that CAP has a minimal effect on healthy brain tissue, and further provide the first evidence for the potential of CAP to inhibit intracranial GBM tumor growth.

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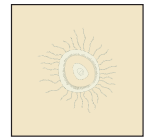
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Photothermal Therapy Generates a Thermal Window of Immunogenic Cell Death in Neuroblastoma

BACKGROUND

Nanoparticle-based photothermal therapy (PTT) has been widely investigated in cancer therapy as a rapid and minimally invasive tumor ablation technique. An emerging area of interest is the effect of PTT on the immune system, since PTT not only causes tumor cell death, but can also release tumor antigens and endogenous adjuvants (e.g. heat shock proteins, damage-associated molecular patterns (DAMPs)) under certain conditions. Immunogenic cell death (ICD) is a highly favorable cell death phenotype that initiates an adaptive immune response and is associated with improved therapeutic outcomes in cancer. Engaging the immune system during PTT is important as it offers the potential for persistent treatment responses and immunological memory.

METHODS

Here, we use Prussian blue nanoparticle-based PTT (PBNP-PTT) on Neuro2a neuroblastoma cells to describe the effects of PBNP-PTT on ICD, and subsequent tumor growth or regression. Three consensus guidelines were measured after *in vitro* PBNP-PTT treatment (ATP and HMGB1 release, calreticulin exposure) by flow cytometry. Neuro2a cells treated *in vitro* with PBNP-PTT were then prophylactically injected into mice, which were then inoculated with untreated neuro2a cells, to examine the *in vivo* effect of immune memory and subsequent tumor rejection.

RESULTS

We describe a thermal “window” of ICD elicited by PBNP-PTT in neuroblastoma. In studies using PBNP-PTT to established localized Neuro2a tumors, we observed that PBNP-PTT conformed to the “more is better” paradigm, wherein higher doses of PBNP-PTT generated higher cell/local heating and thereby more cell death, and consequently improved animal survival. However, *in vitro* analysis of the biochemical correlates of ICD elicited by PBNP-PTT demonstrated that PBNP-PTT triggered a thermal window of ICD. Specifically, the aforementioned markers of ICD were more highly expressed within an optimal temperature (thermal dose) window of PBNP-PTT (63.3-66.4 °C; ~5.6 log(CEM43)) as compared with higher (83.0-83.5 °C; ~12.8 log(CEM43)) and lower PBNP-PTT (50.7-52.7 °C; ~3.3 log(CEM43)) doses. Subsequent vaccination studies in the neuroblastoma model confirmed our *in vitro* findings wherein PBNP-PTT administered within the optimal temperature window (63.3-66.4 °C; ~5.6 log(CEM43)) resulted in long-term survival (33.3% at 100 days) compared with PBNP-PTT administered within the higher (0%) and lower (20%) temperature ranges, and controls (0%).

CONCLUSIONS

Our findings demonstrate a tunable immune response to heat generated by PBNP-PTT, which should be critically engaged in the administration of PTT, both alone and when PTT is administered in combination with immune adjuvants (e.g. TLR agonists) and/or immunotherapies (e.g. immune checkpoint inhibitors) for maximizing its therapeutic benefits.

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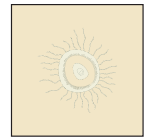
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Novel Roles of MicroRNA-200b in Reversing the Chemoimmuno-resistance by Inhibiting BRCA1 Nuclear Export in Triple Negative Breast Cancer

Triple-negative breast cancer (TNBC) is a subtype of breast cancer that is negative for estrogen and progesterone receptors (ER/PR) and human epidermal growth factor receptor 2 (HER2). It is typically associated with high rate of metastasis and limited targeted treatment options. Chemotherapy is the standard treatment for metastatic TNBC. However, the development of chemo-resistance limits its clinical application. Elevated expression of immune-related genes in TNBC suggests that immunotherapy strategies may provide new therapeutic options for TNBC. Programmed death 1 (PD-1) and programmed death-ligand 1 (PD-L1) immune checkpoint inhibitors have been approved by the FDA for TNBC treatment. However, tumor immune evasion is considered an important obstacle. BRCA1 is a nuclear–cytoplasmic shuttling protein that plays a key role in preventing the development of a malignant phenotype. BRCA1 dysregulation and nuclear export are an important mechanism in cancer development and chemoresistance especially in TNBC. Blocking BRCA1 nuclear export could be used as a strategy to prevent resistance. BRCA1 nuclear export has been reported to be mediated by several proteins such as BRCA1-binding protein 2 (BRAP2) and chromosomal maintenance 1 (CRM1, also known as exportin 1, XPO1). CRM1-mediated events have been implicated in breast cancer and involved in chemoimmunotherapy. microRNA-200b (miR-200b) is a cell-autonomous suppressor of EMT (epithelial–mesenchymal transition) and involved in tumor metastasis. In our present work, we discovered that miR-200b overexpression resulted in significant BRCA1 nuclear retention accompanied by down-regulated expression of CRM1 and STAT1 (signal transducer and activator of transcription 1). Bioinformatics analysis indicated that miR-200b directly targets STAT1, which was confirmed by luciferase assay. We demonstrated that STAT1 is a transcription factor (TF) of CRM1, by both Transfac analysis and chromatin immunoprecipitation (ChIP)-qPCR assay. In patient tissue samples, we found that miR-200b expression was relatively lower in TNBC compared to non-TNBCs. Furthermore, we demonstrated that miR-200b-mediated BRCA1 nuclear retention is associated with significant PD-L1 downregulation, and sensitizes the TNBC cells to chemotherapeutic agents. In addition, high level PD-L1 expression is associated with not only chemoimmuno-resistance but also tumor metastasis. These data provide strong evidence that miR-200b-mediated regulation of BRCA1 nucleus retention is through transcriptional regulation of CRM1 by STAT1, and miR-200b regulates PD-L1 expression in TNBC. In conclusion, this novel dual roles of miR-200b may serve as a strategy in metastatic TNBC therapy by repressing STAT1-mediated CRM1 transcription regulation, and reversing the chemoimmuno-resistance via PD-L1 inhibition.

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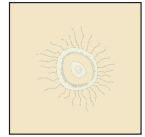
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

miR-203a-3p Regulates GATA6 in Esophageal Carcinoma

Esophageal cancer (EC) is the eighth most common cancer and the sixth most common cause of cancer death worldwide. MicroRNAs (miRNAs) are small non-coding RNAs that are dysregulated in a variety of cancers including EC. We identified a list of dysregulated miRNAs in EC by literature search, including miR-203a-3p, which was reported as a tumor suppressor and dysregulated in many malignancies. Target gene analysis showed that GATA Binding Protein 6 (GATA6) is a potential target of miR-203a-3p. It is reported that GATA6 is a member of zinc finger transcription factors that is amplified or overexpressed in many tumors. Therefore, we hypothesize that miR-203a-3p is a tumor suppressor miRNA by targeting GATA6 in EC. Esophageal squamous cell carcinoma (ESCC) cell lines (KYSE70 and KYSE180) and adenocarcinoma cell lines (JHU-ad1 and FLO-1), along with a normal esophageal cell line, HET-1A, and 9 ESCC FFPE samples were used in this study. The expression levels of miR-203a-3p and GATA6 were determined by quantitative reverse transcriptase PCR (qRT-PCR) assays. Functional analysis was performed by transfecting miR-203a-3p inhibitor or mimic to the above cell lines. MTT assays were used to determine the cell proliferation. Luciferase 3'-UTR-reporter assays were performed for miRNA target verification. We found that decreased cell proliferation was accompanied by significantly lower GATA6 expression in miR-203a-3p mimic transfected cells compared to the mock groups ($p < 0.05$) in four cell lines (KYSE70, Het-1A, JHU-ad1 and FLO-1). When cells were transfected with miR-203a-3p inhibitor in KYSE70, KYSE180, JHU-ad1, cell proliferation rate and GATA6 expression were both increased compared to the inhibitor mock controls ($p < 0.05$). Luciferase activity was significantly decreased when co-transfected with GATA6-WT and miR-203, compared to the control groups in KYSE70, KYSE180 and FLO-1 cell lines ($p < 0.05$). In clinical samples, we found that miR-203a-3p expression was downregulated in 89% of EC tissue compared to the adjacent normal or dysplasia tissue. To further determine the functional relationship between miR-203a-3p and GATA6 in EC, we are in the process of performing invasion assay and other functional assays, and obtaining more clinical samples to determine if miR-203a-3p functions differently in ESCC and adenocarcinoma. Our data has showed a reverse correlation between miR-203a-3p and GATA6 expression in EC, which, along with our bioinformatics analysis, indicates that miR-203a-3p downregulates GATA6 expression by directly targeting its 3'-UTR in EC. Therefore, miR-203a-3p may serve as a novel biomarker for EC management.

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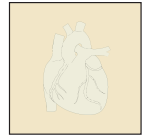
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

RNA Sequencing Identifies Long Non-Coding RNAs Related to Multiple Risk Factors for Cardiovascular Diseases

INTRODUCTION

Cardiovascular diseases (CVD) remains the major cause of mortality partially because it is frequently silent until it strikes. Only 50% of CVD risk is explained by current risk factors, leaving a significant unidentified risk of CVD. In prior studies, advanced RNA sequencing identified blood RNA biomarkers of coronary artery disease (CAD), which are currently being validated in a multi-center trial. Presently, the RNAseq data was reanalyzed to identify RNA biomarkers of other CVD risks.

METHODS

Patients (112) presenting for elective angiography were consented and whole blood was drawn into an RNA preservative for storage at -80°C . RNA was isolated, DNAsed, ribosomal RNA-depleted, and sequenced (SeqLL). Reads were aligned to the human transcriptome, counted, and analyzed for differential expression. A total of 96 samples were satisfactory for analysis, with an average of ~ 5 million informative reads per sample.

RESULTS

Hypertension: 78 transcripts were differentially expressed in hypertensive patients. Many had established relationships with blood pressure regulation, with an interesting change in LINC00467, a known regulator of the DKK axis, and corroborated by a parallel change in dickkopf3 (DKK3). Titin-antisense1 (TTN-AS1), another lncRNA, was also elevated 2-fold in hypertensive patients, and has been associated by GWAS with atrial fibrillation.

Race/ethnicity: African-Americans (AA) are at increased risk of hypertension and stroke. Examination of CAD vs normal in AAs identified 294 DEG, including TTN-AS1. A separate study examining transcripts modulated during heart failure, also observed that TTN-AS1 was regulated.

TTN-AS1 Targets: Analysis of co-expression data suggest that TTN-AS1 modulates certain transcripts by interfering with miRNAs. Several had prior GWAS connections to CVD, including ATP1B1, associated with Long QT syndrome; HDAC9, associated twice with Moyamoya Disease, involving cerebrovascular remodeling and stroke; NME7, associated twice with venous thromboembolism; and SYNPO2L, which is a newly identified GWAS loci for BP regulation and AFib.

CONCLUSIONS

Prior GWAS studies on very large cohorts have identified SNP loci for CVDs, but many have been uninterpretable because they fell within introns, intergenic regions, and/or non-coding transcripts. RNAseq allows us to cross-validate human RNA expression patterns in patients at risk for CVD, with putative risk SNPs, to narrow the candidate list. A top cross-validated hit is TTN-AS1, which is a long non-coding RNA that appears to modulate multiple known risk alleles for CVD, warranting more careful analysis.

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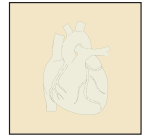
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Progression of Authorship of Manuscripts in The American Journal of Cardiology, 1958-2016

PURPOSE

Manuscript publication is essential in advancing ones career in academia. Consequently, the characteristics of authorship progression in academia has gained interest due to its value. Under this lens publications have become an elemental aspect of an applicants' application in all stages; medical school, residency, fellowship and faculty positions. Various studies looking at authorship developments have been established in other medical subspecialty such as Dermatology, Ophthalmology and Hand Surgery however a similar analysis in Cardiology is imperative. As a result, we explored the progression of authorship in *The American Journal of Cardiology*, a fundamental journal in the history of Cardiology.

METHODS

In this study, manuscripts published in 1958, 1966, 1976, 1986, 1996, 2006 and 2016 were analyzed. Parameters used were gender of published first and last authors, number of authors per article, the authors' qualifications and country of corresponding authors'. A total of 4329 were analyzed. Overtime we hypothesize an increase in authors per article, variety of authors' degrees, medley of countries contributing to authorship and an increase in female authorship.

RESULTS

The mean number of articles per author increased from 1.77 in 1958 to 8.58 in 2016. Similarly, average number of references per article increased from 8.3 in 1958 to 23.4 in 2016. The variety of qualifications of first authorship and last authorship also increased. Particularly, first authors and last authors holding degrees in MD/PhD and Masters. Female first and last authorship showed significant increase over the years. In 1958 female first authors comprised of 3% of all the publications compared to 22% in 2016. Analogously, female last authors accounted for 2% of all publications in 1958 compared to 19% in 2016. There was also a significant contribution in articles originating from "Asia" and "Europe".

CONCLUSION

There has been a significant increase in authors per article, references per article, variety of degrees and contribution from international authors in the *American Journal of Cardiology*. Female authors have increased significantly over the 58 year time period. In our poster presentation the trends observed highlighted similar shifts seen in other medical and academic fields. These characteristics in part can be explained by the increase pressure to publish to further ones career and increase of women into various fields of academia.

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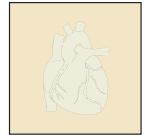
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Characterization of Developmental Changes in Electrical Activity during Cardiac Development of Whole Heart Models

BACKGROUND

Cardiovascular physiology studies have been largely limited to adult models; yet, significant developmental differences exist between the immature and adult heart. The field of pediatric research has largely been limited to immortalized cardiomyocyte cell lines, which lack physiologically relevant action potentials, and primary neonatal myocytes that have a limited life span and lack physiologically relevant automaticity. As a result, our understanding of developmental changes in ion channel expression, t-tubule development, and excitation-contraction coupling have been deduced from 2D simplified cell models. To fully understand cardiac development from neonate to adult, a physiologically-relevant 3D whole heart model is needed to monitor dynamic changes in electrical activity and excitation-contraction coupling.

OBJECTIVE

This study aimed to establish a pediatric research model to monitor developmental changes in electrical activity and excitation-contraction coupling, using both imaging tools and electrocardiograms.

METHODS/DESIGN

Sprague-Dawley rat hearts (3 days–adult) were excised, the aorta was cannulated, and then the heart was transferred to a temperature-controlled constant pressure Langendorff-perfusion system. The perfusate was supplemented with 10 μ M blebbistatin to reduce motion artifacts by mechanically uncoupling electrical and mechanical activity. Calcium (50 μ g Rhod2-AM) and voltage (62 μ g RH237) sensitive dyes were used to stain the heart, signals were acquired using a sCMOS camera (Andor, Zyla 4.2 Plus; >500fps). Electrocardiograms were monitored continuously (lead II configuration) and analyzed using ecgAUTO.

RESULTS/DISCUSSION

Initial results showed that compared to adult cohorts, neonatal rats displayed a longer action potential duration (APD80: adult= 85.9ms, neonatal=95.5ms, $p=0.026$), and a steeper Tau Fall (adults: 33.8ms, neonatal 69.9ms, $p=.012$) which are likely associated with delayed Ito expression. Calcium handling was also slower in the neonatal hearts (Cad80: Adults: 128.9ms, neonatal=138.8, $p=.004$), likely due to immature calcium handling and less robust calcium-induced calcium release. The developing excitation-contraction coupling machinery will be further probed using pharmacological tools to elucidate underlying mechanisms; and the newly developed pediatric model will be used for toxicological screening.

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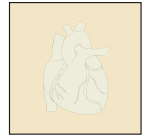
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Smartphone-Based vs. Traditional Dietary Counseling for the Mediterranean Diet in a US Cardiology Patient Population

BACKGROUND

Diet remains the largest uncontrolled risk factor for cardiovascular disease in the United States, and patients with heart disease require more extensive nutritional counseling to reduce their risk of adverse cardiovascular events. Randomized controlled trials conducted in Mediterranean countries have shown that following a Mediterranean diet reduces the occurrence of adverse cardiovascular events, and mobile health technology research demonstrates that smartphone applications help with weight loss.

OBJECTIVES

We tested the hypothesis that the Mediterranean diet can be applied to an American population and result in cardiovascular benefits. Simultaneously, we evaluated whether smartphone-based nutritional counseling results in better adherence to a Mediterranean diet compared with traditional, standard-of-care counseling.

METHODS

100 patients presenting to the cardiology clinic at the GW Medical Faculty Associates and meeting inclusion criteria were enrolled in a 6-month randomized controlled trial. Patients were arbitrarily assigned to receive either standard-of-care (SOC) or smartphone-based nutritional counseling (EXP) on the Mediterranean diet and scheduled for an in-person check-up at 1, 3, and 6 months to assess Mediterranean Diet Score (MDS, a validated measure of dietary compliance), patient satisfaction, weight and various biomarkers of cardiovascular health (e.g., BP, lipids, CRP, HbA1c).

RESULTS

Baseline characteristics, including age, gender, and current cardiovascular status, of patients in the control (SOC) and experimental (EXP) group were statistically similar. Compliance and satisfaction with the Mediterranean diet increased significantly overtime for both treatment groups ($p < 0.001$) but did not vary significantly between the groups ($p > 0.2$). In addition, there was no statistically significant improvement in cardiovascular health overtime or between groups per our results. Patients in EXP did, however, experience significantly greater weight loss compared with SOC ($p = 0.04$).

CONCLUSIONS

Per this US-based study of cardiology patients, the Mediterranean diet can be incorporated into the American lifestyle and adherence to the Mediterranean diet is effectively accomplished by both traditional and smartphone-based nutritional counseling.

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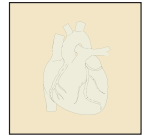
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Validation of Bioelectric Impedance Cardiography for Measuring Diastolic Cardiac Function

PURPOSE

To validate the use of bioelectric impedance cardiography (ZCG) for assessing diastolic cardiac function (DF). Current methods for measuring DF are expensive and often impractical when attempting to assess DF during physical activity or during exercise performed in an upright position. If validated, ZCG may provide a cheaper and more versatile alternative for assessing DF.

METHODS

Recreationally active participants ages 18-45 years old who were free of cardiovascular disease participated in the study. During a single visit, participants received a standard resting clinical echocardiogram followed by an exercise stress echocardiogram employing a treadmill. DF was measured at rest and during an elevated heart rate during the post-exercise stress test cool-down period, respectively. All echocardiogram DF measurements were obtained in a side-lying or prone position. DF variables obtained from echocardiography were the early to late peak ventricular filling velocity ratio (E/A ratio) and early peak filling velocity to early diastolic mitral annular velocity ratio (E/E' ratio). The ZCG device was employed to measure DF concurrently during both echocardiogram assessments for each participant. The early diastolic filling ratio (EDFR) obtained via the ZCG is reported by the device manufacturer to be analogous to the E/A ratio obtained via echocardiography.

RESULTS

To date, 16 subjects have been enrolled in this ongoing study. Results from a Pearson correlation analysis revealed a significant positive correlation between the EDFR and the E/A ratio ($r = 0.467$, $p = 0.009$). No significant correlation was observed between the EDFR and E/E'.

CONCLUSIONS

These preliminary findings of our ongoing study suggest that the ZCG device may be a valid tool for assessing some components of DF. ZCG is less expensive than echocardiography and does not require a trained technician, and can assess global cardiac cycle function during a variety of physical activities in any body position. Recent studies demonstrate that diastolic dysfunction often precedes systolic dysfunction, and is an independent predictor of mortality in some disease models. Our preliminary findings suggest that ZCG may eventually play a role as a less expensive tool to screen for diastolic dysfunction in diverse clinical settings, potentially removing some barriers to detecting early cardiac abnormalities.

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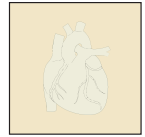
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Differential Roles of p38 MAPKs in Doxorubicin-Induced Cardiotoxicity

Doxorubicin (DOX) is a highly potent anti-cancer therapy agent. However, it has been associated with severe cardiotoxic effects that can result in fatal cardiomyopathies. Previous studies have identified the role of stress signaling pathways, particularly those involving p38 MAPKs in the development of cardiotoxicity. Four different isoforms of p38 MAPKs are expressed in the heart and they have been associated with differing functions. We hypothesized that p38 MAPKs have an isoform-specific role in DOX-induced cardiotoxicity.

We tested this hypothesis in mice and human hearts. Fifteen (15w) and twenty-two (22w) week old mice—WT and with genetic deletion of p38 α , p38 β , p38 γ , p38 δ and p38 $\gamma\delta$ MAPK were treated with either 20 or 30 mg/kg DOX or saline (vehicle) and their survival was tracked over 10 days. Cardiac function was assessed using echocardiography and electrocardiography. Age-, sex-, dose- and p38 MAPK-specific survival responses were studied in these mice. Specifically, while saline-treatment did not influence survival of mice in any group, DOX treatment resulted in varying survival rates in WT mice, with the lowest survival rate observed in 15w male and female mice treated with 30 mg/kg DOX. Interestingly, among young, male p38 mutant mice treated with DOX, survival rates were lower relative to saline treated controls, but not different relative to DOX-treated WT. However, among young, female p38 mutant mice treated with DOX, low survival rates were observed in p38 β , p38 γ and p38 $\gamma\delta$ knockout (KO) relative to saline-treated controls; while p38 δ and p38 β KO had higher and lower survival rates, respectively, relative to DOX-treated WT. Survival rates correlated with improved cardiac mechanical and electrical function in p38 α and p38 δ KO mice, respectively.

Next, we treated human cardiac slices with DOX (0–50 μ M) or DOX (5 μ M) + SB203580 (p38 α and p38 β micro inhibitor, 5 μ M) or DOX (5 μ M) + Compound 62 (pan p38 MAPK inhibitor, 1 μ M). Dose-dependent slowing of conduction velocity (CV) was observed in human slices treated with DOX. SB203580 failed to prevent DOX-induced CV slowing while Compound 62 rescued CV during DOX treatment.

These data indicate the differential roles of individual p38 MAPK isoforms in cardiotoxicity development due to DOX treatment. While deleting p38 α or p38 δ isoforms prevented cardiotoxicity, deleting p38 β promoted it in female mice. Therefore, blocking p38 α and/or p38 δ may be advantageous to prevent DOX-induced cardiotoxicity.

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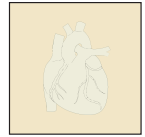
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Risk Stratification of Chest Pain Patients in the Emergency Department by Assessing Diastolic Function Using Tissue Doppler Imaging of Left Ventricular Wall Segments

BACKGROUND

Chest pain is one of the most common chief complaints seen within emergency departments (ED). Diagnostic tests are therefore key to parsing out high risk and low risk chest pain patients. Tissue Doppler Imaging (TDI) is a means of assessing myocardial tissue motion in order to assess the function of the myocardium. Specifically, TDI can detect impaired relaxation of the heart during early diastole, which precedes ischemic changes on electrocardiogram (EKG) and ischemic systolic wall dysfunction on echocardiography. In this proof-of-concept study, we propose that the use of TDI in the ED can function as an objective tool allowing emergency providers to more accurately stratify chest pain patients into high-risk and low-risk groups.

METHODS

Early diastolic left ventricular wall movement (E') was measured in a total of 60 patients using the TDI method at the medial, lateral, anterior, and posterior/inferior mitral annulus. Normal tissue velocity was defined as >9 cm/s for the lateral, anterior, and posterior/inferior walls, and a septal wall speed of >7 cm/s. Studies were performed by two independent operators. Patients with one or more abnormal TDI value by either echocardiographer were considered positive for an abnormal study. The results of the study were compared to a diagnosis of ischemic chest pain determined by the gold standard cardiac workup including EKG findings, HEART score for major cardiac events, troponin levels, stress test, and any further intervention.

RESULTS

The specificity of TDI for detecting ischemic causes was 72.55% (95% CI of 58.02-83.67) with a sensitivity of 100% (95% CI of 39.60-100.00). In addition, the test demonstrated a positive predictive value (PPV) of 22.22% (95% CI of 7.37-48.10) and a negative predictive value (NPV) of 1 (95% CI of 88.29-100.00). Likelihood ratios were calculated as a positive likelihood ratio of 3.64 (95% CI of 2.33-5.70) and a negative likelihood ratio of 0.

CONCLUSION

This proof-of-concept study demonstrated a high specificity and sensitivity for detecting ischemic causes of chest pain and can serve as an adjunct to the current standard chest pain workup and aid in decision making. The study does not imply that TDI can replace other modalities of current chest pain workup. Further studies are needed to investigate the limitations of TDI as well as its indications in the management of patients presenting to the ED with chest pain.

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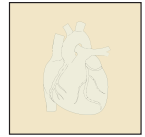
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Transplantation of p53-Silenced Endothelial Progenitor Cells (EPCs) Under Renal Capsule: A Potential Treatment for Diabetic Kidney Disease (DKD)

Diabetic kidney disease (DKD) is a major vascular complication of diabetes, which leads to glomerulosclerosis and poor perfusion. Improving the renal vasculature may help to halt or reverse the kidney injury. Use of mesenchymal stromal cells (MSCs) in diabetic nephropathy showed some positive results. However, endothelial to mesenchymal transformation of endothelial-like structures in the kidney may occur in diabetic kidney disease (DKD) post mesenchymal cell delivery. Here, we investigated whether transplanting EPCs that have p53 gene, transiently silenced, (using Adenovirus) under renal capsule could improve kidney function in DKD mice.

METHODS

C57Bl6 mice were made diabetic by using STZ, next we confirmed proteinuria in STZ-induced type 1 diabetic C57BL/6J mice. We transplanted 0.3 million p53-silenced EPCs, transduced ex-vivo with Ad-p53-sh or Ad-Null-EPCs, bilaterally, under each kidney capsule. Another control was non-STZ normal mouse. Urine was collected at weeks 1, 2, 3 and 4 for volume and protein estimation. Renal blood flow was measured by laser Doppler, by exposing kidneys, immediately prior to sacrifice. Kidneys were harvested post-sacrifice followed by qRT-PCR.

RESULTS

There was no proteinuria after week 2 in the p53sh-EPC transplanted mouse. Enhanced blood flow (3.2 fold) was noted with the delivery of p53sh-EPCs compared to null. The degree of improvement of proteinuria and renal blood flow in the diabetic mice were similar to the non-STZ mouse. Interestingly, markers for neovascularization, such as eNOS (4.5 fold, $p=0.002$) and VEGF-A (1.5 fold, $p=0.03$) were upregulated in kidney tissue, significantly, post-transplantation of p53 silenced EPCs compare to null EPC transplanted kidney.

CONCLUSION

Transient silencing of p53 gene in mouse EPCs help to improve proteinuria, diabetic polyuria, and renal blood flow and may have a prominent therapeutic role in DKD.

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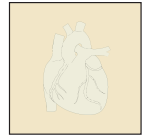
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Effect of Oxytocin on Obstructive Sleep Apnea and Heart Failure

As many as 24% of males and 9% of females within the United States population suffer from obstructive sleep apnea (OSA), which poses significant cardiovascular risks, including sudden death, hypertension, arrhythmias, myocardial ischemia, and stroke. Yet, the primary treatment for OSA, continuous positive airway pressure (CPAP), is poorly tolerated by patients and has a low compliance rate of 50-60%. Intermittent hypoxia and arousals from OSA lead to perturbations of the autonomic nervous system. Such increase in sympathetic activity and decrease in parasympathetic activity are partly responsible for the adverse cardiorespiratory events associated with OSA. Recent studies have shown that activating oxytocin receptors correct the autonomic imbalance in fight-or-flight situations. Therefore, we tested whether or not intranasal oxytocin administration can prevent or reverse adverse cardiorespiratory events by increasing parasympathetic activity and restoring the autonomic balance during apneic and hypopneic events. We saw no statistically significant difference in arrhythmia frequencies between the oxytocin treatment night and the placebo night. However, since the subjects recruited for the study did not have pre-existing heart conditions, it is possible that arrhythmias were too infrequent and random for comparison.

Similar to OSA, heart failure (HF) is marked by an autonomic imbalance: increased sympathetic activity and parasympathetic withdrawal. Although beta blockers, common medication prescribed to HF patients, are able to control the elevated sympathetic activity, it does not address the reduction in cardiac parasympathetic tone associated with HF. Recent animal studies show that increasing parasympathetic tone during HF via vagal nerve stimulation improved left ventricular structure and function. Therefore, we assessed oxytocin neuron activation as a means to improve cardiac function in an animal model of HF. Oxytocin neuron activation did not significantly change arrhythmia frequency. We observed possible ST segment changes, which needs to be further investigated. Oxytocin remains a potential therapeutic agent for OSA and HF, but additional work is needed to optimize its course in treatment.

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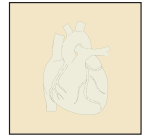
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The Surgical Implantation of Novel Epicardial Pacemakers in Rodents

OBJECTIVES

Rodent hearts have been used as models of cardiac disease for many years in the investigation of cardiovascular physiology. Chronic pacing has been used to induce heart failure or arrhythmia in the past. However, the size and durability of the devices, as well as the viability of the animals following the implantation, have been some of the many challenges. In this study, we present a new technique for the successful implantation of wireless cardiac pacemakers in rat hearts.

METHODS

We present two novel wireless and battery-free pacemakers that are currently under development. One model is completely biodegradable, while the other is not. Anesthesia is induced in the isoflurane chamber and the rats are intubated using standard technique and connected to the ventilator. A left thoracotomy is performed, the lung is mobilized posteriorly, and the pericardium is opened. The pacemaker electrode is sutured to the epicardium using 6-0 monofilament non-absorbable sutures. The receiver portion of the pacemaker is placed in a subcutaneous pocket. After the chest is closed, the rats are extubated and monitored until sternal recumbency is regained. Afterwards, the rats are placed in a cage with radiofrequency (RF) wireless control stimulator and the data was recorded using a standard small animal electrocardiogram (EKG) recording device.

RESULTS

A total of five functioning pacemakers have been implanted. The rats had unremarkable post-operative course and showed long-term survival. The devices were activated and we were able to observe the change of EKG from normal sinus rhythm at 300 to 340 bpm to 400 to 500 ventricular rhythms with wide QRS. Once the remote signal was turned off, we observed a return of cardiac rhythm to normal sinus rhythm.

CONCLUSION

The surgical technique we have developed is an effective and reproducible approach for the implantation of wireless epicardial pacemakers in rats. This will lead to the expanded use of wireless pacemakers in rats that will help recreate human disease patterns in animals.

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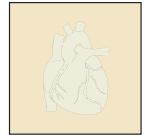
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Skin-Specific Expression of PCSK9 May Provide Novel Link for Increased Cardiovascular Disease Risk in Psoriasis

Cardiovascular disease (CVD) remains the most common cause of death worldwide and is more prevalent in chronic inflammatory states such as psoriasis. Recently, pro-protein convertase subtilisin/kexin type 9 (PCSK9) has gained attention as a novel therapeutic target in CVD due to its LDL cholesterol lowering capabilities. Therefore, we sought to investigate the relationship between PCSK9 and psoriasis. In patients with psoriasis (n=88), circulating PCSK9 levels are elevated compared to those of healthy volunteers (HV) (n=52) (Psoriasis: 253 ng/mL vs HV: 189 ng/mL, $p < 0.001$) and are positively associated with coronary artery calcium (CAC) scores, beyond traditional cardiovascular risk factors ($\beta = 0.38$, $p < 0.004$).

Similarly, in our mouse model of psoriasis, we observe a 1.7-fold increase ($p < 0.0001$) in circulating PCSK9 compared to that of littermate controls. Moreover, there is a robust relationship between circulating PCSK9 levels and psoriasis skin severity ($\beta = 0.92$, $p < 0.001$). We also find that although hepatic PCSK9 protein levels are unchanged in the psoriatic mice, low-density lipoprotein receptor (LDLR), the direct target of PCSK9, is significantly decreased at the protein level. Furthermore, we determine that both PCSK9 mRNA and protein levels are elevated in the lesional skin of psoriatic mice compared to those of littermate controls, a finding we confirmed in our psoriatic human skins. Taken together, we postulate that psoriatic lesional skin, specifically the epidermis, is the source for elevated plasma PCSK9, thereby decreasing hepatic LDLR, and suggesting a potential link between psoriasis and cardiovascular disease.

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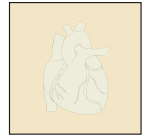
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Prenatal Mono-2-Ethylhexyl Phthalate Exposure Alters Neonatal Cardiomyocyte Physiology

BACKGROUND

Di-(2-ethylhexyl) phthalate (DEHP) is a main component of polyvinylchloride plastics used to soften otherwise rigid plastics. DEHP containing plastics are often used to manufacture medical devices that are used in neonatal intensive care units (NICU). Consequently, NICU patients with immature glucuronidation pathways are often exposed to high levels of phthalates. Furthermore, DEHP and its main metabolite, mono-2-ethylhexyl phthalate (MEHP) have been detected in human amniotic fluid and umbilical cord blood, suggesting exposure to developing fetuses. Phthalates are known endocrine disruptors and prenatal exposure is likely to influence cardiac development and physiology. Phthalates have previously been shown to affect adults, yet little is known about the outcomes on immature cardiomyocytes.

METHODS

Pregnant rats were administered 3.6 mM MEHP treated water ad libitum starting at gestation day 2. Water levels were monitored every two days to calculate total final ingestion of the treated water. Hearts were isolated from 1-2 day old pups and the cardiomyocytes were plated on coverslips as confluent monolayers. The plated cardiomyocytes were loaded with calcium sensitive dyes and externally paced to monitor physiological changes.

RESULTS

In-utero exposure to MEHP prolonged calcium transient upstroke and reuptake phases. Mean time from t0 to 30% of cytosolic calcium reuptake (CaD30) for control cells was 231 ± 0.016 ms and 357 ± 0.034 ms for MEHP treated (p-value=0.01). Calcium transient upstroke duration time to 90% reuptake for control was 56.85 ± 4.8 ms and 95.13 ± 9.5 ms for MEHP cells (p-value= 0.007). Lastly, the maximal rate of capture at pacing frequencies 2 and 3Hz were 100 and 80% for control and 80 and 0% for the MEHP cells, respectively.

CONCLUSION

In-utero MEHP exposure alters cardiomyocyte excitation-contraction coupling, calcium handling and cardiac physiology. Our data suggests that MEHP may adversely affect the activity of Na^+/Ca^+ exchangers (NCX), SR Ca^+ ATPase pumps (SERCA) and/or ryanodine receptor channels. Since MEHP is a known endocrine disruptor, we will investigate downstream effects on cardiac maturation including binucleation and α - and β - myosin heavy chain quantity.

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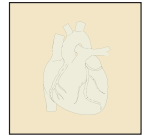
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Assessing Recurrence of Atrial Fibrillation Using Inflammatory Biomarkers

Atrial fibrillation (AF) is a condition where a group of conductile cells in the atria begin to signal independently of the pacemaking cells of the heart. This leads to a rapidly irregular heart rate resulting in an uncoordinated flow of blood through the heart, which increases the risk of life-threatening thromboembolic events. Patients who are candidates for surgery are treated via catheter ablation targeting the aberrant group of cells which cuts the circuit and restores a normal sinus rhythm. About 30% of patients that undergo this treatment have their AF successfully abolished, only for it to reoccur. We aimed to assess the role of inflammatory biomarkers and how they predict the reoccurrence of AF. We recruited 10 patients with AF and isolated peripheral blood mononuclear cells (PBMC) before, one week after, and one month after the catheter ablation. PBMCs were then cultured for 24 hours and their secretions collected and analyzed using ELISA and Multiplex-luminex kits. The future direction of the study is to use a comprehensive panel of biomarkers in order to identify inflammation-dependent AF and to predict AF recurrence in patients post-ablation.

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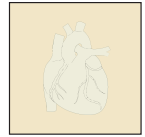
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Extinction of Blood Pressure and Heart Rate Responses to Conditioned Fear

BACKGROUND

Post-traumatic stress disorder (PTSD) is characterized by an impaired ability to extinguish fear associations that trigger exaggerated neurophysiological responses, which may contribute to increased cardiovascular (CV) risk. The objective of this study was to evaluate the effects of learned inhibition or extinction on the conditioned cardio-autonomic response during fear memory recall. We hypothesized that extinction training would lead to a temporary reduction of conditioned heart rate (HR) and systolic blood pressure (SBP) responses. Methods: In male C57BL/6 mice, Pavlovian fear conditioning combined with simultaneous in-vivo telemetry was used to assess CV and behavioral measures in home-cage and testing contexts. The conditioned CV response was evaluated during short-term (STR) (1-hour post-extinction) and long-term recall (LTR) (2 weeks post-extinction) of the CS in the home-cage.

RESULTS

Freezing in response to the CS from Day 1 to Day 2 was reduced in fear conditioned mice ($80\% \pm 7$ vs. $57\% \pm 11$; $p < 0.05$), whereas non-conditioned animals did not respond to the CS on either day. SBP and HR were elevated throughout each session, regardless of whether or not the animals had been previously fear conditioned. Two-weeks after extinction training, fear-conditioned animals in the home-cage context exhibited a strong conditioned CV response to the CS, which remained elevated over the course of four CS presentations (change in SBP $18\text{mmHg} \pm 2$ and HR $166\text{ bpm} \pm 42$; $n = 8$; $p < 0.05$). 24 hours after fear conditioning, we observed increased CV activity in response to the CS (change in SBP $17\text{mmHg} \pm 4.3$ and HR $101\text{ bpm} \pm 34.3$; $n = 9-12$; $p < 0.05$) over 4CS trials. Conditioned mice were then split into two groups: (1) extinction (2) no extinction. The extinction group was repeatedly re-exposed to the CS over two days of extinction training. Both groups went through a final conditioned CV response test in the home cage. In non-extinguished controls, there was a significant increase in SBP during CS exposure ($114\text{mmHG} \pm 2.7$ vs. $124\text{mmHG} \pm 4.3$; $p < 0.05$), while in the extinction group, the SBP response was completely abolished. Heart rate did not change in response to CS exposure in either group at this time point.

CONCLUSIONS

These data demonstrate that both short and long-term recall of fear memory elicit a conditioned blood pressure response that can be temporarily attenuated by extinction training. Furthermore, these data suggest that conditioned blood pressure and heart rate responses may vary in their sensitivity to inhibitory learning.

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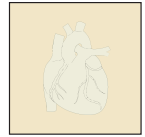
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Impact of Socioeconomic and Geographic Factors on Prenatal Diagnosis of Hypoplastic Left Heart Syndrome (HLHS) and d-Transposition of the Great Arteries (d-TGA)

Congenital heart disease (CHD) is the most common birth defect and persists as a significant cause of neonatal and infant mortality in the United States. Prenatal detection of CHD allows for timely decision making and planning for delivery and may improve postnatal outcomes, especially in specific congenital heart defects, including hypoplastic left heart syndrome (HLHS) and D-transposition of the great arteries (D-TGA). Prenatal diagnosis remains low, however, despite nearly universal use of ultrasound during fetal development. Therefore, defining barriers to diagnosis will be essential to improving these rates. The purpose of the current study was to describe the following socioeconomic and geographic factors in subjects diagnosed with HLHS and d-TGA at Children's National Medical Center: percentage of households living in poverty, median household income, median value of housing, population > 50% of a vulnerable ethnicity (African American, Hispanic, Native American), education level, and distance from a cardiac surgical center.

Retrospective chart review was performed for subjects with HLHS and D-TGA who had their first admission/visit recorded at Children's National Medical Center between January 1, 2012 and December 31, 2016. Using maternal address, cdxzipstream software derived census tract data to assess socioeconomic factors.

105 subjects met inclusion criteria for the study. 59 subjects had a diagnosis of HLHS and 46 had a diagnosis of D-TGA. Census data revealed the mean of households in poverty as 9.58% (range 0.38-33.38%). Average median household income was \$83,142 (range \$25,957-\$250,000) and average median housing value was \$349,425 (range \$89,000-\$1,042,600). 38 census areas were >50% vulnerable ethnicities. On average, census areas were 11.64% Hispanic (range 0-79.94%), 28.13% Black (range 0-99.5%), and 0.32% Native American (range 0-7.43%). 41.54% (range 6.38-76.55%) of persons age 25+ possessed a high school degree and 49.05% (range 5.73-93.34%) of persons age 25+ possessed a bachelor's degree or higher. As a measure of access to care, distance from a pediatric cardiac surgical center was assessed. Census areas were an average of 30.42 miles by car with an estimated 43 minutes of travel time and 33.62 miles using public transportation with an estimated 158 mins of travel time. Results analyzing differences in outcomes and socioeconomic factors between prenatal and postnatal diagnosis are pending.

By evaluating the relationship of socioeconomic and geographic factors to prenatal diagnosis of CHD, interventions can be implemented to eliminate barriers to diagnosis as well as overlapping barriers in clinical management for vulnerable populations.

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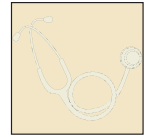
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Not to be Overlooked: The Need for Increased Dialogue Between Patient and Provider Surrounding Medical Foods in IBD

BACKGROUND

Medical foods are treatments with growing evidence for use in a variety of gastrointestinal diseases. They are safe and have proven efficacy in helping to manage inflammatory bowel disease (IBD). They can be used as monotherapy or in addition to traditional therapies. While medical foods offer new, evidence-based options to treat IBD, physician awareness of them remains uncertain. We examined the frequency with which gastroenterologists discussed their use for IBD management and explored associations with gender or race.

METHODS

A retrospective review of all IBD patients seen at an urban university gastroenterology practice in a 6 month period was performed. There were no exclusion factors. Patient age, gender, ethnicity, and disease type were obtained. Records were evaluated for discussions about medical foods as IBD therapy. The association between discussion of medical foods and gender or race were analyzed with a Chi-square test.

RESULTS

268 records were reviewed. Of those, 118 were men and 150 were women, with a mean age of 43. 80 were Black, 143 White, 6 Latino, 10 Asian, and 29 other. 158 had a diagnosis of Crohn's and 109 had ulcerative colitis (UC), while 1 had indeterminate colitis. 8 (3%) in the cohort had a documented discussion about using medical foods to treat IBD. 6 discussed VSL#3 (2 Crohn's, 4 UC), while 2 discussed Ensure (2 Crohn's). There was no association between discussion of medical foods and gender ($P=0.3$) or race ($P=0.9$).

CONCLUSION

Medical foods are emerging in IBD management, with new evidence supporting their use in a diversity of clinical settings. While previously unclear, our study demonstrates that few IBD patients have documented discussions about medical foods. Though some discussions about medical foods may be undocumented, that only 3% of patients had documented discussions suggests clinicians are missing an opportunity to utilize this therapeutic option. Given the growing evidence for therapeutic use of medical foods in IBD, physicians should increase the visibility of their use.

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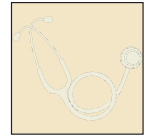
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The Association of Polymorphism rs3736228 within the LRP5 Gene with Bone Mineral Density in a Cohort of Caucasian Young Adults

INTRODUCTION

Osteoporosis is a significant burden for our aging population. Developing a better understanding of the genetic underpinnings of poor bone quality may assist in the future development of prevention strategies. Correa-Rodriguez et al. have identified a group of single nucleotide polymorphisms (SNPs) that were associated with bone mineral density (BMD) in a population of Spanish Caucasians. In particular, they found that SNP rs3736228 in the low-density lipoprotein receptor related protein 5 (LRP5) gene had an influence on BMD. While the role of LRP5 in the Wnt canonical pathway has been fairly well characterized, its association with phenotypic BMD and osteoporosis has only been explored in a limited fashion. The aim of this study is to expand on this, and to replicate the findings of previous studies in a cohort of healthy young adults.

METHODS

Cohort: The University of Calgary cohort from the Assessing Inherited Metabolic Syndrome Markers in the Young (UC AIMMY) study. Participants included consist of 168 healthy, predominantly Caucasian young adults. Phenotypes: height, weight, BMI, and total BMD. **Genotyping:** Allelic discrimination was determined. **Statistical Analysis:** After being tested for Hardy-Weinberg equilibrium (HWE), the data was run through analysis of covariance (ANCOVA).

RESULTS

Using a dominant model, we found that females with one or more copies of the risk T allele of SNP rs3736228 had a significant negative association with total BMD ($p = 0.0347$). However, a similar association was not seen in males in this cohort. We did not find a significant association for this polymorphism and height, weight, or BMI.

DISCUSSION

Polymorphisms in rs3736228 alter the codon in position 1330, downregulating the LRP5 cell surface receptor function. The LRP5 gene has now been shown in multiple studies to be associated with bone quality measures like calcaneal Qualitative Ultrasound (QUS) and BMD. Our study suggests that SNP rs3736228 also influences BMD in healthy young females. This supports the work of Correa-Rodriguez et al that found that when stratifying by sex, females only showed a trend towards significance ($p = 0.092$) in QUS measures.

SIGNIFICANCE

This study expands our understanding of the importance of LRP5 rs3736228 polymorphisms in BMD by extending its relationship to a cohort of predominantly Caucasian college students. While the development of BMD is polygenic, this work broadened the role of SNP rs3736228 across the age span, and the sexual dimorphism seen in musculoskeletal traits.

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Evaluating Outcomes of Elective Robotic-Assisted Colonic Resection for Complicated and Non-Complicated Diverticulitis at a Single Institution

PURPOSE/BACKGROUND

With the incidence of diverticulitis rising, an increasing number of patients are presenting with complicated disease. This analysis compares the outcomes of robotic surgery for elective colonic resection for uncomplicated and complicated diverticulitis at a single institution.

METHODS/INTERVENTIONS

Clinical data from a single institution between 2009 and 2016 was reviewed for robotic assisted cases performed by single colorectal surgeon proficient in robotic surgery. Patients were stratified whether they were diagnosed with diverticulitis versus diverticulitis with stricture, abscess or fistula. Univariate analysis was used to identify differences in intra and postoperative outcomes.

RESULTS/OUTCOMES

The inclusion criteria identified 97 cases during the time of review, of which 27 (27.8%) had a concomitant stricture, fistula or prior abscess. Patients in both cohorts were equally matched regarding preoperative demographics (age, gender, body mass index) and comorbidities (diabetes, hypertension, COPD, heart disease). Total operative time was significantly longer for patients with complicated diverticulitis (325 vs. 227 minutes, $p < 0.001$) as was intraoperative blood loss (390cc vs. 176cc, $p = 0.013$). While the rate of intraoperative conversion (33% vs. 24%, $p = 0.372$) and postoperative complications (7% vs. 3%, $p = 0.317$) was higher for the complicated group, the differences were not significant. Postoperative length of stay was higher for patients with complicated diverticulitis (5.26 days vs. 4.11 days, $p = 0.018$) but there were no significant differences in the rates of readmission or reintervention following robotic surgery.

CONCLUSION/DISCUSSION

Robotic surgery does not have a significantly higher rate of postoperative complication for advanced diverticular disease and should be considered when patients present with prior attacks complicated by abscess, stricture or fistula.

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Acute Hepatic Failure and Oral Amiodarone

INTRODUCTION

Amiodarone is associated with serious complications such as lung toxicity, thyroid dysfunction, and QT-prolongation. Further, hepatic failure from the intravenous (IV) formulation of amiodarone is described in numerous case reports and case series. Although there are reports of elevated liver enzymes from the oral formulation of amiodarone, to our knowledge, none have definitively identified a case of acute hepatic failure from the oral formulation alone. In this case, we report an instance of acute hepatic failure after increasing the oral amiodarone dosage as well as rapid recovery following cessation of the medication.

CASE REPORT

A 61-year-old male with a history of non-ischemic cardiomyopathy with reduced ejection fraction presented with heart failure exacerbation due to atrial fibrillation with rapid ventricular response. He had recently failed cardioversion for atrial fibrillation and was started on a higher dose of amiodarone. In this admission, blood tests revealed elevated BNP (1285) and INR (3.9). Therefore, warfarin was held, and he was started on IV furosemide. His metoprolol was increased for a better rate control and he was continued on his amiodarone.

The next day, his morning tests were significant for elevated liver enzymes (AST/ALT 476/434 from 25/36 one week prior), INR (6.5), and bilirubin (2.3). His kidney function has also deteriorated (BUN/Cr 30/3.0 from 21/2.2). Amiodarone and furosemide were held after his heart rate dropped between 40s and 50s. His repeated laboratory tests revealed a lactate of 8.5 and potassium of 7.4. His systolic blood pressure has then dropped to 80s and 90s. His ALT, AST, INR, and creatinine were peaked to 6702, 3021, 8.2, and 5.1, respectively. Nonetheless, his liver and kidney conditions started showing rapid improvement.

DISCUSSION

A number of case reports focused on IV amiodarone as a cause of acute hepatic failure while the cumulative oral dose is a classical cause of chronic hepatotoxicity. The solvent part of the IV formulation is believed to be the reason for the acute reaction since this solution is not found in the oral form. However, our case sheds light on the possibility of acute hepatic failure following increasing the oral amiodarone dose. Although this patient had a brief episode of hypotension, the chronological sequence of events made us believe amiodarone was the drug involved in the hepatic injury. To conclude, we report an increase in the oral dose, as opposed to the IV form, of amiodarone potentially causing acute hepatic failure.

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Sleep Disorders in Inflammatory Bowel Disease: The Forgotten Discussion

The relationship between sleep disturbances and inflammatory conditions is incompletely understood. Studies have shown that inflammatory bowel disease (IBD) patients have poorer sleep quality, prolonged sleep latency and increased use of sleeping pills compared to controls. Furthermore, patients with clinically active IBD have reported significantly worse sleep than patients with inactive disease. IBD patients in remission with abnormal sleep, may be at increased risk for relapse. This study evaluated physicians' assessment of sleep patterns in IBD patients

A medical record review of consecutive IBD patients seen at a university gastroenterology practice during a 6 months period was performed. Patient age, gender and disease type (Crohn's disease, ulcerative colitis) were obtained. Records were reviewed for documentation of a sleep assessment, sleep disorder or a formal sleep evaluation. A database was created maintaining patient confidentiality. The study was approved by the university IRB.

268 records (118 men, 150 women; mean age 43; 158 Crohn's, 109 ulcerative colitis (UC), 1 indeterminate colitis) were reviewed. Eleven patients (4.1%; 7 Crohn's, 4 UC) had a documented sleep disorder; 6 with obstructive sleep apnea, 2 insomnia, 1 circadian rhythm disorder, 1 with snoring. No other patients had documentation of a sleep discussion or assessment. There was no significant difference the rate of sleep assessment based upon gender, age or disease type ($p=1.000$).

Sleep disorders may have an impact upon clinical outcomes in IBD patients. All IBD patients should be screened and treated for sleep disorders if appropriate. This study reveals that few IBD patients have documented discussions with their gastroenterologists about sleep patterns. While this study is limited due to size and single institutional design, it demonstrates a need for increased sleep evaluation in IBD patients, since early intervention for sleep disorders may improve clinical outcomes.

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Diverse Patient Perceptions in Psoriasis

BACKGROUND

Caucasians are the major population of patients with psoriasis in European countries and the U.S. However, several studies have shown minority populations may suffer from worse quality of life (QoL) and more severe disease. The paucity of psoriasis research in diverse populations as well as sociocultural factors, including access to care, different perceptions of disease, and religious influences, may be the cause of this disparity. No known studies have attempted to assess the racial/ethnic differences and sociocultural variations in patient experiences of psoriasis. Furthermore, no tool exists to measure these differences in patient perceptions.

OBJECTIVE

To conduct focus groups containing psoriasis patients of diverse backgrounds to identify racial, ethnic, cultural, and religious differences in patient perceptions of psoriasis care, treatment, and disease course.

METHODS

Between May 2017 and July 2017, we conducted focus groups of diverse patients with psoriasis from the dermatology clinics at the George Washington Medical Faculty Associates. Patients were asked questions regarding their identity, personal and societal influences on personal perception of their psoriasis, and the societal factors (such as culture, religion, race, and sexuality) which influence their diverse perceptions.

RESULTS AND CONCLUSION

A total of 13 psoriasis patients participated in the focus groups. Patients considered ethnicity, religion, sexuality, and profession as strong definers of their identity. Majority of participants identified that knowing other people with psoriasis of the same ethnicity helped ease anxiety due to psoriasis. Patients of minority origin commonly stated that medical issues were not spoken about in their community, causing them to feel isolated. For patients identifying with the lesbian, gay, bisexual, transgender, and queer (LGBTQ) community, aesthetics was noted to be an important component of the LGBTQ community, which caused greater concern about psoriasis flares in these patients. Patients reported the appearance and the opinions of other people as the most bothersome aspects of their psoriasis. Patients also often felt self-conscious about their skin in their personal and work lives. However, support of family members helped alleviate self-consciousness. Participants wanted better education about psoriasis tailored to their identity. Community education would also benefit the LGBTQ community as peers mistook psoriasis plaques to be related to HIV. Using this data, we are now developing and validating a clinical survey instrument that can be used in research to assess diverse differences in patient perceptions of psoriasis.

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Investigating the Use of Gabapentin to Manage Transient Peripheral Neuropathy in Children Treated with Chimeric 14.18 Antibody

BACKGROUND

Chimeric 14.18 (ch 14.18) is a human-mouse chimeric monoclonal antibody against GD2 ganglioside which is used to treat high-risk neuroblastoma in children, leading to increased survival. However, ch 14.18 therapy causes transient neuropathic pain-like syndrome and allodynia. In children, this transient pain syndrome can be managed with IV opioids safely and effectively. However, opioid use is not devoid of side effects such as respiratory depression or pruritus, which may require medical intervention. Gabapentin, an anti-epileptic drug used for neuropathic pain, may be effective in managing ch 14.18 induced transient neuropathic-like pain and in decreasing opioid use.

OBJECTIVE

The objectives of this study are to assess whether the addition of gabapentin to IV opioids improved analgesia and decreased opioid use in children undergoing ch 14.18 therapy for high-risk neuroblastoma.

METHODS

Electronic medical records were retrospectively reviewed to identify patients with high-risk neuroblastoma undergoing ch 14.18 therapy at Children's National Health System from November 2009 to August 2017. All patients received opioids via nurse-controlled analgesia (NCA) or patient-controlled analgesia (PCA). Demographic data, gabapentin doses, opioid use, pain scores, and pain location were recorded from their first cycle and last cycle of ch14.18. The data was compiled and analyzed to obtain 24 hours opioid consumption (mg/kg/d) and mean daily pain score for each patient. Daily opioid use was log transformed, and daily mean pain score was square root transformed for analysis.

RESULTS

29 patients were identified. 7 of the 29 children received gabapentin in addition to opioid PCA while undergoing ch 14.18 therapy. During the first cycle of therapy, root transformed average pain score in patients without gabapentin was 1.12 vs.0.83 with gabapentin. These values decreased to 0.60 vs. 0.69 respectively during the last cycle. Log transformed daily opioid use were -0.83 mg/kg/d in those not receiving gabapentin vs. -0.55 in those receiving gabapentin during the first cycle, and -0.91 vs. -0.86 respectively during the last cycle.

CONCLUSIONS

There was an overall decrease in average daily pain scores and opioid use between the first and last cycle but was not statistically significant. The addition of gabapentin did not decrease pain scores or opioid use during the first or last cycle. Due to the small sample size and the retrospective nature of this study, these results warrant further exploration of analgesic adjuncts to improve analgesia and reduce opioid use in children with transient neuropathic pain syndrome during ch14.18 therapy.

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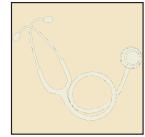
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PARP-1 Silencing Upregulates FOSL1 Transcription, Enhances Angiogenesis And Accelerates Ischemic-Diabetic Wound Healing

OBJECTIVE

People with combined ischemic and diabetic wounds of the lower extremities have the highest risk for limb loss, especially for those without surgical revascularization options. Better medical therapy to enhance angiogenesis is needed for limb salvage. We have demonstrated that Poly-ADP-Ribose polymerase (PARP-1) is hyperactivated in hyperglycemic/hypoxic (Hg/Hp) cells and in ischemic/diabetic murine wounds. This study tests the efficacy of PARP-1 inhibition or silencing in ischemic-diabetic wound healing and further elucidates the role of PARP-1 in angiogenesis.

METHODS

A model of dorsal bipedicle flap-ischemic wounds on diabetic mice was used. The wounds were treated topically with nanoparticle-encapsulated siPARP-1 or vehicle. Wound closure rate and perfusion was analyzed using digital photography and Laser Doppler scanning, respectively. Angiogenetic markers in the tissues were measured by immunohistochemistry. In-vitro endothelial tube formation assay was performed using HUVECs cultured under hyperglycemic and hypoxic conditions.

RESULTS

Wounds treated with topical siPARP-1 significantly accelerated wound healing compared to vehicle (from $25\% \pm 5\%$ to $40\% \pm 8\%$ ($n=7$, $p < .05$) by day 6 and from $50\% \pm 15\%$ to $75\% \pm 3\%$ ($n=7$, $p < .05$) by day 12, and also exhibited improved tissue perfusion ($50\% \pm 5\%$ increase in perfusion units over control on day 6, $n=47$ $p < 0.05$). Improved capillary density was also observed in the siPARP-1 treated wounds detected by immunohistochemistry for SMA ($250\% \pm 35\%$ increase in mean fluorescence intensity over control on day 12, $n=4$, $p < 0.05$) and CD31 ($125\% \pm 15\%$ increase in mean fluorescence intensity over control on day 12, $n=4$, $p < 0.05$). In-vitro angiogenesis assay showed that PARP-1-silencing significantly enhanced endothelial tube formation of hyperglycemic/hypoxic HUVECs (15 ± 4 complete polygons as compared to 0 in untreated, $n=4$, $p < 0.05$). Human angiogenesis PCR-array analysis of pro-angiogenic factors revealed that PARP-1 silencing upregulated FOSL1 transcription by 5-fold ($n=4$, $p < 0.05$). Interestingly, co-silencing of FOSL1 in PARP-1 silenced HUVECs resulted in loss of endothelial tube formation.

CONCLUSIONS

PARP-1 silencing is an effective strategy to promote ischemic-diabetic wound healing. Our data suggest that PARP-1-FOSL1 is a potential novel axis in angiogenesis and PARP-1 could be a promising therapeutic target for improving angiogenesis in ischemic-diabetic wounds.

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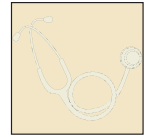
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Mixed Immune Response in Pediatric Severe Asthma

RATIONALE:

Severe asthma account for 5-10% of all patients but >70% of healthcare cost. While the majority of asthma is thought to be driven by a Th2 immune response, recent data suggests Th1 and Th17 responses may play a role in severe asthma. Few studies have evaluated Broncho alveolar lavage (BAL) cytokines in pediatric severe asthma. In this pilot study, we hypothesize that children with severe asthma exhibit a mixed Th2 and Th1/Th17 response based on BAL cytokine profiling.

METHOD:

BAL samples and data were collected from children undergoing bronchoscopy for severe refractory asthma symptoms or chronic cough. MSD multiplex kits were used to measure Th1 (IFN- γ , IL- β , TNF- α), Th2 (IL-5, IL-13, TSLP) and Th17 (IL-17A, IL21, IL-23, and IL-33) cytokines in BAL. Data collected included demographics, asthma history, serum IgE and eosinophils, BAL neutrophil and eosinophil count. Asthma severity was defined based on NAEPP criteria. BAL results and clinical characteristics were analyzed comparing severe asthma to non-severe asthma subjects.

RESULTS:

A total of 22 children were included in this study of which 17 BAL samples were analyzed (77.2% male, median age 6.0 yrs (SED \pm 1.1), 72.7% African American). Overall, median FEV1 was 86% predicted (SED \pm 3.2), serum IgE 80IU/ml (SED \pm 145.8) and serum eosinophilia 0.34K/mcl. Children with severe asthma were older [10.0 vs. 2.0 years ($p < 0.001$)], received a higher number of systemic steroid courses in the past year [3 vs. 2 ($p = 0.05$)], and had a higher median BAL eosinophil (14 vs. 0% ($p < 0.001$)). After correcting for age, there was no increase in any BAL cytokine in severe vs. non-severe asthma. Unlike findings in non-severe asthma, there was a significant positive correlation in the severe asthma cohort between IL-13 and TNF- α ($p = 0.003$), IL-5 with Th17 (IL-23, IL-33) ($p = 0.001$ for both), and IL-13 with Th17 (IL-23, IL-33) ($p = 0.017, 0.023$ respectively).

CONCLUSION:

In pediatric patients with severe asthma, BAL samples showed multiple correlations between Th1, Th2, and Th17 cytokines. This reflects a mixed immune response of different T-helper cells unique to severe asthma in children. This may help explain inadequate responses to current treatment measures, including steroids. Further studies are needed to evaluate mechanisms for this mixed response in epithelium, smooth muscle and sub-epithelial structures, which may lead to other therapeutic targets for severe, therapy resistant asthma.

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Perioperative Complications and Impact of Age on Revision Total Knee Arthroplasty

INTRODUCTION

Age has been shown to be a significant factor in predicting rates of many postsurgical complications. Our study aimed to analyze the NSQIP database to see how increasing age impacts rates of complications after revision total knee arthroplasty, as it has not been significantly studied up to this point.

METHODS

Revision total knee arthroplasty cases were selected out from the NSQIP database using CPT codes 27486 and 27487. Statistical analyses were done using SPSS statistical software. Demographics and comorbidities were analyzed using chi-square for categorical variables and one-way ANOVA for continuous variables. Linear regression models were used to evaluate for independent predictors of postsurgical complications. Only demographics and comorbidities with differences in age groups that showed p-values of less than 0.200 were included in the regression to control for confounding variables.

RESULTS

Complications were shown to correlate with older age groups. However, age was only found to be an independent predictor of rates of UTI, transfusion, and pneumonia.

DISCUSSION

Surgeons should continue to take age into account when evaluating patients as surgical candidates and be especially weary of age when performing revision total knee arthroplasty in patients who have risk factors for the complications that we found to occur at higher rates in older groups.

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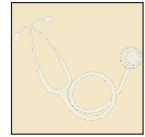
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5-ALA Induced Fluorescence in Hormone Secreting Pituitary Adenomas

INTRODUCTION

Cushing's Disease (CD) is caused by millimeter-sized corticotropinomas (microadenomas) that lead to supraphysiological levels of glucocorticoid. Up to 40% of microadenomas are not visualized on gold-standard MR imaging. Pituitary adenomas metabolize exogenous 5-ALA (an endogenous metabolite) to protoporphyrin IX (PpIX) at rates 20-50 times higher compared with normal tissues. PpIX intensely fluoresces red (635nm) when excited with blue light (375-440nm), enabling its use as an intraoperative fluorescence imaging agent. 5-ALA is now an FDA approved prodrug. We examined the efficacy of ALA-induced-PpIX fluorescence in human derived adenomatous and normal pituitary samples. We explored the modulation of PpIX conversion with CRH or dexamethasone (DEX), and subcellular localization of PpIX.

METHODS

We used flow cytometry for PpIX intensity analysis. A human-derived corticotropinoma, it's adjacent normal gland, murine normal pituitary cells, and AtT20 cells were incubated with 5-ALA (300 nM) with/without DEX (1 μ M) or CRH (50nM). For confocal microscopy, live cells imaged for PpIX (405nm/615nm) and mitochondrial (550nm/615nm) fluorescence.

RESULTS

We found a 10-fold-increase in 5-ALA induced PpIX fluorescence intensity in human-derived adenomatous compared to adjacent normal pituitary tissue ($p < 0.05$). AtT-20 cell lines ($n=6$, $p < 0.05$) fluoresced 7-fold more intensely compared to normal murine pituitary tissue ($n=3$, $p < 0.05$). The addition of DEX, before or after 5-ALA exposure, increased the fluorescence intensity by 31% ($n=4$, $p < 0.05$). The addition of CRH did not have a significant effect on 5-ALA fluorescence ($n=3$, $p < 0.05$). We saw localization of 5-ALA to mitochondria, and mitochondrial disruption in 5-ALA treated At-T20s.

CONCLUSIONS

Our results support the use of 5-ALA for fluorescence guided resection in hormone secreting microadenomas. The supraphysiological levels of glucocorticoids, as seen in CD, may enhance the 5-ALA fluorescence in corticotropinomas. We confirm the mitochondrial localization and disruption by 5-ALA, a basis for photodynamic therapy.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Increased Severity of Recurrent Acute Pancreatitis versus First Time Pancreatitis in ED Patients

STUDY OBJECTIVE

Approximately 30% of patients with one episode of acute pancreatitis experience a recurrent episode. The objective of this study is to compare the severity of the first-time episode versus recurrent episodes of acute pancreatitis based on CT scan.

METHODS

Study was conducted as part of a retrospective chart review at a single academic urban emergency department from 2012-2016. Criteria for inclusion included clinical symptoms of pancreatitis, age greater than or equal to 18 years, ED diagnosis of acute pancreatitis, and, an abdominal CT scan within 24 hours of triage. Exclusion criteria were traumatic cause of acute pancreatitis and pregnancy. Charts were reviewed by a trained abstractor using structured data collection sheets which included data elements such as a history of acute pancreatitis and the results of an abdominal CT scan. Data abstraction was confirmed for interrater reliability. CT Scans were graded using the Modified CT Severity Index (MCTSI) which grades acute pancreatitis by the presence of inflammation, fluid accumulation, necrosis or extra-pancreatic findings.

RESULTS

283 patients were included in the study. Of these, 110 patients resented with recurrent acute pancreatitis and 173 patients presented with first-time acute pancreatitis. We calculated the mean MCTSI score in both groups and found a significantly higher rate of severity in recurrent acute pancreatitis versus first episode (2.09 vs. 1.43, $p < 0.05$.)

CONCLUSION

Patients with recurrent acute pancreatitis are more likely to present with a more severe episode of acute pancreatitis than patients presenting with first-time acute pancreatitis.

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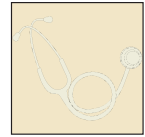
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Impact of COPD on 30-Day Postoperative Complications Following Total Hip Arthroplasty

INTRODUCTION

The demand for Total Hip Arthroplasty (THA) has rapidly risen and continues to due to high success rates of this procedure and the growing aging population. Particularly in Chronic Obstructive Pulmonary Disease (COPD), studies have indicated an increased risk of various postoperative complications across several surgery types. Despite the prevalence of COPD, very little has been investigated regarding postsurgical complications in patients with COPD following a THA. The aim of the current study is to utilize the NSQIP database and determine differences in short-term postoperative complications after undergoing THA, comparing patients with and without COPD.

METHODS

In total, 74,814 patients were included in the analysis looking at how COPD contributes to the rates of postoperative complications in primary THA. Data was obtained from the National Surgical Quality Improvement Project Database years 2005-2014, with readmission/reoperation data beginning in 2011. THA cases were selected out of the database using current procedural terminology (CPT) code 27130. On univariate analysis, p-values were calculated using chi-square for categorical variables and one-way ANOVA for continuous variables. On multivariate analysis, logistic regression was used to control for preoperative comorbidities and calculate p-values.

RESULTS

On multivariate analysis and after controlling for contributing comorbidities, having COPD was found to be an independent predictor of superficial surgical site infection (OR: 1.74), pneumonia (OR: 3.69), reintubation (OR: 2.65) failure to wean (OR: 3.45), urinary tract infection (OR: 1.46), needing a postoperative transfusion (OR: 1.19), and sepsis (OR: 1.97). COPD also independently predicted whether a patient would be discharged home or not (OR: 1.50).

DISCUSSION

Although COPD has been linked to negative postoperative outcomes across several surgeries, few studies have examined postsurgical complications in patients with COPD following a THA. Our study found patients with COPD to have higher rates of superficial surgical site infection, pneumonia, reintubation, failure to wean, urinary tract infection, needing a postoperative transfusion, and sepsis. COPD also independently predicted whether a patient would be discharged home or not. Managing high-risk surgical patients requires a better understanding of possible complications a patient faces and enhancing perioperative conditions to improve outcomes. Given our study identified certain complications as independent risk factors for patients with COPD, surgeons and other healthcare providers can use this information to more accurately counsel patients and make perioperative adjustments accordingly.

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Toward Improving the Quality Assurance Self Reporting in Anesthesia

INTRODUCTION

The mainstay of quality assurance (QA) programs in anesthesia is the end-of-case self report. It is well recognized that many adverse events that occur during cases are not reported, however the extent of under reporting is difficult to estimate. Medications that are not used routinely, such as pressors, anti-hypertensive agents, antidotes and reversal agents may be used as "indicators" since their use provides a window into the true incidence of adverse events (AE) during anesthesia.

In this report, we analyzed our QA database and EMR to compare the incidence of reported AE with the use of indicator medications. While the true incidence of adverse events is not knowable, analysis of indicator medications use might bridge the gap.

METHODS

AE and indicator medications as documented in Epic Anesthesia (Epic Systems, Verona WI) are made available in a Qlikview (Qliktech, Radnor PA) anesthesia dashboard. The date range from January 2013 to June 2015 was selected and all reported QA indicators and all indicator meds from this time were extracted into a spreadsheet (Excel, Microsoft, Bellevue WA).

Some indicator medications were used either for prophylaxis (planned) or to manage an AE (unplanned) i.e. diphenhydramine to prevent or treat allergy. We therefore determined thresholds for each drug that would relate to an AE and (AE yes or no) was added to the spreadsheet.

Descriptive statistics were used to determine the rate an AE was reported correctly associated with classes of medications and individual medications.

RESULTS

During the study period, 804 incidences of administrations of indicator medications were recorded. In many instances multiple administrations occurred for the same AE, resulting in 514 unique cases. In 157 (31%) of unique cases, administrations were deemed planned, leaving 357 cases to analyze if an AE was documented.

In 303/357 (85%) cases, AE were not recorded, leaving only 15% that were documented correctly. Different classes of medications were reported incorrectly with Anti-Croup, and Anti-Hypertensives not recorded 100% of the time indicating that their use was not even considered to be an AE. Opioid and benzodiazepine reversal agents and antiarrhythmic agents were recorded correctly only 50% of the time. Individual drugs usage record ranged from adenosine with 100% correctly acknowledging the AE to esmolol, labetalol, and hydralazine not correctly identified with an AE 100% of the time.

CONCLUSION

Our study shows significant underreporting of adverse events during anesthesia. With EMR, indicator meds administration can be used to identify unreported AE. Combination of education and creative programming that directs the provider to report the use of drugs indicative of an AE would likely improve QA self report and provide a more accurate incidence of adverse during anesthesia.

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Risk factors for Venous Thromboembolism in Obese Women Undergoing Cesarean Delivery

INTRODUCTION

Venous thromboembolism is a leading cause maternal mortality in the developed world, responsible for 9.3% of maternal deaths in the US. Obesity and cesarean deliveries are established risk factors for pregnancy related VTE. Guidelines for prophylactic use of anticoagulation in obese women undergoing cesarean delivery are heterogeneous across major organizations. We therefore sought to identify risk factors that make obese patients who deliver via cesarean section more likely to develop VTE and help guide targeted anticoagulation in this population.

METHODS

We conducted a secondary analysis of data from the Maternal-Fetal Medicine Units Network (MFMU) Cesarean Registry Database using a case control design. Cases were identified as obese women, with pre-pregnancy BMI >30 Kg/m², who underwent cesarean deliveries and subsequently developed deep venous thrombosis or pulmonary embolism. These women were compared to a control group of similar obese women, who also underwent cesarean deliveries but did not develop DVTs or PEs. Analyses of risk factors associated with VTE were performed using Chi-Square Test and Fisher's Exact Test.

RESULTS

Each of the identified 43 VTE cases was matched with 4 controls, for a total of 172 controls. Increased risk of VTE were noted in women with endometritis OR of 4.58 (95% CI: 1.86 - 11.2, $p=0.0004$). Other significant risk factors for VTE includes receiving a blood transfusion with OR 17.07 (95% CI: 4.46–65.3, $p=0.0001$) and having a coagulopathy 27.73 (95% CI: 3.24 - 237.25, $p=.0003$).

CONCLUSION

Important risk factors for VTE in obese women undergoing cesarean deliveries include endometritis, intraoperative or postoperative transfusion, and coagulopathy. The presence of one or more of these factors may warrant addition of pharmacologic thromboprophylaxis.

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Impact of Age on 30-Day Postoperative Complications Following Spine Surgery

INTRODUCTION

Age has been shown to increase risk of postoperative complications. The current study is the largest known study of postoperative complications after spine surgery by age cohort, using the National Surgical Quality Improvement Program (NSQIP) database.

METHODS

A retrospective analysis NSQIP data of 46,509 patients undergoing spine surgery from 2005 to 2014 was performed using specific Current Procedural Terminology (CPT) codes. 30-day postoperative data was collected, analyzed, and broken into age cohorts <30, 30-39, 40-49, 50-59, 60-69, 70-79, and 80-89, to determine differences in complications by age group.

RESULTS

46,509 patients were analyzed. Age was a significant predictor of deep surgical site infection, reoperation rate, pneumonia, pulmonary embolism, unplanned intubation, urinary tract infection, requiring postoperative transfusion, postoperative myocardial infarction, cardiac arrest requiring resuscitation, and DVT. Older patients also had longer overall hospital stays and higher rates of hospital readmission. There was no difference in the rate of superficial SSI based on age groups and the highest rate of wound disruption was found in the <30 age group.

DISCUSSION

Age is a significant predictor of most 30-day postoperative complications after spine surgery. Higher rates of complications in older age cohorts, as well as increased length of stay and higher readmission rates, suggest the need for individualized counseling and decision-making around spine surgery in the elderly.

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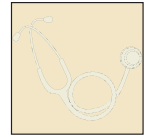
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Perinatal Outcomes of Women Undergoing Cesarean Delivery After Prior Myomectomy

OBJECTIVES

The purpose of this study was to evaluate maternal and neonatal outcomes after prior myomectomy in women undergoing planned cesarean delivery.

STUDY DESIGN

We conducted a retrospective cohort study using the Maternal Fetal Medicine Units Cesarean Registry database comparing women undergoing a cesarean delivery with a history of prior myomectomy to women undergoing a cesarean delivery without a history of a prior myomectomy. Inclusion criteria were singleton gestations at term undergoing planned cesarean delivery. Exclusion criteria were stillbirth, cesarean delivery indication for non-reassuring fetal heart rate, macrosomia, abruption or previa or women undergoing planned trial of labor after cesarean. Primary outcome was incidence of blood transfusion. Maternal and neonatal outcomes were compared secondarily. Logistic regression was used to adjust for confounders.

RESULTS

The entire study population included 73,257 deliveries; 34,002 women met inclusion criteria, of which 367 had a prior myomectomy and 33,635 were controls. The demographics, which varied by maternal age, race and number of prior cesareans were adjusted for when calculating maternal outcomes. The rate of intraoperative transfusion in the prior myomectomy group was 1.4% (5/367) compared to 0.4% (131/33,635) in the control group (aOR 2.8; 95% CI 1.15-6.79). The prior myomectomy group had a higher incidence of postpartum transfusion rate (2.5%, 9/367) compared to the control group (1.2%, 416/33,635) (aOR 2.03 (1.06-3.92), uterotonics usage (5.4%, 20/367) compared to the control group (3.5%, 1,165/33,635; aOR 1.57; 95% CI 1.01-2.45), bowel injury (0.5%, 2/367) compared to the control group (0.0%, 14/33,635; aOR 8.13; 95% CI 2.05-8.91) and cesarean hysterectomy (1.4%, 5/367) compared to the control group (77/33,635; aOR 3.43; 95% CI 1.32-8.91). Neonatal outcomes were not different between groups.

CONCLUSION

Prior myomectomy in women with term, singleton gestations undergoing planned cesarean delivery was associated with a 180% increased risk of intraoperative transfusion compared to the control group. Neonatal morbidity was not statistically different between the groups.

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The Effect of BMI on Rates of Postoperative Complications after Open Reduction and Internal Fixation of Distal Radius Fractures – A Study on the National Surgical Quality Improvement Project Database

BACKGROUND

A patient's Body Mass Index (BMI) has a wide variety of correlations in the orthopedic perioperative setting including post-operative complications. With the current increasing obesity epidemic in the population, understanding the effects of BMI across surgical outcomes can help highlight specific populations that may warrant further management. This study examines the outcomes of patients categorized by BMI receiving operative treatment for distal radius fractures.

METHODS

A retrospective cohort study was conducted using the American College of Surgeons National Surgical Quality Improvement Program database. Patients who underwent operative management for distal radius fractures between 2007 and 2014 were identified and stratified into groups based on World Health Organization BMI guidelines: (1) <18.5, (2) 18.5-24.9, (3) 25-29.9, (4) >30. Univariate and multivariate analysis were used to evaluate the incidence of multiple adverse events within 30 days after operation.

RESULTS

A total of 6,078 subjects were included in this study, with patients who were underweight having the highest percentage of complications at 4.5%. Underweight patients were seen to have an increased likelihood of developing sepsis ($p=0.003$), myocardial infarction ($p<0.001$) and progressive renal insufficiency ($p<0.001$). There were no observed differences seen between BMI groups amongst other comorbidities. Multivariate analysis did not identify BMI as an independent risk factor for any post-operative complications.

CONCLUSION

Relative to non-obese patients (BMI ≥ 30) were not observed to be at an increased risk for any post-operative complications. On the contrary patients underweight (BMI<18.5) were found to be at increased risk for developing sepsis, progressive renal insufficiency, and myocardial infarction. Overall complications for operative treatment of distal radius fracture were low for all groups, and patients who stand to benefit from operative treatment should still receive treatment.

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Erector Spinae Plane Block for Post Thoracotomy Pain in a Pediatric Patient

BACKGROUND

Ultrasound-guided erector spinae plane block (ESB) is a recently described interfascial block in which local anesthetic (LA) is injected around the erector spinae muscle at the level of the fifth thoracic (T5) spinous process. Local anesthetic spread at this location can block both the dorsal and ventral rami of the thoracic spinal nerves. Among other indications, ESB is proposed to have potential uses in thoracic surgeries.

CASE

A 17 year old, 127 kg, male patient presented for video-assisted thoracoscopic surgery (VATS) for lobectomy and excision of mass. History was significant for an undifferentiated sarcoma of the right chest, status post 3 cycles of chemotherapy. After intravenous (IV) induction of general anesthesia, a 37French, left-sided double lumen tube was placed and confirmed with fiberoptic guidance. Due to difficulty obtaining adequate surgical exposure, a decision was made to convert the procedure to an open thoracotomy.

The patient received 300 microgram fentanyl, one gram acetaminophen, and 3 milligram (mg) morphine throughout the procedure. Upon completion of the surgery and before emergence from anesthesia, an erector spinae plane block was performed for post-operative pain control. With the patient in the left lateral decubitus position, a linear ultrasound transducer was placed 3 cm lateral to the T5 spinous process. The trapezius, rhomboid major and erector spinae muscles were identified, along with the transverse process of T5. A short bevel, 22 gauge, 9 cm echogenic needle was advanced under ultrasound guidance until contact was made with the T5 transverse process. After slight retraction, 20 milliliters of 0.5 % ropivacaine LA was deposited underneath the erector spinae muscle and satisfactory spread of LA visualized. Ten mg of dexamethasone were mixed with the LA to prolong the duration of action of the block.

In the recovery unit, the patient complained of 4 out of 10 pain. His pain scores for the first 24 hours post operatively were less than or equal to 5 and treated with 650 mg acetaminophen. After 24 hours, his pain levels increased and he was started on IV Patient-controlled analgesia with hydromorphone.

DISCUSSION

ESB is a relatively new and easy to perform ultrasound guided technique that can be used to achieve good post-operative pain control for patients undergoing thoracic surgeries. This can be especially useful in patients where epidural analgesia is either technically difficult or contraindicated.

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Wearable Augmented Reality Goggles Using 3D Computerized Tomography to Simulate Pedicle Screw Placement

Augmented reality has shown potential to enhance surgical navigation and visualization. Our objective was to demonstrate whether head-mounted display augmented reality (HMD-AR) technology projecting reconstructed 3D and 2D computerized tomography (CT) images can be accurately superimposed over a lumbar model and used to simulate placement of pedicle screws with no additional real-time fluoroscopy. CT imaging was obtained of a phantom composed of L1-L3 *Sawbones* vertebrae in opaque silicone. CT images and virtual trajectories of appropriate angle and depth were integrated into the *Microsoft HoloLens* using the *Novarad OpenSight* application allowing the user to view the virtual trajectory guides and CT images superimposed on the phantom in two- and three-dimensions. 22-gauge spinal needles were inserted following the virtual trajectories to the point of contact with bone. Repeat CT revealed actual needle trajectory, allowing comparison with preprocedural planning. Registration of AR hologram to phantom showed a roughly circular deviation with maximum average radius of 2.5 mm. Users averaged 200 seconds to place a needle. Extrapolation of needle trajectories into pedicles showed that of 36 needles placed, 35 (97%) would have remained within the pedicles. Compared to the edge of the bone, needles placed approximated a mean distance of 4.69 mm in the mediolateral direction and 4.48 mm in the craniocaudal direction. We effectively simulated pedicle screw placement using HMD-AR on a lumbar model with no additional fluoroscopy. This technology has potential to enhance safety and efficiency in selected surgical procedures.

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Predictive Value of Pulmonary Function Testing in the Evaluation of Pulmonary Hypertension in Sarcoidosis

BACKGROUND

In sarcoidosis patients, pulmonary hypertension (PH) is associated with significant morbidity and mortality. Early identification of sarcoidosis-associated pulmonary hypertension (SAPH) has substantial clinical implications. While a number of pulmonary function testing (PFT) variables have been associated with SAPH, the optimal use of PFT's in screening for SAPH is unknown.

OBJECTIVES

To examine the predictive value of PFT's for echocardiographic PH in a cohort of sarcoidosis patients.

METHODS

We conducted a retrospective cohort study of patients with sarcoidosis from a single center over a period of five years. All consecutive adult patients with a diagnosis of biopsy-proven sarcoidosis (determined by review of the medical chart) who underwent PFT and echocardiographic testing were included. Echocardiographic risk of PH (either intermediate or high) was determined by the presence of echocardiographic PH signs and tricuspid regurgitant jet velocity. Data analysis was performed using multivariate logistic regression analysis with least absolute shrinkage and selection operator.

RESULTS

Of the 156 patients included in the study, 42 (27%) met the criteria for echocardiographic PH. Roughly equal proportions met the criteria for intermediate risk (45%) as did for high risk of PH (55%). The percent predicted of diffusion capacity for carbon monoxide (%DLCO) and forced vital capacity (%FVC) were predictive of echocardiographic PH. No other PFT variables outperformed these two markers, and the incorporation of additional PFT variables failed to significantly enhance the model.

CONCLUSIONS

The %FVC and %DLCO emerged as being predictive of echocardiographic PH in this cohort of biopsy-proven sarcoidosis patients. Potentially reflecting the multifactorial pathogenesis of PH in sarcoidosis, incorporation of other PFT variables failed to enhance screening for PH in this population.

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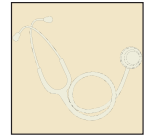
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Parental Compliance for Two-Stage Fowler-Stephens Laparoscopic Orchiopexy: Is Everyone Following Up for the Second Stage and, If Not, Who is at Risk?

PURPOSE

Patients undergoing a two-stage Fowler-Stephens laparoscopic orchiopexy for intra-abdominal testes are typically recommended to undergo the second stage 4-6 months after the first stage. As part of a quality care initiative, our study examined if patients were in fact following up within this window and, if not, why patients were lost to follow up.

MATERIALS AND METHODS

We retrospectively reviewed a cohort of 105 patients who underwent the first stage of a 2-stage Fowler-Stephens orchidopexy at our institution between 1/2005 to 1/2015. Bivariate and multivariate analyses were performed to compare clinical, surgical, and socioeconomic factors. Patients identified as having undergone the first but not second stage procedure were contacted in an attempt to schedule the second stage procedure.

RESULTS

Of the 105 patients, the mean and median interval between the 1st and 2nd stage procedure was 7.2 months and 5 months (2-65 months). Twenty-seven of the 105 patients (25.7%) followed up >6 months after their first stage procedure. Four (3.8%) did not ever undergo a second stage procedure at our institution. Three patients were not able to be contacted. Contact was re-established with one patient who subsequently underwent the second stage of the procedure at 8 years of age, 45 months after the first stage procedure. **The parents chose to not follow up for the second stage due to fear of another procedure under general anesthesia, despite knowledge that a second procedure would be required.** Of patients who completed the second stage of their Fowler-Stephens, those that were older were less likely to have followed up within 4-6 months. The OR for older children was 0.78 with a p-value of 0.02.

CONCLUSION

Although uncommon, some patients offered a two-staged operation will not follow up for the second stage, highlighting the importance of thorough counseling. As patients with undescended testicles get older, they are less likely to follow up within the recommended time frame. Protocols for routinely contacting patients 3 months after a first stage Fowler-Stephens orchidopexy could potentially improve parental compliance with standard recommendations for timing of the 2nd stage.

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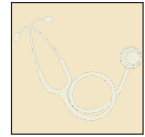
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Effect of Early Discharge on Postoperative Comorbidity and Complications for Patients Undergoing Revision Total Knee Arthroplasty

BACKGROUND

Total knee arthroplasty (TKA) is becoming an increasingly common procedure to alleviate knee pain often associated with osteoarthritis (OA) of the knee. As the number of TKAs performed continue to increase, there remains a debate regarding efficacy of discharging patients earlier than the conventional 3-4 days in the postoperative period. A variety of studies have begun to show that early discharge has an economical benefit, while causing either a reduction or no difference in patient outcomes. This study aims to determine effect of early discharge on postoperative complications in those that undergo revision TKA.

METHODS

A retrospective cohort study was conducted using data collected through the American College of Surgeons National Quality Improvement Program Database. All patients who underwent revision TKA between 2007 and 2014 were identified and stratified into groups based on discharge date. The incidence of adverse events following surgery was evaluated with univariate and multivariate analyses where appropriate.

RESULTS

Patients that were discharged earlier were found to be less likely to develop a deep wound infection, urinary tract infection, sepsis or require a reoperation in the OR within 30 days. Furthermore, earlier discharge was found to be an independent risk factor for these complications.

CONCLUSIONS

Patients that are discharged earlier have a decreased risk for a variety of complications in the postoperative period, while reducing economic burden. If patients are appropriate candidates, surgeons should consider early discharge as a viable option even in the revision TKA population.

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ANA negative scleroderma

BACKGROUND

Systemic Sclerosis (SSc) is an autoimmune disease characterized by inflammation, fibrosis, and vasculopathy. More than 90% of patients with SSc test positive for anti-nuclear antibodies using immunofluorescence (IF-ANA) as well as for scleroderma specific extractable nuclear antibodies such as topoisomerase (Scl-70), centromere, THTO, U3RNP, U1RNP and RNA Polymerase III. However, a small subset of scleroderma patients test negative for anti-nuclear antibodies. The purpose of this study was to investigate whether scleroderma patients with negative IF-ANA had different characteristics when compared to scleroderma patients with positive IF-ANA.

METHODS

This study was IRB approved and all patients consented to be included in the study. At the time of data lock, 65 patients fulfilled diagnostic criteria for systemic sclerosis. Data was collected on patient demographics, autoantibody profile, and disease characteristics.

RESULTS

Of the 65 patients, 49 had positive IF-ANA and 16 had negative IF-ANA. There was no significant difference in age, sex, race or scleroderma subtype (sine, limited, diffuse, or localized) between the IF-ANA positive and negative groups. The IF-ANA negative group were more likely to have positive U3RNP ($p=0.009$).

CONCLUSION

The U3RNP is one of the nucleolar antibodies which is known to be missed using direct ANA testing; however, this study shows that this antibody subtype may also be missed using the IF-ANA test. This is an important finding since scleroderma patients with U3RNP are at higher risk for life threatening complications of scleroderma including pulmonary hypertension and pulmonary fibrosis.

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Cochlear Implant Symmetry via Template

In cases of severe to profound sensorineural hearing loss (SNHL), cochlear implantation (CI) restores the ability to process auditory signals and allows for verbal language acquisition. Along with advances in technology, modern CIs have a slimmer physical profile that allows for fixation using a direct subperiosteal pocket technique that obviates the need for drilling a bone well in the parieto-occipital cortex. With the overall trend in pediatric bilateral CI favoring the less invasive direct subperiosteal technique, we propose a reliable method using materials available in any operating room to achieve optimal, symmetric placement in real time. This “mirror template”, developed by the Senior Author (BKR), employs a simple folding and tracing to allow precise, yet timely pocket placement on the right and left sides of the temporal bone. Our method exploits the thinner profile of the most recent receiver-stimulator (R/S) models, and may be safely and reliably performed in our youngest patients, including those under 12 months of age. Clinicians have a duty to optimize the aesthetic aspects of prosthetic devices; regarding cochlear implants, aesthetic considerations largely focus on R/S placement. Psychological analysis of the human perception of beauty shows that symmetry has a significant and independent input into the perception of beauty for both males and females. We reviewed 11 bilateral cochlear implantation cases performed by the Senior Author using the direct subperiosteal pocket technique with our proposed template. Excellent symmetry has been seen in all cases following the implementation of the “mirror template,” and has translated to high patient and family satisfaction regarding aesthetics and symmetry.

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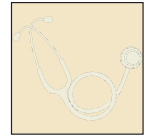
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Affective Communication in Routine Diabetes Care for Adolescents and Young Adults

High quality communication between health care providers (HCPs) and adolescents and young adults (AYAs) with type 1 diabetes (T1D) may contribute to better diabetes self-care and health outcomes. Health communication reflects both informational content and how information is conveyed, including affect and tone. The aim of this study was to assess HCP affective communication and the relationship between HCP affective communication and glycemic control in AYAs with T1D.

As part of a larger study of AYA-HCP health communication, routine clinic visits for 69 AYAs with T1D (M age 17.81 yrs; 56.5% female) and 8 HCPs (88% female) were audiorecorded. Clinic visits were coded using the Roter Interaction Analysis System (RIAS), a validated coding structure assessing verbal and non-verbal exchanges in a medical encounter. HCP global affective ratings were used to create two composite variables—positive HCP affect (e.g. attentiveness; respectfulness; Cronbach's $\alpha = 0.82$) and negative HCP affect (e.g. anger; dominance; Cronbach's $\hat{\alpha} = 0.75$). Hemoglobin A1c (A1c) was taken from the medical chart.

The mean A1c was 8.97% (± 2.30). Descriptive analyses of positive and negative HCP affect indicated that HCPs expressed a high level of positive affect ($M = 4.21$) and a relatively low level of negative affect ($M = 2.80$). Negative affect was positively associated with HbA1c. After controlling for salient covariates (e.g., HCP, race, regimen), A1c accounted for a significant portion of the variance in negative affect during the clinic visit ($\text{Adj } R^2 = .36, \beta = 0.57, p < 0.001$).

This sample of HCPs predominantly exhibited positive affect during routine T1D visits. Glycemic control was not associated with positive affect, but higher A1c was associated with more negative affect. This finding suggests elevated A1c levels may elicit more negative affect in routine diabetes care. Future research should examine these associations over time, including how AYA-HCP health communication quality predicts long-term glycemic control.

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Impact of a Dedicated Cardiac Anesthesiology Team on Peri-Operative Outcomes in Children with Congenital Heart Disease Undergoing Non-Cardiac Procedures

Children with Congenital Heart Disease (CHD) undergoing noncardiac surgery are at higher risk for adverse perioperative (Ramammorthy, 2010, Faraoni, 2016) and less likely to survive cardiac arrest (Ramammorthy, 2010). The perioperative team is often confronted with the question about who should care for these patients when undergoing non cardiac surgery. Our objective was to identify those patients at highest risk for adverse outcomes and to examine if using a risk stratified approach to allocate care of these patients would mitigate the risk of adverse events under anesthesia.

We conducted a single center retrospective cohort study of children with CHD who underwent non cardiac surgery between June 2014 - December 2015. Perioperative outcomes and survival data were reviewed and compared to that reported in the literature.

We identified 131 patients with CHD undergoing a total of 171 non-cardiac surgical procedures during the study period all cared for by a cardiac anesthesiologist. The majority of patients taken care of by the cardiac anesthesia team had either major (45%) or severe (45%) CHD when utilizing the ACSNSQIP classification system. Patients with severe CHD represented the highest risk for perioperative events accounting for all intra-and post- operative cardiac arrest events at 0.6% (CI 0.0-3.2) and 1.7% (0.4-5.0) respectively. Moreover, patients with severe CHD accounted for the majority (83.3%) of the 3.5% (CI 1.3-7.5) of patients requiring post-operative reintubation. There was no correlation between age, sex, type of surgery and perioperative arrest/30 day mortality.

Children with severe CHD are at increased risk of perioperative complications including cardiac arrest, death, and reintubation. At Children's National Medical Center these patients undergo a comprehensive risk stratification and multidisciplinary planning which includes intraoperative care by a dedicated cardiac anesthesia team and the incidence of intraoperative cardiac arrest is below what has been reported in the literature.

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A Curious Case of Aortopathy

Cystic Medial Degeneration (CMD) is a disorder of typically large arteries, particularly of the aorta, and can be associated with congenital vascular diseases such as Ehlers Danlos or Marfan syndrome. CMD can be a diagnostic challenge for rheumatologists as it is a known vasculitis mimicker, thus PET scan is a vital diagnostic tool in differentiating between vasculitic and non vasculitic etiologies when evaluating large vessel aneurysms. Here we present a case of a dilated aortic aneurysm and new onset Deep Venous Thrombosis (DVT) in a young patient where radiotracer uptake was noted on PET with initial concern for vasculitis, however histopathology revealed cystic medial degeneration.

A 28-year-old African American male with past medical history significant for surgically-managed congenital patent ductus arteriosus presented to an outside hospital with right lower extremity pain and swelling with Venous Dopplers revealing a large occlusive distal DVT extending from the common femoral and popliteal veins. CT angiography revealed a 5.9 cm mid ascending thoracic aneurysm, and a 3.2 cm pulmonary artery dilatation. The patient was transferred to our institution for further surgical management of his aortic aneurysm.

Laboratory Evaluation revealed an ESR of 0, and CRP 37.1. HIV, RPR, Hepatitis B surface antigen, Hepatitis b Core antibody, Quantiferon Gold, ANA-IFA, Anti-dsDNA, Rheumatoid Factor, anti-CCP, ACE, C3, C4, HLA-B27, HLA-B51, and ANCA panel were all within normal limits. PET/CT revealed increased radiotracer uptake throughout the right lower extremity vasculature and a small focus in the ascending aorta. MRI/MRA of the brain revealed enlarged bilateral internal carotid artery aneurysms. Pulse dose methylprednisolone therapy was initiated following results of PET and patient underwent successful surgical aortic root aneurysmal repair. Surgical Pathology of aortic tissue revealed cystic medial degeneration without evidence of prominent lymphocytic infiltrate in the intima and tunica media; though a small focal lymphoplasmacytic infiltrate was identified in the aortic adventitia "without strong morphologic evidence of vasculitis." Familial genetic aortopathy panel returned positive for a heterozygous missense mutation in the Smooth Muscle Alpha Actin Protein (ACTA2).

This case illustrates the necessity of maintaining a broad differential when considering the etiology of arterial aneurysms in varying size vessels in a young patient. In our patient, radiotracer uptake was noted in the aorta and lower extremity vessels, but histopathology of aortic tissue was consistent with cystic medial degeneration. Mutations in the ACTA2 protein are associated with familial syndromes of Thoracic Aorta Aneurysms, premature Coronary Artery Disease and Moya Moya Disease.

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Effect of Preoperative Transfusion on Postoperative Complications After Total Hip Arthroplasty

Primary total hip arthroplasty (THA) is among the most common surgical procedures and clinically known to cause significant intraoperative blood loss requiring peri- and post-operative transfusion. Multiple studies have shown post-operative transfusions are associated with greater complications and subsequent prolonged recovery, however limited studies exist in determining whether similar post-operative risks are observed in THA patients receiving pre-operative transfusions. Based on studies conducted on post-operative transfusions, it was hypothesized that pre-operative transfusions would be associated with an increased risk for post-operative complications.

In total, 74,814 patients from the National Surgical Quality Improvement Project Database between 2005-2014 were studied with specific readmission/reoperation data beginning in 2011. Complications were divided post-operative complications (directly related to the procedure), and non-operative complications (not associated with procedure), and co-morbidities were controlled during multi-variate analysis.

Pre-operative transfusion in THA patients was found to be an independent predictor of organ space infection (OR: 5.41), pneumonia (OR: 2.66), failure to wean (OR: 13.84), urinary tract infection (OR: 3.42), cardiac arrest (OR: 5.83), transfusion post-operatively (OR: 5.94), and non-home discharge (OR: 3.18).

Overall, patients receiving blood products prior to a primary THA are at increased risk of operative and non-operative complications including increased infection risk, prolonged hospital stay, discharge to a non-home facility, and potential cardiac arrest leading to resuscitation. Future medical decision making regarding pre-operative anemia management in primary THA cases should entail a careful risk-benefit analysis of transfusion and potentially include higher thresholds to transfuse preoperatively as well as, close monitoring in order to prevent complications.

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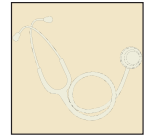
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Dexmedetomidine as a Non-Opiate Adjunct to Multimodal Perioperative Pain Control in Pediatric Patients Undergoing Craniofacial Reconstructive Surgery: A Retrospective Study

PURPOSE

Craniofacial (CF) reconstruction surgery involves a surgical approach to the CF region to repair cranial vault and facial deformities. The surgery is extensive, often requiring wide scalp dissections and multiple osteotomies and is associated with significant postoperative pain and analgesic requirements. Dexmedetomidine is a highly selective alpha-2 receptor agonist that mediates central nervous system sympathetic activity and pain modulation, thus producing both analgesia and sedation. Intraoperative use of dexmedetomidine could be particularly helpful in these surgeries as a means of reducing postoperative opioid administration and opioid-induced side effects. We hypothesized that intraoperative administration of dexmedetomidine in children undergoing CF reconstructive surgery would have a greater reduction in postoperative opioid requirements, pain, sedation scores, and opioid-induced side effects compared to patients who did not receive dexmedetomidine.

METHODS

All patients with craniosynostosis who underwent either CVR or BFOA at Children's National Health System between July 1, 2013 and June 30, 2017 (48 months duration) were retrospectively evaluated. Thirty-nine patients received dexmedetomidine intraoperatively while 41 patients did not receive dexmedetomidine. Demographic data was analyzed and a multitude of continuous and categorical perioperative variables were assessed. Primary outcome measure was mean postoperative morphine equivalent requirements. Secondary outcome measures included presence of opioid related side effects, pain scores, mechanical ventilator days, and ICU and hospital length of stay. Normality of all continuous outcomes was determined and means were compared using a student's t-test. Categorical outcomes were compared using a Fisher's exact test. A p-value of <0.05 was considered statistically significant.

RESULTS

There were significant demographic differences in terms of age and weight between the two groups in which those receiving dexmedetomidine were younger and weighed less than those that did not receive dexmedetomidine. Intraoperative dexmedetomidine use was not associated with significantly lower postoperative opioid requirements or pain scores. However, patients who received higher doses of intraoperative dexmedetomidine did have significantly lower rescue medication administration for nausea and vomiting postoperatively.

CONCLUSION

Contrary to the hypothesis, dexmedetomidine was not associated with reduced postoperative opioid requirements or pain scores in children undergoing CF reconstructive surgery. Interestingly, our findings suggest that dexmedetomidine may be protective in terms of postoperative opioid-induced nausea. A prospective, randomized controlled trial is needed to better analyze the relationship between intraoperative dexmedetomidine use and postoperative opioid requirements, opioid-related side effects, and pain scores in children undergoing such surgery.

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Purpuric Lesions and Non-Healing Ulcerations: An Unusual Presentation of Multiple Myeloma

Cryoglobulinemic vasculitis is a small vessel vasculitis that can be associated with various pathologies, including infection, autoimmunity, and malignancy. Diagnosing cryoglobulinemic vasculitis can be challenging due to its widely varying presentation and limited sensitivity with isolated laboratory testing. Here we present a case of cryoglobulinemic vasculitis associated with multiple myeloma.

The patient is a 64 year old woman with a past medical history of type 2 diabetes, hypertension, hyperlipidemia, hypothyroidism, asthma, and atrial fibrillation. She had a prior history of lower extremity purpuric lesions and ulcerations that responded to high dose steroids many years back. Several skin biopsies revealed both cutaneous vasculitis and thrombotic vasculopathy, an initial bone marrow biopsy was non-diagnostic, and labs indicated a worsening paraproteinemia on UPEP and positive serum cryoglobulins. She presented to an outside hospital with altered mentation, acute renal failure, and suspected pneumonia and cellulitis, and was later transferred to our hospital for further evaluation of progressive necrotic wounds.

On presentation, the patient's physical exam revealed necrotic tissue of the bilateral knees, fixed areas of non-blanching reticular reddish-blue to purple discoloration of both upper and lower extremities, and scattered petechiae, palpable purpura, and lower extremity ulcers. Labs were significant for the presence of serum cryoglobulins, elevated serum free kappa to lambda light chain ratio, serum IFE with hypogammaglobulinemia, urine IFE with prominent M spikes and IgG monoclonal protein with kappa light chain specificity, Hgb of 6.5, platelets of 146, peak creatinine of 1.8, prolonged PT of 16.5 and INR of 1.34, and a UA with proteinuria.

Rheumatology and Hematology-Oncology were consulted during this admission, and a bone marrow biopsy revealed kappa light chain multiple myeloma as the underlying etiology of the patient's Type 1 cryoglobulinemic vasculitis. A regimen of cyclophosphamide, bortezomib, and dexamethasone was initiated, however treatment was complicated by septic shock and encephalopathy, and ultimately the patient died from complications of her disease.

This case demonstrates the importance of maintaining a broad differential in the setting of worsening cutaneous vasculitis and multi organ failure that includes cryoglobulinemia. When serum cryoglobulins are detected, a thorough evaluation for underlying causes including infectious, rheumatologic, and hematologic etiologies should be pursued. Often, initial evaluation may not yield a cause of cryoglobulinemia. Given that long-term prognosis relies upon rapid diagnosis and treatment of the underlying disease process, close interval follow up and consideration of repeat investigation when paraproteinemia progresses is crucial.

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Who is Saying What About Inflammatory Bowel Disease on Twitter?

BACKGROUND

With about 330 million active users and its growing media attention globally, Twitter is a powerful tool for conveying information to the general population. There is limited data on the utilization of Twitter for disseminating medical information. This study evaluated messages on Twitter regarding Inflammatory Bowel Disease (IBD).

METHODS

Social Feed Manager (SFM; version 1.10.0; GW University, 2017), a software that mines social media platforms, was used to extract information regarding IBD-related tweets and their accounts over a 10-day period. We queried Twitter for terms related to IBD and categorized messages by geographic origin, type of user, and message content. Only tweets in English were included. Statistical analysis was conducted using a two-tailed Fisher's Exact Test with a significance set at $p < 0.05$. The study was approved by the university IRB.

RESULTS

Our study analyzed 629 consecutive IBD-related messages worldwide. The vast majority of tweets came from the USA (41.7%) and UK (35.7%), with fewer from Canada (9.9%), South America (8.5%), Asia (3.2%), and Australia (0.9%). These messages were posted by 578 distinct users, with patients (20.9%) and clinicians (21.1%) being the most common. General disease information was discussed by patients and support groups more than by clinicians, industry, foundations, and advocates (39.2% vs. 23.6%; $p=0.0002$), with symptoms being discussed by patients more than all other groups (23.1% vs. 8.0%; $p=0.0001$). Disease management was discussed by clinicians, industry, and foundations more than by patients, advocates and support groups (52.9% vs. 28.5%; $p=0.0001$). Direct recommendations were made more by clinicians and industry than other groups (5.6% vs. 0.8%; $p=0.0018$), with industry making more recommendations than clinicians (13.2% vs. 3.3%; $p=0.0353$).

CONCLUSIONS

This study reveals that Twitter is utilized by a variety of people and provides diverse messaging about IBD. Patients and support groups tweeted more about general disease information, while clinicians, industry, and foundations tweeted more about disease management. Patients alone discussed symptoms in their messages. Clinicians and industry made more management recommendations than any other group, while industry made more direct recommendations than clinicians. It is critical that users are aware that Twitter messaging provides unfiltered medical information and that the validity of message content always should be considered.

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The Utility of Smart Phone Applications and Fitbit as a Screening Tool for the Diagnosis of Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is considered to be the most prevalent sleep disorder, with 2-4% of the adult population suffering from the disease. OSA causes severe hindrances to the patient's daily life, by causing excessive sleepiness, memory loss problems, poor work performance, erectile dysfunction, personality changes, and depression. Untreated OSA can also lead to high blood pressure and cardiovascular diseases. Currently, the gold standard for objective sleep measurements, and therefore diagnosis of OSA, is polysomnography (PSG). PSG, however, is limited by its time-intensiveness, high cost, intrusiveness, and temporality; not only does it interrupt the patient's daily life, it is unable to provide information on the patient's sleep pattern over multiple days. In this study, we implement the new Fitbit Alta HR and two most popular smartphone applications to compare their results to that of PSA.

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Gastric Abscess with Gastro-Duodenal Fistula Formation as a Manifestation of Gastric Crohn's Disease

INTRODUCTION

Clinically significant gastroduodenal involvement of Crohn's disease (CD) is rare, affecting only 0.5–4% of CD patients. Gastric abscesses from CD are not well-documented in the existing literature. In this report, we present a rare case of CD complicated by a gastric abscess with fistulization to the duodenum.

CASE

A 32-year-old male with CD complicated by perianal and enterocutaneous fistulas s/p right hemicolectomy and ileostomy presented with two weeks of progressive abdominal pain and purulent drainage from his ileostomy site. Physical exam was notable for generalized abdominal tenderness. Labs were pertinent for WBC $15 \times 10^3/\text{mm}^3$, platelets $646 \times 10^3/\text{mm}^3$, Na 124 mmol/L, and CRP 67 mg/L. He was started on ciprofloxacin and metronidazole. CT revealed a gastric antral stricture with two small collections or fistula in the ventral gastric wall. EGD showed a soft subepithelial lesion with an overlying 3–4 mm white-based ulcer located in the gastric antrum adjacent to the pylorus which produced a large amount of purulent drainage after biopsy. Purulent material was also seen actively draining into the duodenal bulb from an unvisualized source, likely a fistula from the antral abscess.

DISCUSSION

Our case presented with a gastric abscess complicated by an antral-duodenal fistula draining purulent material. The antral abscess was confirmed endoscopically with biopsy enhancing drainage.

The recommended treatment for intramural gastric abscesses has generally been surgical drainage in combination with antibiotics. Follow-up imaging will determine if further intervention, endoscopic or surgical, is necessary in this patient. This is the first case of a gastric abscess from Crohn's disease that had fistulized to the duodenum resulting in spontaneous drainage that was enhanced by endoscopic intervention. Awareness of this rare complication and therapeutic options is important to optimize clinical outcomes.

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Efficacy of Outpatient Ketamine Infusions in Different Chronic Pain Conditions

Ketamine, an NMDA antagonist, has shown to be effective in chronic pain relief. This study seeks to examine the efficacy of outpatient ketamine infusions in patients with various chronic pain diagnoses.

We examined data on patients undergoing ketamine infusions, subdividing patients based on their pain diagnosis into nonexclusive categories: neuropathic pain, generalized pain, chronic postoperative pain, and chronic pain with a psychiatric diagnosis. Patients completed the Brief Pain Inventory prior to 1-day or 3-day outpatient ketamine infusions and again 2-4 weeks after the infusions. We measured pain scores pre and post infusions and on follow up visit.

A random effects mixed model was used to test the time effect for pain and accounted for within-subject autocorrelation of the pain scores.

There were 224 patients: 143 patients with neuropathic pain (64%), 49 with generalized pain (22%), 80 with chronic post-op pain (36%), and 63 with psychiatric diagnoses (28%). There was a significant drop in mean pain level from pre to post infusion ($p < .0001$) for all diagnoses, with the mean pain level dropping from 7.6 (95% confidence interval 6.8 to 8.5) to 6.8 (95% ci 6.0 to 7.7) after adjusting for covariates.

Outpatient ketamine infusions significantly improved outcome measures in patients with each of the above diagnosis groups. Closer analysis shows that improvement in various quality of life measures differed amongst chronic pain conditions.

Further study with larger sample groups may help elucidate ketamine's broad therapeutic effect in treating chronic pain.

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Risk for Post-Spinal Surgery Complications Associated with Pre-Operative Blood Transfusions

INTRODUCTION

The frequency of spinal surgeries has increased dramatically in the United States over the past decade and, as with all surgeries, spinal procedures carry inherent risks for complications after the operation. Recently, it has been recognized that procedures in which intra-operative/post-operative blood transfusions are administered carry a higher risk of postoperative morbidity and increased length of hospital stay (Seisean *et al.*). Despite this, there is little literature, currently, analyzing post-operative complications associated with blood transfusions taking place 72 hours prior to spinal operations. The aim of this study was to investigate the prevalence of pre-operative blood transfusions in spinal surgeries and elucidate the associations that exist between those transfusions and post-operative complications.

MATERIALS & METHODS

We retrospectively analyzed cases of spinal surgeries between 2005 and 2014 from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database with the exception of 2009 due to incomplete data. A total of 37,201 patients who had undergone spinal procedures were studied. Patients receiving pre-operative blood transfusions within 72 hours of surgery were documented. Demographic factors, including sex and age, were noted. Comorbidities included in this analysis include body mass index (BMI) and American Society of Anesthesiologists (ASA) score. Post-operative complications were stratified into major and minor categories. Chi-squared test, Fisher's exact test, and ANOVA were used to perform univariate testing where appropriate, while multivariate analyses were performed to determine independent risk factors for complications.

RESULTS

With the exception of pneumonia ($p=0.096$), blood transfusions prior to spinal surgeries were associated with increased risk for all major and minor complication criteria analyzed, with major complications including myocardial infarction (MI), deep venous thrombosis (DVT), pulmonary embolism (PE), stroke, peripheral nerve injury, deep wound infection, organ cavity infection, sepsis, and death ($p<0.05$). Minor complications included urinary tract infections (UTI), superficial surgical site infections, wound dehiscence ($p<0.05$), and pneumonia ($p=0.096$). Average BMI, age, and other factors from the complications criteria were similarly associated.

DISCUSSION

Overall, patients receiving blood transfusions within 72 hours prior to undergoing spinal procedures had increased rates of several post-operative complications. Among these complications, the most notable include superficial and deep wound infections, MI, pneumonia, DVT, stroke, and even death. Armed with this knowledge, surgeons would better be able to predict, and therefore mitigate, such post-operative complications in these patients. Future research in this area, directed toward stratification of risk based on the patient's need for pre-operative blood transfusion and procedure type, would provide further insight into preventing post-operative complications after spinal surgeries.

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Impact of Food Allergy on the Growth of Children with Moderate-Severe Atopic Dermatitis

BACKGROUND

Atopic dermatitis (AD) is a chronic inflammatory skin disease that affects 10-20% of children in the United States. Significant sleep disturbance due to itching, and increased metabolic demands due to rapid skin turnover and chronic inflammation, are thought to impact the growth of children with AD. Between 15-40% of children with AD have food allergy as well, which can also have adverse growth consequences. This study aims to determine the impact food allergy status has on height, weight and BMI Z-scores of children with moderate-severe AD.

METHODS

A detailed food allergy history was acquired on children aged 2-20 years old enrolled in a natural history of atopic dermatitis protocol at the NIH who were identified as having moderate-severe AD. The children were categorized into three groups based on their food allergy (FA) status: IgE FA: those with IgE-mediated FA to the most common food allergens—cow's milk, egg, wheat, soybean, and/or peanut; Skin Only: those avoiding any of the most common food allergens due to worsening of their AD upon ingestion of the food; and No FA: those nonallergic to food following an unrestricted diet. The height, weight, and BMI were compared between the three patient subgroups as well as between patients who avoided milk and did not avoid milk.

RESULTS

The BMI Z-score (0.08 ± 0.98) of the IgE FA group was significantly lower than in the Skin Only group (0.77 ± 1.07 ; $p=0.04$) and No FA group (0.99 ± 1.17 ; $p=0.003$). The weight Z-score (-0.42 ± 1.12) of the IgE FA group was significantly lower than in the Skin Only group (0.45 ± 1.14); $p=0.047$) and No FA group (0.58 ± 1.12 ; $p=0.007$). The average BMI Z-score of the Skin Only group was significantly above zero ($p=0.003$). 3/10 (30%) of the Skin Only group were overweight or obese compared to 7/42 (16%) in the IgE FA group. The average BMI Z-score of the No FA group was significantly above zero ($p<0.001$). 12/25 (48%) of the No FA group were overweight or obese compared to 7/42 (16%) in the IgE FA group.

CONCLUSIONS

The growth of children with AD is significantly impaired by the simultaneous presence of IgE FA, particularly milk allergy. In contrast, patients with moderate-severe AD alone are more likely to have elevated BMI and weight. These data suggest that all children with moderate-severe eczema warrant close nutritional follow-up.

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Characterization of Pediatric Bowel and Bladder Dysfunction via Pupillometry

Bowel and Bladder Dysfunction (BBD) refers to a heterogenous group of voiding disorders, accounting for an estimated 40 percent of pediatric urology visits. Symptoms of BBD include enuresis, urgency, and urinary retention, often accompanied by constipation. While the role of the autonomic nervous system (ANS) in regulation of voiding is well-characterized, it is not known if children presenting with BBD exhibit distinct patterns of ANS activity that could be measured for diagnosis, or targeted for intervention. Pupillometry allows for assessment of systemic ANS activity, and therefore could elucidate differences in ANS function among BBD patients. This study aimed to determine whether a pupillary response can be characterized for BBD.

The goal of this study was to use pupillometry to compare the pupillary responses of BBD patients to controls pre- and post-voiding. Both BBD patients and controls were recruited from the urology clinic at Children's National. Using scores from the Dysfunctional Voiding and Incontinence Scoring System (DVISS) questionnaire, subjects were identified as BBD patients or control patients. Pupillometry was then conducted before and after voiding.

BBD patients showed a significantly larger maximum pupil size in the pre-voiding condition relative to controls. Additionally, several pre- and post-voiding parameters showed near-significant differences. The changes in values pre- and post-voiding were also compared, and BBD patients showed significantly larger changes in both minimum pupil size and in average constriction velocity. These results suggest that BBD patients may have a distinctive profile of ANS activity, and that this profile may be detectable in a clinical setting via pupillometry. The role of the autonomic nervous system in voiding behavior is well described, with the parasympathetic nervous system (PNS) more active during voiding, and the sympathetic nervous system (SNS) more active during the retention phase in healthy patients. The larger maximum pupil size seen in the pre-voiding condition among BBD patients could indicate relatively higher SNS activity during the retention phase. This is consistent with a finding from a study of cardiac autonomic activity among BBD patients, which found higher baseline heart rates relative to controls. Additionally, the significantly larger changes in minimum pupil size and average constriction velocity between pre- and post-voiding conditions among BBD patients could indicate greater variability in ANS activity related to voiding behavior. The results could be applied toward a diagnostic tool for identify patients with BBD dysautonomia, versus patients with behavioral, anatomical, or other causes of urinary symptoms.

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Impact of a Student-Led Rheumatology Interest Group on Medical Student Interest in Rheumatology

BACKGROUND

Based on data from the 2005 Rheumatology Workforce Study the demand for rheumatologists will continue to increase in the coming decades. Demand for rheumatologists outstrips the current supply of trained rheumatologists. The American College of Rheumatology has implemented several strategies to try to increase medical student interest in Rheumatology including programs such as Choose Rheumatology! The purpose of this observational study was to investigate impact of development of a student led Rheumatology Interest Group and the Choose Rheumatology! program on medical student interest in Rheumatology at a single institution.

METHODS

In April 2015 a student led Rheumatology Interest Group was established at our institution. As part of the inaugural meeting the "Choose Rheumatology!" team presented on careers in rheumatology, several faculty gave testimonials on why they had chosen Rheumatology, and patients spoke on the impact their rheumatologist had on their lives. Follow up meetings included a meeting on finding research projects and two joint injection workshops. To assess medical student interest in rheumatology we retrospectively collected data and following initiation of the interest group based on four parameters: the number of medical student abstract submissions to the GW Research Day, the number of medical students enrolling in the rheumatology elective, and the number of manuscripts published by faculty with medical students. In order to account for the variable time periods in the pre and post intervention groups, the mean number of student-rheumatology interactions per 6 months in the pre and post intervention periods was assessed for each parameter. Data analysis was performed using GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego, CA).

RESULTS

Student interest in the rheumatology elective significantly increased following the Interest Group intervention with a mean number of students per 6 months period ($p=0.012$). The number of abstract submissions also significantly increased ($p=0.003$). The number of manuscripts submitted by student-faculty dyads has also increased ($p=0.002$).

CONCLUSION

A simple and low cost intervention of development of a student led interest group coupled with a Choose Rheumatology! Campus visit has dramatically impacted student interest in Rheumatology at a single institution.

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Impact of Chronic Kidney Disease on Postoperative Complications Following Revision Total Knee Arthroplasty

BACKGROUND

Total knee arthroplasty (TKA) is a common orthopedic procedure that is becoming increasingly common in the United States. With an aging population the per capita number of TKAs have doubled from 1991 to 2010 and this rate is projected to grow exponentially over the next decade.

Chronic kidney disease (CKD), characterized by a gradual loss of kidney function, is a growing national trend in the United States and is associated with medical comorbidities and increased incidence of postoperative morbidity and mortality. CKD is particularly common amongst an aging population, many of whom are likely to receive a TKA at some point in their lifetime. This study examines the impact of pre-operative kidney function on the risk of post-operative complications for revision total knee arthroplasty.

METHODS

A retrospective cohort study was performed from data collected via the American College of Surgeons National Quality Improvement Program Database from 2005 to 2014. Patients who had undergone revision TKA were identified by CPT code and further stratified based on pre-operative GFR. Univariate and multivariate analyses were conducted appropriately.

RESULTS

In total, 8,454 patients were identified for this study. Decreased GFR was shown to have a significant increase in overall complications, pneumonia, renal insufficiency, renal failure, urinary tract infection, sepsis, septic shock, death, extended hospital length of stay and unplanned return to OR. Multivariate analysis revealed GFR to be an independent risk factor for extended length of stay, renal insufficiency and renal failure.

CONCLUSION

This evidence suggests a trend of higher post-operative complication rates among patients with CKD receiving revision TKA, with particular risk stratified based on worsening CKD stage. In particular, patients with less than 30 GFR had an almost 30% chance of incidence for development of a postoperative complication. Surgeons should carefully consider CKD stage and GFR status when determining patients who would appropriately benefit from revision TKA.

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Prognostic Factors that Predict Failure of Manipulation Under Anesthesia for the Stiff Total Knee Arthroplasty: A Systematic Review

PURPOSE

Failure to maintain a functional arc of motion following primary total knee arthroplasty (TKA) causes significant impairment and patient dissatisfaction. Manipulation under anesthesia (MUA) remains a validated treatment for post-operative stiffness. However, prognostic factors associated with MUA failure remain unknown.

METHODS

A systematic review of the literature was performed to identify studies that reported prognostic factors associated with adverse clinical outcomes for patients who underwent MUA for post-operative stiffness.

RESULTS

7 studies analyzing prognostic factors associated with MUA outcomes were included. Several studies note pre-MUA ROM to be a significant prognostic factor affecting post-MUA ROM at final follow-up. Knees with 70 degrees of flexion pre-MUA.

CONCLUSIONS

The strongest prognostic factor for decreased ROM after MUA is severe pre-MUA stiffness. However, even among this challenging group of patients, a substantial gain in function is still expected with MUA.

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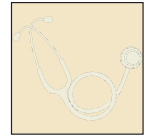
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The Impact of Anesthesia Type on Postoperative Outcome and Complications in Patients Undergoing Revision Total Knee Arthroplasty

BACKGROUND

Revision total knee arthroplasty is an increasingly common procedure and is effective in treating knee osteoarthritis, but has higher complication rates than primary total knee arthroplasty. Anesthetic choice offers a perioperative risk factor that has been extensively studied in primary total knee arthroplasty, showing favorable results for regional anesthesia compared to general anesthesia. Anesthetic choice in revision total knee arthroplasties can be optimized to reduce complications and improve health outcomes.

METHODS

A retrospective study was conducted using the American College of Surgeons National Surgical Quality Improvement Program database. Patients who underwent revision total knee arthroplasties between 2007 and 2014 were divided into three anesthesia cohorts. Univariate and multivariate analyses were used to analyze perioperative factors.

RESULTS

From 9899 patients, 6435 received general anesthesia, 3098 received regional anesthesia, and 366 received Monitored Anesthesia Care/IV Sedation. Patients receiving general anesthesia had increased risk for six adverse outcomes compared to patients receiving regional anesthesia, and one adverse outcome compared to patients receiving Monitored Anesthesia Care/IV sedation. General anesthesia independently increased risk for deep surgical site infection, urinary tract infection, and sepsis compared with regional anesthesia. General anesthesia was shown to be an independent risk factor for having an extended length of hospital stay compared with regional anesthesia or Monitored Anesthesia Care/IV sedation.

CONCLUSION

Patients receiving general anesthesia have increased likelihood for developing adverse postoperative outcomes relative to patients receiving regional anesthesia and Monitored Anesthesia Care/IV sedation. Though complication rates remained low, anesthesiologists must consider the implications of anesthetic choice on postoperative outcomes.

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The Use of Single Nucleotide Polymorphisms in LOXL1 as a Genetic Marker for Pseudoexfoliation Syndrome in Ethiopian Patients

Pseudoexfoliation Syndrome (PEX) is a systemic disease characterized by fibrillary, proteinaceous deposits that accumulate preferentially in the eyes. It is the most common cause of secondary open angle glaucoma worldwide and has been shown to have a strong association to single nucleotide polymorphisms in the lysyl oxidase-like 1 (LOXL1) gene found on chromosome 15q24.1. These mutations have been previously seen in Swedish and Icelandic populations. We are interested in studying the large population of Ethiopian patients at the Medical Faculty Associates (MFA), who have a high prevalence of PEX. The main goal of the study is to assess variations in the LOXL1 gene among this patient population, and its correlation to PEX. Blood samples will be drawn and sent for genetic testing, and we will analyze for different polymorphisms. Patients will first be recruited—about 80 subjects will be involved in the study. 20 patients will also be recruited without PEX to serve as a control. Blood samples will be drawn and genome analysis will be performed to study variations within the LOXL1 gene.

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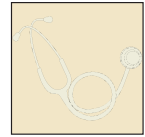
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Impact of Adductor Canal Saphenous Nerve Block on Perioperative Pain Management for Children Undergoing Anterior Cruciate Ligament Repair: A Retrospective Study

BACKGROUND

Anterior cruciate ligament (ACL) reconstruction is a common orthopedic procedure that is associated with significant postoperative pain. Femoral nerve blocks (FNB) provide better analgesia and decrease opioid requirements after ACL reconstruction compared to intra-articular local anesthetic. However, FNBs are associated with decreased quadriceps and hamstring strength, which may delay healing and present an increased risk for falls. There is increasing interest in performing adductor canal saphenous nerve blocks (SNB) for ACL reconstruction, which provide a purely sensory blockade to the knee.

OBJECTIVE

To compare the perioperative opioid requirements and immediate postoperative outcomes following SNB vs. FNB in children undergoing general anesthesia for ACL reconstruction.

METHODS

This is a retrospective study of 105 patients, ages 11 through 18, who underwent ACL reconstruction at Children's National Health System between July 2014 and July 2017. As part of their intraoperative anesthetic management, patients received a FNB, SNB, SNB with local anesthesia, or local anesthesia alone depending on surgeon preference. Intraoperative, postoperative, and perioperative opioid requirements were examined along with use of other rescue analgesics, postoperative pain scores, post anesthesia care unit (PACU) length of stay, and admission rate.

RESULTS

With the exception of gender, no significant differences were observed between the groups in regards to demographics. Males more commonly received a FNB, SNB with local anesthesia and local anesthesia alone while females more commonly received a SNB (0.041). There was no difference in ASA class, length of surgery, length of tourniquet time, and whether additional procedures were performed. Total intraoperative morphine milligram equivalents (MME) and total perioperative MME were significantly greater in patients who received local only vs. a FNB ($p=0.018$ and $p=0.035$) and vs. a SNB ($p<0.001$ and $p<0.001$). No significant difference in total intraoperative and total perioperative MME was observed between patients receiving a FNB vs. a SNB. There were no significant difference in postoperative pain scores, PACU length of stay, admission rates, and postoperative MME between the groups.

CONCLUSIONS

Both FNBs and SNBs significantly decreased intraoperative and perioperative opioid use compared to local anesthesia only in pediatric ACL reconstruction. While both blocks led to similar analgesic efficacy and opioid use, a SNB may be a safer option due to the purely sensory blockade and sparing of quadriceps and hamstring weakness. More studies should be conducted on adductor canal SNBs to further validate its usefulness in children undergoing ACL repair.

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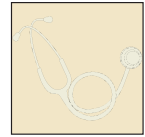
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Trends in Authorship Demographics of Publications in the Journal of Pediatric Orthopaedics from 1985 to 2015: A 30-Year Longitudinal Analysis of Pediatric Orthopaedic Literature

PURPOSE

Academic authorship has increasingly gained importance with established criteria for professional promotion. Although authorship demographic trends have been studied in other surgical and medical specialties, authorship trends have not been studied for publications in pediatric orthopedic surgery. This study sought to elucidate the evolution of authorship demographics in a major pediatric orthopedic surgery journal.

METHODS

The number of authors, gender of the first and last authors, academic degrees, and geographic origin of the corresponding author in *The Journal of Pediatric Orthopaedics* in the years 1985, 1995, 2005, and 2015 were recorded. Only original, published work was analyzed. Statistical analyses with p-values less than 0.05 were considered significant. The Monte Carlo method of the Cochran-Armitage trend test was used for statistical analysis of authorship trends and to evaluate the changing authorship demographics in relation to time elapsed over the 30 year period.

RESULTS

A total of 597 articles were reviewed. The mean number of authors per article increased significantly from 3 in 1985 to 4.8 in 2015 ($p < 0.0001$). Female first authorship significantly increased over the study period from 7.2% in 1985 to 27.0% of publications in 2015 ($p < 0.0001$). There was no difference in the proportion of first authors who held an MD/PhD, PhD, Master's or Bachelor's degree since 1985. There was a significant decrease in proportion of the number of last authors with solely an MD ($p = 0.001$), with an increase in proportion of the number of last authors with an MD/PhD during the study period ($p = 0.002$). During the study period, a decrease in the proportion of first authors who held solely an MD was seen. There has been significant growth in publications originating outside of "North America," with 74.5% originating from "North America" in 1985, decreasing to 71.0% in 2015 ($p = 0.031$).

DISCUSSION

There has been a significant increase in the number of authors per article in *The Journal of Pediatric Orthopaedics*. Similar to other studies, we noted increased number of authors, shifts in the degrees most commonly held by authors, and a greater representation of international authors in the pediatric orthopedic surgery literature. In addition, the proportion of manuscripts primarily authored by female authors has increased significantly in the past thirty years, with the largest increase occurring between 1995 and 2015.

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Impact of COPD on Postoperative Outcome and Complications in Patients Undergoing Primary Total Knee Arthroplasty

BACKGROUND

Total knee arthroplasty (TKA) is one of the most common operating room procedures performed in the United States and has been increasing over the past decade as the population continues to age. The incidence of chronic obstructive pulmonary disease (COPD) in the aging population has been steadily increasing as well. As a result, a larger percentage of patients who undergo TKA have COPD. In this study we assessed the following: (1) What demographics and comorbidities are most likely to present concurrently in patients with COPD? (2) Are patients with COPD undergoing TKA at increased risk for development of postoperative complications within 30 days? (3) Do patients with COPD have a higher propensity for extended hospital stay or unplanned return to operating room? (4) Does COPD act as an independent risk factor for development of postoperative complications within 30 days?

METHODS

A retrospective cohort study was conducted utilizing data collected via the American College of Surgeons National Quality Improvement Program Database. Patients who underwent primary TKA from 2005 to 2014 were included in this study. Complications were classified into operative, directly related to surgical procedure, and non-operative, indirectly related to surgical procedure. Univariate and multivariate analyses were conducted on appropriate data.

RESULTS

COPD was an independent risk factor for complications including deep surgical site infections (DSSI), pneumonia, re-intubation, failure to wean > 48 hours, progressive renal insufficiency, acute renal failure and cardiac arrest requiring resuscitation. Patients with COPD were additionally found to have longer hospital stays and non-home discharge.

CONCLUSION

There is a growing trend of higher complication rates in patients with COPD and other comorbidities undergoing TKA. The evidence discussed here supports the notion that COPD can incur longer hospital stays and complications that involving respiratory, cardiac, and renal systems. Overall complication rates in the post operative period, however, remained low for patients with and without COPD. Total Knee Arthroplasty remains an efficacious and relatively safe procedure.

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Legionnaire's Disease Presenting with Severe Rhabdomyolysis and Acute Renal Failure: A Case Report

Legionnaire's disease is caused by *Legionella* species, and is a recognized but rare cause of rhabdomyolysis. *Legionella* species live in water, and exposure to inoculated water systems leads to transmission of the disease, and commonly causes pneumonia in infected individuals. While the mechanism of muscle destruction legionella infection causes is not fully understood, the prevailing theory is that rhabdomyolysis is linked to an endotoxin released by the bacteria into the blood stream. Massive muscle necrosis manifests as limb weakness, muscle pain, swelling, and gross pigmenturia due to the release of electrolytes, myoglobin, and other sarcoplasmic proteins into the bloodstream. A common complication of this is acute kidney injury due to myoglobin obstruction of renal tubules and direct glomerular cytotoxicity. We present a case of a 49 year old woman presenting a week following heavy rainfall in the mid-Atlantic region with lower extremity weakness, calf and thigh pain, cough and shortness of breath, subsequently found to have severe rhabdomyolysis and acute kidney injury. Her initial laboratory values showed creatinine kinase levels elevated to 423,920 U/L, acute renal failure (Creatinine 8.9 mg/dL, BUN 60 mg/dL), transaminitis (AST 1,798 U/L, ALT 440 U/L), and hyponatremia (Na 128 mmol/L). Initial chest x-ray was notable for a right lower lobe hazy consolidation, and urine legionella antigen was positive. Subsequent work up including hepatitis, HIV, urine toxicology, thyroid stimulating hormone, nasal PCR and flu swabs, and blood and urine cultures were all negative. The patient was started on levofloxacin and aggressive intravenous fluid hydration. Our case highlights the value of including a broad infectious work up when investigating the cause of rhabdomyolysis, as early diagnosis and initiation of treatment can prevent life threatening complications of the disease. We also review the epidemiology, clinical and laboratory findings, and treatment of Legionnaire's disease causing rhabdomyolysis.

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Effects of a Formal Educational Class on the Quality of Life in Patients Diagnosed with Hypothyroidism

BACKGROUND

Hypothyroidism is a chronic disease that requires self-care skills such as healthy diet, exercise, and a daily medication regimen where timing of food intake is essential. There are many barriers that affect a patient's self-management of their illness which may result in a reduction in quality of life. Adequate education is essential for patients with hypothyroidism to be able to manage their disease, and to live with the best quality of life possible. Many studies have been conducted to assess the perceived health status of patients with hypothyroidism, but few have examined the effects of a formal educational program on quality of life.

OBJECTIVES

The purpose of this study is to determine if a formal hypothyroidism educational class will improve the ThyPRO-39us quality of life survey among patients diagnosed with hypothyroidism.

METHODS

In this prospective pretest-posttest design study, 40 patients diagnosed with hypothyroidism recruited from a private endocrinology practice in Fairfax, Virginia were asked to complete the ThyPRO-39us quality of life survey, after which they attended a 45-minute formal hypothyroidism educational class hosted by myself, the nurse practitioner. Four weeks after the class, they were mailed the same ThyPRO-39us surveys which they completed. SPSS23 was used for statistical analysis and paired t-tests were performed to determine any significant changes in the ThyPRO-39us composite and subscale scores on quality of life.

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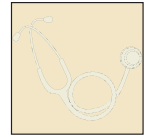
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ACL Growth with Age in the Skeletally Immature: An MRI study

BACKGROUND

The current knowledge of morphological changes during growth of the ACL in the skeletally immature patient is limited.

PURPOSE

To establish normal ACL growth trajectories in skeletally immature patients utilizing serial magnetic resonance imaging (MRI) examinations.

MATERIALS AND METHODS

A retrospective review of patients aged 0 to 18 years who had undergone at least two serial magnetic resonance imaging (MRI) examinations of the same knee for reasons other than ACL tear was performed. A total of 365 MRIs were reviewed. The parameters measured included physeal status, sagittal length of the ACL, diameter of the ACL in the sagittal and coronal plane, ACL-tibial inclination angle, femoral transcondylar width and intercondylar notch width, the anterior and posterior borders of the ACL attachment, anterior-to-posterior dimension of the tibia, and tibial epiphyseal height. A Pearson correlation coefficient was calculated to determine the direction and strength of each measurement taken compared to age. Growth curves were created for individual parameters by calculating average growth vectors across quarter year age intervals. This produced a predictive model for the rate of growth for ACL parameters at different ages.

RESULTS

Of the 147 patients included, 50.3% were female. Ages at time of MRI ranged 1.3 to 21.7 years, inclusive of all MR images available (average 13.5 years, SD 3.60). The Pearson correlation coefficient for each measurement examined showed statistically significant relationship relative to age, with varying degrees of strength. The ACL grows in length and diameter with age, and younger patients had more oblique, anteriorly attached ACLs compared to older patients. The ACL length growth model shows three distinct phases of growth: patients age 1.5 to 5.75 years average 2.25 mm of growth per year (mm/yr); patients aged 6 to 11.5 average 1.46 mm/year; and growth begins to plateau at age 11.75, reaching 0 mm/year by age 18.5 years. The ACL sagittal diameter growth model shows an average of 0.45 mm/year between 1.5 and 14.5 years old, after which growth slows until it stops at age 18.75.

CONCLUSION

In the skeletally immature patient, the ACL grows in length and diameter in the coronal and sagittal planes in an approximately linear fashion until age 18. Additionally, the tibial insertion of the ACL becomes more posterior and the orientation of the tibial insertion more vertical with age. This model aids clinicians in predicting normal ACL parameters for reconstruction procedures in the skeletally immature patient, specifically in very young patients.

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Insurance Coverage of Patch Testing: A Retrospective Review in a University Dermatology Clinic

BACKGROUND

Patch testing is considered both cost effective and beneficial to quality of life in patients with allergic contact dermatitis (ACD). Furthermore, increased number of allergens tested has been shown to correlate with increased relevant test results. However, health insurance providers and plans have differing allergen testing limits and guidelines for coverage. A more robust understanding of how patch testing contributes to patient financial burden is needed.

OBJECTIVE

To determine differences in insurance coverage and out-of-pocket (OOP) patient costs of patch testing.

METHODS

A retrospective chart review of patients at the George Washington University Dermatology Clinic receiving patch testing between January 1, 2015 and June 30, 2017 was performed. Data regarding patient demographics, testing plans, testing regimens, and calculated OOP costs were collected. Means of continuous variables were compared using Student's T-test and proportions of categorical variables were compared using Fisher's Exact Test.

RESULTS

Of the 414 charts reviewed, 367 met inclusion and exclusion criteria. Of the 367 patients, 316 had private insurance, including CareFirst® (N=162), United Healthcare® (UHC) (N=49), Aetna® (N=39), and Cigna® (N=38), while 51 patients were insured by Medicare. Patients with private coverage were 45.7 years old on average, compared to a mean age of 70.5 for Medicare patients. Medicare patients paid \$180.06 in OOP costs on average, which was significantly less than CareFirst® patients (\$396.58, $p < 0.01$) and all privately-insured patients combined (\$403.70, $p < 0.01$). No significant differences in average OOP costs between patients of different individual private insurers were found. About 65% of UHC patients encountered allergen limits, in comparison to about 21% of Aetna® patients ($p < 0.0001$), 1.2% of CareFirst® patients ($p < 0.0001$), and 0% of Cigna® patients ($p < 0.0001$). The highest percentages of patients encountering treatment changes due to private insurance coverage were found in Aetna® (about 15%) and UHC (about 14%) patients, which contrasted 0% of both CareFirst® and Cigna® patients.

LIMITATIONS

This study did not control for differences in insurance coverage due to age or patient preference for paying OOP costs.

CONCLUSION

Allergen limitations imposed by insurance coverage are associated with altered treatment plans in patients undergoing patch testing. Further studies are warranted to delineate whether the cause of differences in OOP costs between privately and publically insured patients are due to confounding age-based differences in healthcare expenses and/or preferences.

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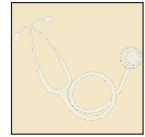
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Biphasic Anaphylactic Reactions and Emergency Department Observation Times

BACKGROUND

The biphasic reaction is a feared complication of anaphylaxis management in the emergency department (ED). The traditional recommended ED observation time is 4-6 hours after complete resolution of symptoms for every anaphylaxis patient. However, there has been great controversy regarding whether this standard of care is evidence-based.

METHODS

Articles were selected using a PubMed, MEDLINE search for the keywords "biphasic anaphylaxis", yielding 155 articles. Articles were filtered by English language, and the keyword biphasic in the title. Case reports and case series were excluded, narrowing to 33 articles. Then, articles were filtered by relevance to the ED setting, and studies conducted in outpatient clinic settings were excluded, narrowing the search to 16 articles. All remaining articles were reviewed and findings were discussed.

RESULTS

The reported mean time to onset between the resolution of initial anaphylaxis and biphasic reaction ranges widely by study from 1-72 hours with the majority of studies reporting the mean time to onset greater than 8 hours. A delay between anaphylaxis symptom onset and administration of epinephrine of 60-190 minutes was reported to correlate with biphasic anaphylaxis in three studies. Anaphylaxis requiring >1 dose of epinephrine to achieve symptom resolution was also reported to correlate with biphasic reactions in two studies. No definitive conclusions about the role of corticosteroids in preventing biphasic reactions can be made at this time however; a couple small studies have shown that they may decrease the incidence of biphasic reactions. Additional risk factors correlated with biphasic reaction vary widely between studies and the generalizability of these risk factors is questionable.

CONCLUSIONS

There is a need for further research to identify true risk factors associated with biphasic anaphylaxis and to clearly define the role of corticosteroids in biphasic reactions. However, given the low incidence and rare mortality of biphasic reactions, patients who receive epinephrine within one hour of symptom onset and who respond to epinephrine with rapid and complete symptom resolution can probably be discharged from the ED with careful return precautions and education without the need for prolonged observation.

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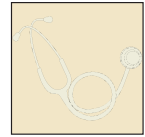
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Perioperative Complications and Impact of Diabetes Mellitus Severity on Revision Total Knee Arthroplasty

BACKGROUND

Total knee arthroplasty (TKA) is a common and effective treatment of knee osteoarthritis. As the amount of TKAs performed increases, so does the number of TKA failures and subsequent revisions. Diabetes mellitus (DM) has been shown to increase complications following orthopedic procedures. For these reasons, it is important to understand the association between severity of DM and the risk of perioperative adverse events following revision TKA.

METHODS

A retrospective cohort study was conducted using the American College of Surgeons National Surgical Quality Improvement Program database. Patients who underwent revision TKAs between 2007 and 2014 were identified and recorded as having non-insulin-dependent DM (NIDDM), insulin-dependent DM (IDDM), or no DM. Univariate and multivariate analysis were used to evaluate the incidence of multiple adverse events within 30 days after revision TKA.

RESULTS

A total of 9,921 patients who underwent revision TKA were selected (without DM = 7845 [79.1%]; NIDDM = 1349 [13.6%]; IDDM = 727 [7.3%]). Patients with NIDDM were found to have an increased risk of developing 1 of 20 adverse events studied compared to patients without DM, while patients with IDDM were found to have an increased risk of developing 6 of 20 adverse events compared to patients without DM.

CONCLUSION

Relative to patients with NIDDM, those with IDDM have a greater likelihood of developing more adverse perioperative outcomes than patients without DM. Although complication rates remain relatively low, orthopedic surgeons must consider the implications of diabetes and insulin dependence on patient selection, preoperative risk stratification, and postoperative outcomes.

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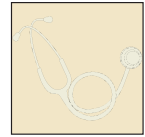
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Current Trends in Surgical Airway Management of Patients with Robin Sequence

BACKGROUND & PURPOSE

Robin sequence (RS) is the clinical triad of micrognathia, glossoptosis, and airway obstruction. Mortality rates range as high as 65%, though improved nutritional support and airway management may reduce this rate. In severe cases, surgical intervention may be indicated to relieve airway obstruction. Though the efficacy of certain surgical interventions (e.g. tracheostomy, tongue-lip adhesion - TLA, mandibular distraction osteogenesis - MDO) in improving patient outcomes is well established, algorithms dictating decision making and peri-operative protocols are poorly defined. To aid in establishment of distinct protocols among surgeons treating RS, we designed a survey to elucidate current practice trends.

METHOD/DESCRIPTION

A 22-question survey was designed on SurveyMonkey (www.surveymonkey.com) and sent via e-mail to members of the American Cleft Palate-Craniofacial Association and International Society of Craniofacial Surgeons. Questions were related to surgeon experience in treating RS, and peri-operative protocols. Responses were collected for 8 weeks.

RESULTS

A total of 151 responses were collected. Most respondents were surgeons practicing in North America (82.8%), in a university hospital setting (81.5%), and had completed a fellowship in pediatric plastic surgery or craniofacial surgery (76.2%). Pre-operative protocols varied widely. While 78.8% of respondents performed direct laryngoscopy, only 49.7% routinely obtained pre-operative polysomnography. Minimum apnea hypopnea index (AHI) for surgical intervention ranged from 30 (6.8%). 74.2% reported MDO as their most common primary surgical modality, with 12.6% primarily utilizing TLA. Similarly, only 45.7% perform TLA. Surgeon experience influenced operative selection, with 80% of those in practice 0-5 years primarily utilizing MDO, compared to 56% in practice >15 years. Among those performing MDO, there were variations in osteotomy selection (inverted L ramus-39.3%, angle-37.8%), distraction vector (horizontal-64.0%, oblique-22.1%), type of device (internal-80.0%, external-23.1%), and use of virtual surgical planning (yes/sometimes-50.0%, no-50.0%). 25.2% did not incorporate a latency phase. Daily activation length mostly ranged from 1.0mm (45.1%) to 2.0mm (32.3%), with most choosing an endpoint of class 3 occlusion (56.0%) or "as far as possible" (28.4%). There was no consensus on consolidation phase (4-6 weeks-20.0%, 6-8 weeks-31.3%, 8-10 weeks-19.1%, >10 weeks-25.2%). Most respondents (90.3%) reported low rates (0-24% of patients) of required secondary intervention for apnea after distraction.

CONCLUSIONS

Surgical airway management in patients with RS varied widely. Clear trends were not identified in preoperative evaluation, type of surgical intervention, intraoperative or postoperative protocols, though MDO was utilized more than other modalities, particularly among younger surgeons. Further studies and collaborative efforts will help guide standards of care in the airway management of these patients.

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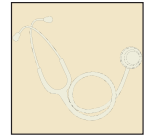
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Postoperative Complications and Impact of Gender on Revision Total Knee Arthroplasty

BACKGROUND

Knee osteoarthritis is a common form of arthritis often treated by total knee arthroplasty (TKA). Complications often arise after TKAs, which may necessitate revision TKAs and further treatments. However, there remains a paucity in the literature regarding influence of gender on post-operative complications rates of those undergoing revision TKA.

METHODS

A retrospective cohort study was conducted using the American College of Surgeons National Surgical Quality Improvement Program database. Patients who received revision TKAs between 2007 and 2014 were identified and recorded as male or female. Univariate and multivariate analysis was used to evaluate the incidence of multiple adverse events within 30 days of revision TKA.

RESULTS

This study included 9,914 patients who underwent revision TKA (females= 5728 [57.8%]); (males= 4186 [42.2%]). Male patients were shown to be at greater risk for developing seven of 17 complications compared to female patients, and female patients were shown to be at greater risk for UTI development. Multivariate analysis showed males as an independent risk factor for 4 complications, and females as an independent risk factor for UTI development.

CONCLUSION

Male patients were more likely to develop more complications post-operatively than female patients. Although the possibility of developing complications is relatively low, orthopedic surgeons should be aware of increased post-operative complication rates when counseling patients who undergo revision TKA.

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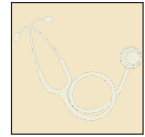
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The Cilioretinal Artery is Protective Against Choroidal Neovascularization in Age-Related Macular Degeneration

IMPORTANCE

A hemodynamic role in the pathogenesis of age-related macular degeneration (AMD) has been proposed, but a relationship between retinal vasculature and late AMD has not been investigated.

OBJECTIVE

To determine if the presence and location of a cilioretinal artery may affect the risk of developing late AMD in the age-related eye disease study (AREDS).

DESIGN, SETTING, AND PARTICIPANTS

Retrospective analysis of prospective, randomized, clinical trial data from 3647 AREDS participants. Fundus photographs of AREDS participants were reviewed by two masked graders for the presence or absence of a cilioretinal artery, and if any branch extend within 500 μ m of the center of the macula. Multivariate regressions were used to determine the association of the cilioretinal artery and vessel location, adjusted for age, sex, and smoking status, with the prevalence of choroidal neovascularization (CNV) or central geographic atrophy (CGA), as well as AMD severity score, for eyes at randomization and progression at 5 years.

MAIN OUTCOMES AND MEASURES

Association of cilioretinal artery with prevalence of and progression to CNV or CGA.

RESULTS

Among AREDS participants, 26.9% of subjects had a cilioretinal artery in one eye, and 8.4% had the vessel bilaterally. At randomization, eyes with a cilioretinal artery had a lower prevalence of CNV (5.0% vs. 7.6%, OR 0.66, $P=0.001$), but no difference in CGA (1.1% vs 0.8%, OR 1.33, $P=0.310$). In eyes without late AMD, those with a cilioretinal artery also had a lower AMD severity score (3.00 ± 2.35 vs. 3.19 ± 2.40 , $P=0.019$). At 5 years, eyes at risk with a cilioretinal artery had lower rates of progression to CNV (4.1% vs 5.5%, OR 0.75, $P=0.050$), but no difference in developing CGA (2.2% vs. 2.7%, OR 0.83, $P=0.354$) or change in AMD severity score ($+0.65 \pm 1.55$ vs. $+0.73 \pm 1.70$, $P=0.112$). In subjects with a unilateral cilioretinal artery, eyes with the vessel showed a lower prevalence of CNV than the fellow eyes (4.7% vs. 7.2%, $P=0.012$).

CONCLUSIONS AND RELEVANCE

The presence of a cilioretinal artery may be protective against the development of CNV, but not CGA. This finding suggests a hemodynamic contribution to neovascular AMD pathogenesis.

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Impact of Age on Postoperative Outcomes Following Laparoscopic Hysterectomy: A NSQIP Analysis

Laparoscopic Total Hysterectomy, Laparoscopic Assisted Vaginal Hysterectomy, and Laparoscopic Supracervical Hysterectomy are all methods used to perform hysterectomies. These are amongst the most common gynecological surgeries for several different gynecological conditions including uterine leiomyomas, adenomyosis, idiopathic abnormal uterine bleeding, endometriosis, gynecological malignancies, pelvic inflammatory disease, and uterine prolapse.

The purpose of this study is to investigate the impact of age on postoperative outcomes and complications following laparoscopic hysterectomies. The four age groups analyzed are <60, 61-70, 71-80, and >80. This information will allow gynecologic surgeons to use age as an independent variable to risk stratify patients undergoing laparoscopic hysterectomies.

The adverse events that will be analyzed are death, cardiac arrest, stroke, sepsis, myocardial infarction, renal failure, thromboembolic events, wound-related infection, on ventilator >48 hours, unplanned intubation, renal insufficiency, return to operating room, wound dehiscence, readmission, pneumonia, urinary tract infection, and extended length of stay.

This is a retrospective observational study that includes data from the National Surgical Quality Improvement Program database on all laparoscopic hysterectomies from 2007 to 2016. They will be identified by the following CPT codes: Laparoscopic Total Hysterectomy: 58570, 58571, 58572, 58573, Laparoscopic Assisted Vaginal Hysterectomy: 58550, 58552, 58553, 58554, and Laparoscopic Supracervical Hysterectomy: 58541, 58542, 58543, 58544

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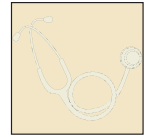
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Chronic Steroid Use in Patients Undergoing Lumbar Decompression Surgery and Postoperative Infectious Complications

INTRODUCTION

It has long been established that corticosteroids have a negative impact on the human immune system's ability to function at an optimal level. Many past studies have shown that patient's will have higher rates of infection if they are taking chronic steroids. What has yet to be established is just how much of an increased risk patients on chronic steroids have for infection after undergoing lumbar decompression surgeries, of which there are thousands per year. We hypothesize that patients on chronic steroids will have higher rates of surgical site infections and higher rates of other infections (UTI, pneumonia, etc.) after undergoing lumbar decompression surgery of the spine.

METHODS

To test our hypothesis, we looked at the ACS National Surgical Quality Improvement Program (NSQIP) database data from 2005-2014. Using CPT codes, we selected out all spine surgeries where the purpose of surgery was to decompress an area of the lumbar spine, including herniated discectomies, laminectomies, among others. Chi-square analysis was done to evaluate for differences among the steroid and non-steroid groups for demographics, preoperative comorbidities, and postoperative complications. Binary regression analysis was done to determine if chronic steroid use independently predicts rates of postoperative infections.

RESULTS

Though chronic steroid use was not found to increase rates of surgical site infections, chronic steroid use was found to independently predict rates of pneumonia (OR: 3.06, $p=0.030$) and septic shock (OR: 3.79, $p=0.008$).

DISCUSSION

While steroid use has been established as immunosuppressive, it has not been established to what extent steroid use increases infection rates postoperatively in lumbar decompression surgeries, of which there are thousands each year. Spine surgeons should remain vigilant regarding postoperative infections in patients on chronic steroids, especially as it relates to pneumonia and propensity to decompensate into septic shock as these occur at significantly higher rates than the general population.

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Initial Impressions with the Flexible Robot

BACKGROUND

In 2000, the da Vinci surgical robot became the first FDA approved surgical robot for use in laparoscopic surgery. Since that day, its use has grown exponentially in fields such as abdominal, thoracic and pelvic procedures. Adoption in other specialties, however, has been limited. Due to design limitations, it is not suited for use in small or confined spaces. Use of the da Vinci in otolaryngology has been especially limited as many of the procedures involve the use of natural orifices and aligning the large arms in such a small space makes usability and visibility of the surgical site extremely difficult. Recently, a new surgical robot, the Medrobotics Flex robot, designed specifically for use in otolaryngology, hopes to address the shortcomings of the da Vinci robot in head and neck surgery. An improved robotic surgery experience in otolaryngology might help spur more widespread adoption.

MATERIALS AND METHODS

A literature review was conducted using the PubMed database to investigate the effectiveness of both the da Vinci surgical robot and the Medrobotics Flex robot, focusing on their use in transoral robotic surgery. To do this, a MeSH search was done using the terms: otolaryngology and robotic surgery with keywords transoral, limited to the last 10 years. Parameters to be compared include: surgical site visualization, operative time, complication rate, length of hospital stay, cost and surgeon impressions.

RESULTS

A total of six articles investigating the Medrobotics Flex robot and five articles investigating the da Vinci robot in transoral robotic surgery were analyzed. The data available for the Medrobotics Flex includes brief case studies, cadaveric studies and one larger clinical trial for FDA approval, focused primarily on surgical site visualization and feasibility where 75/80 surgical sites could be visualized and 72/80 could be treated.

DISCUSSION

Despite the limited data available on the Medrobotics Flex robot, it is apparent that the flexible endoscope design with wristed instruments improves access to sites that were previously difficult to reach using traditional rigid endoscopes and instruments. Though some studies have shown potential benefits when using the da Vinci surgical robot in transoral robotic surgery, such as improved access, tremor reduction and 3D visualization, the increased cost and lack of haptic feedback has restricted adoption of the da Vinci in ENT. Additional studies are needed to develop inclusion exclusion criteria to better exploit the benefits of this new technology in head and neck surgery.

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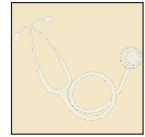
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Pupillometric Assessment of Small Doses of Opioid in a Pediatric Population

According to the CDC, opioid prescriptions in the United States have more than tripled from 1999-2014, which has correlated with the staggering increase in opioid-involved drug overdose deaths. This pattern of prescription is thought to be a major contributory factor to the increase in drug overdose in America, as four out of five new heroin users started by misusing prescription painkillers. Providers need the means to objectively monitor analgesic efficacy of treatment in patients with pain to mitigate unnecessary analgesic prescribing.

It is well established that mu opioid agonists like morphine cause miosis, an effect to which tolerance does not occur. This suggests a utility in using pupil size and responsiveness as a pharmacokinetic analogue of bioavailability. An infrared pupillometer is a device that produces a short light stimulus and subsequently measures parameters of the pupillary light reflex (PLR) including maximum and minimum pupil size (MAX, MIN), maximum constriction velocity (MCV), latency period before constriction onset (LAT), change in pupil size (DELTA), and average constriction velocity (ACV). Current data supports the efficacy of using infrared pupillometry to detect high dose opioid presence, but no research exists judging its efficacy in monitoring low dose therapeutic levels.

We enrolled 15 patients between the ages of 7 and 18 on the pain medicine service receiving low dose opioids on patient controlled analgesia (PCA). The pupillometer was used to take a baseline PLR, and repeated measures were taken 10 and 15-minutes post PCA dose infusion.

We found that the pupil size at 10 and 15-minute time points were significantly smaller than the baseline for the parameters MAX ($p=.0016$, $p=.0010$) and MIN ($p=.0250$, $p=.0070$). Additionally, it was found that LAT was significantly longer from baseline at the 15-minute measure ($p=.0350$), and there was a significant difference between the 10 and 15-minute time points for the MIN ($p=0.0251$).

This evidence supports the sensitivity of the pupillometer in evaluating opioid activity. Furthermore, in concordance with previous research, the MIN is significantly correlated with opioid concentration dose-dependently across the 15-minute measurement window.

Before applying the pupillometer to clinical pain medicine, more research comparing pupillometric parameters with blood levels of opioid metabolites will serve to determine detection limits. Providers could use this tool to monitor treatment efficacy by using these parameters to assess steady state equilibrium and to determine dosing intervals. Furthermore, the pupillometric parameters could elucidate individuals' metabolic capacity for different opioids in order to prescribe therapeutic levels.

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Vitamin C: The Next Step in Sepsis Management?

Sepsis is a life-threatening medical condition, affecting approximately 26 million people worldwide every year. The disease is a continuum, marked by dysregulated inflammation and hemodynamic instability leading to shock, multi-system organ dysfunction, and death. Over the past decades, there has been a focus on the early identification and treatment of sepsis primarily with bundled and goal directed therapy. Despite these advances, morbidity and mortality has remained high, prompting investigation into novel therapies. Vitamin C is a water-soluble vitamin that plays a role in mediating inflammation through antioxidant activities and is also important in the synthesis of cortisol, catecholamines, and vasopressin, which are key mediators in the disease process. Emerging evidence provides cursory data in support of the administration of vitamin C in addition to standard therapy to ameliorate the effects of inflammation and improve hemodynamic stability in patients with sepsis and septic shock; however, further evidence is needed to support this practice. This review discusses the physiologic role of vitamin C as well as the recent literature and evidence for the use of vitamin C in patients presenting with sepsis.

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Whose Job is it Anyway? A Look at Proton Pump Inhibitor De-Escalation Patterns in Patients Receiving Prescriptions from GI versus Non-GI Providers

INTRODUCTION

Proton pump inhibitors (PPI) are amongst the most widely prescribed classes of medication in the United States, commonly prescribed by primary care providers and specialists from a variety of disciplines. Indications for the initiation and maintenance of PPI therapy are well established. However, because they are so widely prescribed, responsibility for the management of PPIs is often diffused over a patient's numerous providers. This study evaluated the rates of PPI de-escalation in patients receiving PPIs from GI versus non-GI prescribers.

METHODS

A retrospective chart review was conducted of patients currently on PPI therapy seen by a faculty gastroenterologist at an urban university medical center over a 12-month period. Data was collected regarding the indication, length, and prescriber of PPIs and whether there was a documented PPI de-escalation discussion. De-escalation was defined as attempts at reduction in dose, reduction in frequency, or complete discontinuation of the PPI. Patients prescribed PPIs for Barrett's esophagus or gastrointestinal bleeding were excluded. A Microsoft Excel database maintaining subject confidentiality was used. Statistical analysis was conducted using a two-tailed Fisher's Exact Test, significance set at $p < 0.05$.

RESULTS

A total of 600 charts were initially reviewed, of which, 324 were included in the analysis. PPIs were primarily prescribed by GI providers in 141 patients and non-GI providers in 183 patients. Of the 141 patients prescribed PPIs by their GI provider, 41 (29%) had documentation of an attempt to de-escalate therapy. Of the 183 patients prescribed PPIs by a non-GI provider, 25 (16%) had a documented de-escalation discussion. There was a significant increase in the frequency of documented attempts at PPI de-escalation amongst patients whose PPIs were primarily prescribed by GI providers versus non-GI providers ($p = 0.0008$).

DISCUSSION

PPIs are highly effective, safe, and commonly prescribed in patients suffering from GERD or similar GI complaints. However, these medications are not without their risks and there is evidence to suggest that patients with uncomplicated GERD who have obtained symptomatic relief with PPIs, should be able to successfully de-escalate their therapy. Our data suggest that gastroenterologists are more likely to have a discussion of PPI de-escalation if the patient's primary PPI prescriber is a GI provider as compared to a non-GI provider (29% vs 16%, $p = 0.0008$).

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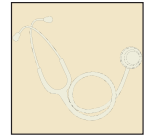
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Postoperative Complications and Impact of Gender on Operative Treatment of Distal Radius Fractures

BACKGROUND

Distal Radius Fracture Repair procedures remain commonly performed. While numerous studies have attempted to differentiate gender impact on operative outcomes, the literature remains inconclusive. In particular, gender impact on orthopedic procedures is controversial. In our study, we examined the effects of gender on postoperative complications following distal radius fracture repairs. We predict that males will have increased morbidity and mortality following operative treatment of distal radius fractures than their female counterparts.

METHODS

Data was collected from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) for all operative treatments for distal radius fractures from 2007 through 2014. Data includes preoperative demographic information and risk factors, perioperative events, and complications occurring within 30 days of initial surgical intervention.

Subjects were identified using Current Procedural Terminology (CPT) codes. Primary CPT codes 25607, 25608, 25609 were used to identify patients receiving operative treatment for distal radius fractures. Two cohorts were defined in this study: (1) Male and (2) Female.

Data on patients' demographics, comorbidities, and postoperative complications were analyzed with univariate and multivariate analyses on SPSS software. Univariate analysis was performed using Pearson's Chi-square for categorical variables or one-way ANOVA for continuous variables. Variables with $p < 0.05$ were selected for multivariate analyses. For the multivariate analyses, Poisson logistic linear regression analyses were performed to determine independent associations of risk factors for post-operative complications. Multivariate analysis results were reported as odds-ratios and 95% confidence intervals. A p-value of < 0.05 was used.

RESULTS

A total of 6,450 subjects were included in this study. Females comprised the majority of the study, with 4,675 (72%) patients. There were 1,775 male patients included in this study (28%). In total, there were 196 postoperative complications (4.2%) amongst females, and 75 postoperative complications (4.8%) seen in the male cohort. Men have an increased likelihood of failure to wean from anesthesia ($p = 0.022$). There was no observed difference between males and females amongst all other comorbidities. Multivariate analysis did not identify gender as an independent risk for post-operative complications.

SUMMARY

There was no difference in postoperative complications based on gender analysis. Furthermore, Gender was not determined to be an independent risk factor for any post-operative complication. Overall complications for operative treatment of distal radius fractures were low for both groups. Based upon our results, risk for postoperative complications should not be stratified based off gender. Patients who stand to benefit from operative treatment of distal radius fractures should receive treatment.

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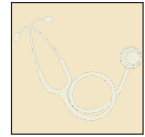
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Longitudinal Follow-Up of Patients with Scleroderma Sine Scleroderma

INTRODUCTION

Scleroderma is an autoimmune disease characterized by inflammation, vasculopathy, and fibrosis. Scleroderma Sine Scleroderma is a subtype of scleroderma in which there is autoantibody positivity as well as internal organ involvement without skin involvement. The purpose of this study was to investigate longitudinal outcomes in a cohort of patients with scleroderma sine scleroderma.

METHODOLOGY

This research was conducted via the STOP Scleroderma Study, a biospecimen and data repository approved by The George Washington University IRB (051427). All subjects gave written informed consent for longitudinal collection of their data. Of the 66 scleroderma patients enrolled in the STOP scleroderma study at the time of data lock, 17 fulfilled criteria for scleroderma sine scleroderma. Data was collected on baseline demographics, and longitudinal measures of disease activity were collected at each clinical visit including the modified Rodnan skin score and the Medsger severity score. Data was analyzed using GraphPad Prism (version 5.0).

RESULTS

Organ involvement was seen in 4 of the 17 patients who had sine scleroderma at enrollment with a mean follow up of 5.90 ± 4.65 years. There was no significant difference in age between patients with (54.13 \pm 13.26 years) and without organ involvement (41.19 \pm 2.84 years, $p=0.138$). Of the patients who developed organ involvement, 50.00% were African Americans and 50.00% Caucasians. There was no significant difference in race between patients with complications and without complications ($p=0.272$). Internal organ involvement included pulmonary (11.76%), GI tract (5.88%), cutaneous (5.88%), and vascular (11.76%) complications.

CONCLUSION

In this cohort of patients with scleroderma sine scleroderma, only 23.53% of patients developed internal organ involvement during follow-up indicating scleroderma sine scleroderma generally carries a good prognosis. Ongoing longitudinal follow up of this cohort is planned.

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Missed Opportunities for Attempts at De-Escalation of Proton Pump Inhibitor Therapy

INTRODUCTION

Proton pump inhibitors (PPI) are amongst some of the most widely prescribed classes of medication in the United States. While long term treatment is appropriate in certain situations, attempts to should be made to reduce, or discontinue their use in many patients.

METHODS

A retrospective chart review of patients with a PPI listed as a current medication seen by a faculty gastroenterologist at an urban university medical center over a 12-month period was conducted. Data was collected to determine the indication for PPI use, reason for clinic visit, and whether or not there was a documented discussion of de-escalation of PPI therapy. De-escalation was defined as attempts at reduction in dose, reduction in frequency, or complete discontinuation, of the PPI. Patients prescribed PPI's for Barrett's esophagus, Helicobacter pylori infection, and gastrointestinal bleeding were excluded. A Microsoft Excel database maintaining subject confidentiality was used. Statistical analysis performed via two-tailed Fisher's Exact Test, $p < 0.05$.

RESULTS

A total of 600 charts were initially reviewed, of which, 324 were included in the analysis. Of the 324 patients, 141 patients were prescribed a PPI by a gastroenterologist. 72 out of 141 were seen for GERD, and 69 seen for non-GERD reasons. 29 patients (40%) seen for GERD had documented discussions of de-escalation, compared to 12 (17%) of patients being seen for non-GERD reasons. A missed opportunity exists for attempts at de-escalation in patients who are prescribed a PPI by a gastroenterologist, yet being seen for a chief complaint unrelated to GERD ($p = 0.0031$).

DISCUSSION

Proton pump inhibitors are amongst the most commonly prescribed medications in the United States. There is evidence to suggest that patients with uncomplicated GERD who have obtained symptomatic relief with PPIs, should be able to successfully de-escalate their therapy. Our data show that when a gastroenterologist is the prescriber of a patient's PPI, and the patient is being seen for a GERD related chief complaint, the likelihood of a documented de-escalation discussion is much greater than compared to when a patient is presenting for a non-GERD related chief complaint (40% vs 17%, $p = 0.0031$). While PPI's are quite safe, and overall, well tolerated, nevertheless, their continued use in a patient should be re-evaluated periodically. There appear to be missed opportunities to for attempts at de-escalation of PPI during non-GERD related visits.

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The Pivotal Role of MRI in the Diagnosis of Listeria Rhombencephalitis

Sixty-six year-old female presented to the Emergency Department with history of several days of headache, malaise, chills, and fatigue with accompanying nausea, vomiting, and inability to tolerate oral intake. She had no history of fever and remained afebrile at the time of presentation. Physical exam and immediate lab values were non-contributory; CSF was obtained and sent for analysis. The patient was placed preemptively on acyclovir, as viral meningitis was the admitting diagnosis. MRI of the brain showed abnormal FLAIR signal hyperintensity and enhancement involving the entire cisternal segment of the left trigeminal nerve, which extended dorsally along the nerve fiber tracks to the left trigeminal nucleus. Abnormal signal extended inferiorly from this nucleus to the left cerebellomedullary junction and upper cervical cord.

Extensive involvement of the trigeminal nerve, brain stem along with CSF findings of lymphocytosis, increased protein and decreased glucose made listeria rhombencephalitis the most likely diagnosis. This was confirmed later by positive CSF growth on the 5th day of the admission.

Listeria is the third leading cause of foodborne related death in US with case fatality rate of 20%. Delay in the early diagnosis increases the associated morbidity and mortality, as the pathogen respond only to the few particular drugs, which typically are not included in the empirical therapy. Specific diagnoses with blood/CSF culture are negative in 40% of the cases with additional challenge added by non-specific clinical history.

The specific tropism of the bacteria for the brainstem and cerebellum with specific imaging findings on MRI are pivotal in early diagnosis. This understanding fosters improved care and decreased morbidity and mortality in this patient population.

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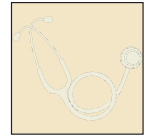
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Perioperative Complications and Impact of Operation Time on Revision Total Knee Arthroplasty

BACKGROUND

Total knee arthroplasty (TKA) is a common and effective treatment of knee osteoarthritis. As more TKAs are performed, there will be more subsequent revisions and failures. In multiple studies, operation length was shown to be a risk factor for postoperative infection and venous thromboembolism. Thus, it is important to understand the association between length of operation time and the risk of these various postoperative complications following revision TKA.

METHODS

A retrospective cohort study was conducted using the American College of Surgeons National Surgical Quality Improvement Program database. Patients who underwent unilateral revision TKAs between 2007 and 2014 were identified and sorted into three different cohorts- below standard operation length (BSOL), standard operation length (SOL), and above standard operation length (ASOL). SOL was defined as between 40-100 minutes. Univariate and multivariate analyses were used to evaluate the incidence of multiple 30-day adverse outcomes after revision TKA with statistical significance as $p < .05$.

RESULTS

Patients that were BSOL were more likely to develop a deep surgical site infection (OR 3.3; CI 1.2-9.0; $p=0.017$) compared to SOL. Patients that were ASOL were more likely to develop a pulmonary embolism (OR 2.5; CI 1.1-6.1; $p=0.038$), but less likely to develop an organ/space infection (OR 0.5; CI 0.4-0.7; $p < 0.001$) or sepsis (OR 0.5; CI 0.3-0.6; $p > 0.001$) compared to patients with SOL.

CONCLUSION

Relative to patients with SOL, those with BSOL or ASOL have a greater likelihood of developing certain postoperative complications. However, there were also certain decreased risks associated with ASOL, particularly infection. Orthopedic surgeons should keep in consideration the implication of operation time as a risk factor for postoperative outcomes.

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A Case of Mistaken Identity: HSP Masquerading as Urticaria

An 8-year-old boy with an atopic history presented to the ED with back pain, cough, diarrhea and two weeks of bruising and arthralgias. He denied fevers, abdominal pain, or gross hematuria. Vital signs were normal. His elbows, knees and ankles were tender to palpation without restricted range of motion. Skin exam was notable for petechiae, palpable purpura, ecchymoses at various stages of healing, and evanescent urticarial plaques on the trunk, upper and lower extremities, buttocks, and genitalia. CBC, CMP, coagulation studies, ANA, RF, Lyme serologies, and urinalysis were normal. C4 complement was low and ASO titers were elevated.

Punch biopsies showed peri- and intravascular infiltrate of neutrophils and eosinophils involving the superficial and deep vascular plexuses. Direct immunofluorescence (DIF) demonstrated IgA vascular deposition. These findings are consistent with Henoch-Schonlein purpura (HSP).

HSP is the most common small vessel vasculitis in children. Clinical presentation classically includes palpable purpura, arthritis, abdominal pain, and nephritis, though not necessarily concurrently. On skin biopsy, HSP demonstrates a neutrophilic infiltrate and IgA deposition in the superficial to mid-dermal vessels. HSP is a self-limited disorder, but 2% of patients will have permanent renal sequelae; thus, close follow-up is required. Our patient had atypical HSP, in which the cutaneous manifestation included urticaria.

HSP typically follows an upper respiratory tract infection but can also follow exposure to other infectious agents. Mucosal IgA and microbial antigen complexes disseminate hematogenously and deposit in vessel walls, inducing complement activation, mast cell degranulation, and neutrophil chemotaxis. Proteolytic enzymes cause vessel wall damage, resulting in palpable purpura. Superficial vessel involvement leads to urticaria and purpura while deep vessel involvement leads to bullous or necrotic lesions. Similar to HSP, acute urticaria develops after exposure to an infectious agent, medication, or allergen. The binding of these substrates to mast cells causes histamine release and leakage of plasma into the dermis. This creates classic erythematous and evanescent wheals.

Conditions associated with immune dysregulation are found in a significant number of HSP patients. Our patient's history of atopy may have played a role in his unusual cutaneous features. We present this case to highlight an atypical presentation of HSP involving urticaria.

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Is Cognitive Rest Following a Head Injury Associated with Prolonged Concussion Symptoms?

BACKGROUND

Recent studies have suggested that cognitive rest may not lead toward a faster recovery from acute concussions. Furthermore, the latest international consensus concussion guidelines note the appropriate amount of cognitive rest remains undetermined. Additionally, somatization has recently been shown to be a risk factor for prolonged concussion symptoms (PCS).

OBJECTIVE

Our objective was to determine the relationship between cognitive rest and PCS. Additionally, we sought to determine the relationship between somatization and PCS, while also considering the interaction with cognitive rest.

DESIGN/METHODS

A prospective cohort study of 5-18 year olds diagnosed with an acute concussion in a tertiary care children's hospital emergency department was conducted from January through December 2017. Participants completed the post-concussion symptom inventory (PCSI) and Children's Somatization Inventory (CSI) at diagnosis.

Emergency department provider recommendations on rest from school were collected. Follow-up calls were completed at 1 week to determine time off from school as a proxy of cognitive rest. Rest was categorically analyzed. PCSI scores were re-assessed at 4 weeks.

RESULTS

A total of 89 patients have been enrolled with a median age of 10.0 (IQR: 8.5-13.0). 58% (N=52) of the patients are male. 82.0% (N=73) completed 7-day follow-up. 24.7% (N=18) of patients took no time off from school; 42.5% (N=31) took 1-2 days off; and 32.9% (N=24) took 3 or more days off from school. 24% had prolonged concussion symptoms. Logistic regression analysis was used to compare the rest tertiles to PCS, with no time off as the reference category. When compared to the shortest rest tertile, the longest rest tertile had a 1.35 fold increase in prolonged concussion symptoms, which was not statistically significant (95% CI: 0.31–5.91). When compared to the shortest rest tertile, the medium rest tertile had a 0.50 fold decrease in prolonged concussion symptoms, which was also not statistically significant (95% CI: 0.10–2.42). In the longer rest tertiles, somatization scores trended higher in the group with PCS ($p = 0.15$).

CONCLUSION(S)

In our preliminary pilot data, patients who took more time off from school did not show decreased likelihood of prolonged concussion symptoms. Furthermore, patients with somatization may be at particular risk of rest associated with prolonged concussion symptoms. Further larger scale studies, including randomized trials, are necessary to determine the risk of rest on prolonged concussion symptoms.

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Outcomes of Paradoxical Vocal Cord Motion Diagnosed in Childhood

Paradoxical vocal cord motion (PVCM) is a condition where the vocal cords inappropriately and intermittently adduct during inspiration. In the pediatric population, PVCM is an affliction of adolescents. A variety of etiologies including laryngeal hyper-responsiveness, sensory defects, psychogenic origins, irritant exposure and more have been suggested however, the exact etiology of PVCM is not well understood. This arguably contributes to the prolonged time between symptom onset and definitive diagnosis. While the current mainstays in PVCM treatment include speech therapy, biofeedback and patient education, there remain key unanswered questions including: do patients continue to experience episodes of dysfunction after achieving early control with biofeedback, do patients still practice vocal cord relaxation techniques, and does PVCM affect participants' quality of life? This cross sectional study assesses the outcomes for patients diagnosed with PVCM at Children's National Health Center over a 10-year period. Chart review identified fifty-two patients with PVCM, these patients were then given a REDcap-based survey assessing participants' time from symptom onset to diagnosis, treatments recommended to them, their continued use of treatments, persistence of symptoms and impact on quality of life. Data collection and analysis is ongoing.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Emergency Department Opioid Prescriptions for Shoulder Dislocations 2005-2015

INTRODUCTION/BACKGROUND

Shoulder dislocations are frequently related to sports and outdoor activities. Many reduction techniques for simple anterior shoulder dislocations can be successfully performed in the field with simple or no analgesics. Despite this, many patients in U.S. EDs continue to be treated with opioid analgesics. To assess this, we performed an analysis of the medication administration dynamics of closed shoulder dislocations in U.S. EDs.

OBJECTIVE

To analyze dynamics and trends in medication administration for closed shoulder dislocations in U.S. EDs.

METHODS

We analyzed shoulder dislocation ICD codes from the CDC's 2005-2015 National Hospital Ambulatory Medical Care Survey, determined the medications prescribed, and subsequently applied appropriate statistical analyses.

RESULTS

Patients with closed shoulder dislocations of any type totaled over 2 million between 2005-2015. The majority, 71.1% (95% CI 64.7-76.7, $p < 0.0001$), received opioids while in the ED, with 47.4% (95% CI 41.4-53.4, $p < 0.0001$) receiving an opioid as their first medication and 33.9% (95% CI 28.6-39.8, $p < 0.0001$) receiving opioids as a prescription at discharge. Concurrently, 38.6% (95% CI 32.8-44.8, $p < 0.0001$) of patients were administered NSAIDs in the ED, 11.4% received muscle relaxers (95% CI 8.32-15.31, $p < 0.0001$) and 3.3% (95% CI 1.6-4.66, $p < 0.0001$) received lidocaine injections. Between 2005-2015, the administration of opioids experienced a relative change overall of -10.2%, excepting hydromorphone and fentanyl, which increased 14.6% and 12.2%, respectively.

CONCLUSIONS

Most patients presenting to EDs with shoulder dislocations received opioids in some form. NSAIDs, muscle relaxers and lidocaine injections were comparatively underutilized. We conclude that shoulder dislocations are a significant source of opioid overprescription. Providers should feel comfortable reducing shoulder dislocation without the use of opioids.

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Review of a Medical Pre-Clinical Curriculum for Competencies in Caring for Patients Who Are LGBT, Gender Nonconforming, or Born with DSD

PURPOSE

This review aimed to assess whether the George Washington University medical, pre-clinical curriculum met any of the Association of American Medical College's (AAMC) 30 professional competencies to improve health care for people who are lesbian, gay, bisexual, transgender (LGBT), gender nonconforming, or born with disorders of sex development (DSD).

METHODS

Relevant sessions were reviewed based on instructors' PowerPoint slides, audio recording of sessions (when available), assigned pre-session material, and notes taken by a student. Content and objectives from each session were mapped to corresponding AAMC competencies, and each competency was qualitatively graded as completely met, partially met, or unmet.

RESULTS

This review found that 18 of the 30 AAMC competencies were completely or partially met. Of the 12 competencies that were unmet, the majority fell into the domains of professionalism, systems-based practice, inter-professional collaboration, and personal/professional development. Mandatory sessions specific to LGBT/DSD health care totaled 7.5 hours, and an additional 13 hours addressed broader topics of sexual health.

CONCLUSIONS

Strengths of the curriculum included greater than the national average of 5 hours of LGBT-related content, access to LGBT patients on panels, and inclusion of gay and lesbian patients in standardized patient exercises. While psychological and social determinants of health for LGBT patients were addressed, the curriculum lacked similar material for patients who are gender nonconforming or born with DSD.

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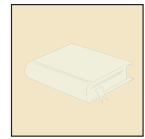
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Deeper Look into Medical Foods: Where is the Best Patient-Centered Information?

BACKGROUND

An assortment of medical foods, formulated to be consumed or administered enterally under the supervision of a physician, have established roles in the management of Inflammatory Bowel Diseases (IBD) as adjunctive or stand-alone therapies. The internet is a common method patients use to look for health-related information. Our aim is to evaluate and assess the quality and readability of information about medical foods found on the internet.

METHODS

Using Google search engine, we retrieved the first 100 websites using the search term "Medical Foods and IBD." Information was categorized by academic (journal/abstract), commercial (products for sale), informational (leaflets) or personal (blogs). Information quality was evaluated using the DISCERN instrument. DISCERN scores were categorized as Excellent 63-75, Good 51-62, Fair 39-50, Poor 27-38, and Very Poor < 26. The readability was assessed using Flesch-Kincaid Grade Level calculation. We conducted a one-way ANOVA between website subcategories of DISCERN and readability level.

RESULTS

A total of 25 websites were evaluated after the exclusion of inaccurate and duplicate websites. The average DISCERN score for all sites was in the poor category (38) and every subcategory was also poor or fair (Academic 43, Informational 40, Commercial 29, and Personal 33). The average Flesch-Kincaid grade level for all subcategories was at or above high-school level (13). There was no difference between DISCERN scores ($P=0.17$) or readability levels ($P=0.425$) among website subcategories.

CONCLUSION

This study demonstrated that the overall quality of websites was poor and the reading level was above the American Medical Association's recommended sixth grade level. Contrary to expectation, academic websites were only of fair quality. Moreover, non-academic websites traditionally targeting patients were at or above high school reading level. Therefore both health consumers and providers lack access to high quality, easy to understand information regarding Medical Foods in IBD.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Knowledge Retention Across Curricular Models: An International Collaboration

Anatomy is one of the first subjects taught in medical school, and its retention over time has been strongly debated (Waterston and Stewart, 2005). Physicians have commented on medical students' poor anatomical knowledge in surgically oriented clerkships (Jurjus et al., 2014). Literature also shows that correlating clinical and anatomical sciences throughout early medical education may improve anatomical knowledge retention (Jurjus et al., 2016; Zumwalt et al., 2010). With major medical school curricular changes happening globally, more quantitative data confirming this correlation is needed.

The medical curriculum at The George Washington University (GWU) School of Medicine recently transitioned from a discipline-based curriculum to an integrated system-based one, and an evaluation of anatomical knowledge retention between classes in the different curricula was conducted. Students from the last class of the discipline-based curriculum and those from the first and second classes of the new, integrated curriculum completed a 27-question test before starting their clinical rotations. Scores were then analyzed and compared between classes.

The results demonstrated a significant increase in retention ($p=0.012$), with a mean score based on the old curriculum of 56.28% (SD=24.6%), as compared to a mean score of 63.98% (SD=23.48%) based on the new curriculum.

The results show that integration enhances retention in the anatomical discipline. To strengthen these findings, we are conducting an international multicenter study, in collaboration with four other medical schools that have very different curricula: The American University of Beirut (Lebanon), Balamand University (Lebanon), Palermo University (Italy), and University College Cork (Ireland). A uniform baseline pre-test will be given at the end of pre-clinical anatomy instructions and a post-test will be given prior to students going into the relevant clinical rotations, and retention drop will be measured accordingly. The effectiveness of different curricula will be evaluated by comparing baseline and final test scores. This multicenter study will offer unique insights and comparisons of various curricular models.

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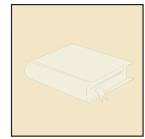
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Use of Ultrasound to Teach Living Anatomy to Graduate Students

Ultrasound technology is used to reinforce gross anatomy instruction in many medical sciences programs. However, this technology has not transferred into common practice for anatomy instruction in non-medical graduate courses. The addition of ultrasound sessions provides a clear view of local anatomy and could help graduate students transfer anatomy from didactic content onto a living, moving body. This modernized approach to instruction complements the rapidly evolving technological advances in science education and may assist with spatial understanding, knowledge retention, and student engagement. Our main objective of this study was to determine the efficacy of ultrasound sessions in order to aid comprehension and retention of gross anatomy.

We tested our hypothesis with two cohorts of students (n=48) who were enrolled in both graduate-level gross anatomy, and a parallel course that was designed to introduce imaging techniques for visualizing normal anatomy. During these courses, students participated in three interactive, two-hour long ultrasound sessions that corresponded to the gross anatomy lecture material. At the end of the semester, the students took a final examination and lab practical, which was scored and averaged to evaluate their content mastery. They also filled out a questionnaire to assess their learning experience and interest level in the sessions. The questionnaire results were analyzed, and the words and phrases that were used most frequently to describe the sessions were collected.

Analysis of the 31 questionnaires that were completed, demonstrated that 96.77% (30) of the students felt that the ultrasound sessions aided in their anatomical comprehension. Despite the fact that the students had a limited background in ultrasound technology or anatomy, 90.32% (28) of them felt that they had adequate knowledge from the gross anatomy lectures to be able to benefit from the sessions. Furthermore, the students unanimously "agreed/strongly agreed" that ultrasound technology should be used for anatomical instruction for graduate students. Free response data showed that while students found the sessions to be helpful, they sought more and longer sessions, and smaller group sizes. The average score of the combined final examination and lab practical was 79% correct, indicating that students had an appropriate level of understanding of anatomical concepts related to ultrasound technology for a graduate anatomy course. Overall, this study supports the idea that using ultrasound technology to reinforce gross anatomy instruction to graduate students may be an effective and engaging method of instruction that will aid in comprehension and retention of the content.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Medical Students in a Hybrid Microscopic Anatomy Instructional Setting

MOTIVATION

As the number of hours dedicated to histology and pathology instruction in medical school declines, there is a need for innovative methods of instruction. At The George Washington University (GWU), medical students adapted the use of a hybrid teaching approach that combines formal lectures in histology and pathology, self-guided laboratory experiences, and independent study with the microanatomy and pathology atlas (MAPA) e-learning tool. This study aims to assess and compare the effectiveness of this hybrid model as GWU transitions to this approach.

The purpose of this study is to evaluate the hybrid model in its effectiveness and learning experience as perceived by the students. This study's hypothesis is that principles of e-learning, when applied to a hybrid microanatomy instruction, will lead to increased student satisfaction and improved performance.

APPROACH

As GWU transitions to this hybrid model, different classes of medical students encountered different elements of the new course structure. Both first and second year medical students will complete a survey on the perceived effectiveness of the separate elements of this hybrid model to compare experiences. In addition, attendance records and test scores in histology and pathology will also be gathered to evaluate the efficacy of this new curriculum relative to the transitional curriculum.

PRELIMINARY RESULTS

In one component of the study, students who completed the survey demonstrated an overall satisfaction with new e-learning tool, MAPA. Among the class of 2021, 58% of those who responded stated that MAPA was exceptional or exceeded expectations, while 42% stated it met expectations. Of those who participated from the class of 2020, 57% thought the MAPA tool to be exceptional or exceeding expectations, and 36% believed MAPA met their expectations.

The results from the student examinations in histology and pathology have yet to be examined, and will be included at a later date. In addition, this study will further investigate the qualitative components of this model through personal interviews with students.

PRELIMINARY CONCLUSION

The new curriculum was designed to combine various teaching methods: the lecture, small group, and independent study with the MAPA e-learning tool. There appears to be an upward trend in satisfaction between the two classes of medical students who experienced either the transitional or new curriculum. Preliminary results from both classes show that the MAPA e-learning tool was reported to enhance their learning of histology and pathology. The students in the new curriculum described an overall better learning experience than those in the transitional curriculum, which supports the hypothesis.

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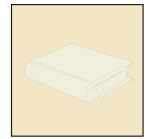
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Non-Traditional Medical Student Experiences on Clinical Rotations

BACKGROUND

According to the Association of American Medical Colleges (AAMC), the average age of matriculation was 24 years over the past four years (AAMC, 2016). This indicates that students are taking at least 2-3 years to pursue additional work or life experiences prior to entering medical school. Students with increased life experience have reported a better transition to clinical years compared to their younger counterparts (Shacklady et al., 2009).

PURPOSE

This study aimed to identify how characteristics of the non-traditional medical students impact their experience on clinical rotations.

METHODS

An anonymous online quantitative survey was sent to medical students enrolled in clinical rotations at The George Washington University School of Medicine and Health Sciences from June through August 2017. Non-traditional students were defined as students that had at least one year between undergraduate study and entering medical school. Survey questions were adapted from a qualitative study on the experiences of mature-aged medical students (Jurjus et al., 2017).

RESULTS

A total of 57 students responded to the survey resulting in a 16% response rate. Average age upon entering medical school was 24 years. The majority (82%) of the respondents were classified as non-traditional, with most (53.2%) taking 1-2 years before matriculating into medical school. Most non-traditional students reported working in a healthcare setting (23.3%), followed by attending graduate school (14.6%). Non-traditional students identified age, previous work experience, and life experiences as having a very strong impact on their clinical rotation experience. These students also cited preparedness as the most important clinical attribute seen in high-performing peers.

CONCLUSION

These findings support the earlier hypothesis that non-traditional students gain valuable experience from their time between obtaining their undergraduate degree and starting medical. We are currently expanding our survey to three other institutions in order to increase our sample size. This will further help to understand the role previous life experience plays in students' clinical experience.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Model to Translate Rehabilitation Evidence into Practice

In light of the Impact Act of 2014 and a series of bundled payment initiatives, many post-acute care (PAC) providers are or will be in a state of transition while they try to provide high-quality care with an increasing focus on lowering costs. The current and impending changes in PAC present a unique opportunity for the collection and dissemination of emerging local innovative strategies PAC providers are developing to address these challenges.

We propose the creation of Mobilizing Post-Acute Care, a free open-access medical education (FOAM) PAC portal of resources and community of experts, as a mechanism to translate research into practice. The use of FOAM has become a growing trend across medical specialties, with the FOAM philosophy that high-quality medical education and resources can, and should be free and accessible to all. Consumers of FOAM are encouraged to re-use and modify resources to fit their needs, but a common critique is FOAM content is not peer-reviewed and therefore the value, validity, and utility of the information shared is suspect. Mobilizing PAC will disseminate FOAM content designed to assist in the development, evaluation, and dissemination of field-tested and innovative practice models, evaluation strategies, and policies that enhance healthcare value in PAC settings. Mobilizing PAC resources will be developed and shared by, a multidisciplinary, collaborative, and expansive PAC community, to improve communication, collaboration, and the timely dissemination of evidence-based and novel strategies within the PAC community.

Mobilizing PAC will create a space for dynamic conversation among providers, researchers, and consumers in the PAC community. Mobilizing PAC is modelled after our successful Urgent Matters FOAM program, which serves as a dissemination vehicle for novel strategies on improving emergency department patient flow and quality by engaging audiences in educational webinars, blogs, podcasts, as well as an annual innovation award that recognizes leading innovations in emergency medicine. Urgent Matters started in 2002 as a ten-hospital collaborative Learning Network that provided breakthrough research on patient flow measurement and improvement. Now with over 7,500 subscribers and an editorial board composed of top Emergency Physician groups in the United States, Urgent Matters has grown to a nationally-recognized resource for innovative strategies and tools in the emergency medicine community. Mobilizing PAC will use the Urgent Matters model and employ similar dissemination channels to provide a collection of enduring, tailorable, and effective solutions for others in the PAC community to improve their delivery of care and patient outcomes.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

GWSMHS Interdisciplinary Emergency Medicine/Trauma Surgery Ultrasound Curriculum Augmentation

The intention of this project was to provide more cohesive structure to the Extended Focused Abdominal Sonography in Trauma (eFAST) curriculum provided during the Trauma Surgery rotation at George Washington School of Medical Health Sciences (GWSMHS). Currently, the curriculum consists of a basic introductory module to the physics of ultrasound and the use of different ultrasound modalities as well as one to two hands-on practice sessions in the Emergency Department during which rotating students are guided through the eFAST. This project was composed of two steps. First, a literature review of eFAST curriculum provided at other medical schools in the United States. Second, improvement of an educational video to be viewed by GWSMHS students beginning the Trauma Surgery rotation, in order to provide an asynchronous learning module.

The intention of the literature review was to learn from the approaches that other schools have taken in teaching ultrasound, and to discover whether any other schools have used an asynchronous module in an interdisciplinary learning environment in their approach (as we planned to do). A number of the articles reviewed looked at the feasibility of adding ultrasound to their curriculum, and shared the details (learning objectives, structure, timelines) of their proposed curriculum. Overall, schools found that the addition of ultrasound to curriculum was well received by students, and improved educational outcomes. While inclusion of ultrasound into undergraduate medical education is a hot topic in medical education, and a number of schools are developing innovation new curriculums to apply it, there was no other school developing an asynchronous module to introduce ultrasound to medical students, which makes the project at GW unique.

I will continue to work with my fellow medical student and with Dr. Ogle to improve the asynchronous learning module, as well as to develop an assessment for 3rd year medical students entering the trauma surgery rotation.

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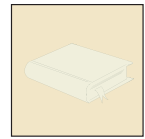
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Exercise as Adjunctive Therapy in Inflammatory Bowel Disease: An Educational Intervention Can Increase Physician Awareness

Exercise has been shown to be safe and have symptom reduction in patients with inflammatory bowel disease (IBD). However, there has been inconsistent incorporation of physical activity in IBD management recommendations. This study evaluated physician awareness of exercise upon IBD and evaluated the impact of an educational intervention upon integrating exercise into IBD treatment plans.

Surveys were administered to physicians in a gastroenterology university practice which addressed the frequency of inquiring about and recommending exercise to IBD patients. A week following survey administration, a brief educational presentation of the current data on the effect of exercise upon IBD was given. Physicians were subsequently surveyed about whether the presentation was helpful and the likelihood that exercise would be recommended to IBD patients. Likert scales were used to evaluate ordinal data. All surveys were anonymous.

9 of 14 physicians (64.3%) completed the initial survey. Most indicated that IBD patients were rarely or never asked about their physical activity (0 always, 0 usually, 2 sometimes, 6 rarely, 1 never), and that most patients rarely or never received recommendations for exercise (0 always, 2 usually, 1 sometimes, 4 rarely, 2 never). Following the educational presentation, 9 of 14 physicians (64.3%) responded and indicated that the information was helpful and that increased effort would be made to discuss exercise (5 strongly agreed, 4 agreed). No respondents were neutral, disagreed or strongly disagreed with recommending exercise to IBD patients.

This study demonstrated that physicians inconsistently ask or recommend exercise to IBD patients and that an educational intervention can increase physician awareness of the therapeutic effects of exercise upon IBD. While this study is limited based upon sample size and self-reporting, it can serve as a basis for additional investigations that focus on exercise, IBD and optimization of clinical outcomes.

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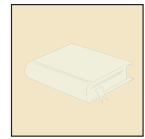
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluation and Recommendations for GW Public Health Curriculum

In response to the evolving health care system, The George Washington University School of Medicine and Health Sciences is integrating a curriculum in Clinical Public Health - the application of principles of public health, population health, and leadership to medical care and health systems decision-making - into its medical education program. This project involved analysis of a specific component of this curriculum, namely, Clinical Sciences and Reasoning case-based sessions. 27 sessions were analyzed, and suggestions for further integration of clinical public health topics were generated. Some examples of the suggestions proposed are included below:

- 1) Intersection of health and other public service sectors
 - a. Health and Housing—understanding housing interventions for various exposures (Pediatric Anaphylaxis Case)
 - b. Health and Schools—understanding the physician’s role in the creation of an Individualized Education Program/504 Plan (Developmental Delays Case)
- 2) Provider resources
 - a. Disease Reporting—understanding department of health requirements for disease reporting (TB case)
 - b. Resource Guide—can be applied to several cases. For cases involving student presentations, one student per group will present on “Community Resources.” The student will compile a list of DC-specific community, patient, and/or provider resources relevant to the case. These resources can be pooled across classes to make a comprehensive “Resource Guide” which can then be used by students in their clinical years.
- 3) Behavioral Health
 - a. Choice architecture - opt out vs. opt in, etc. (Vaccination Debate Case)
- 4) Prevention
 - a. For several cases (e.g. Chronic Kidney Disease Case), ask students to discuss/present on what steps could have been taken to prevent the case from having occurred in the first place?
- 5) Population Health
 - a. Opioid Epidemic—misconceptions, mitigation strategies, etc. (Back Pain Case)

This research project is part of the continuing overall assessment of progress to-date of the new GW Clinical Public Health curriculum and development of improvements and new program directions. This project will have significant impact on the healthcare community. Individual health is increasingly influenced by a wide range of community and population determinants of health. Today, therefore, the scope of practice for clinicians must encompass both individual and community health by drawing on principles of public health, population health, health policy, health systems, and leadership in order to enhance the quality of care delivered and effectively promote the health of our patients and communities. The further development of GW’s clinical public health curriculum is thus integral to the success of its students.

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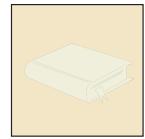
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Gender Differences in Self-Evaluation of Medical Student Competency During Mid-Point of Inpatient Pediatrics Clerkship

BACKGROUND

Self-assessments are increasingly utilized in medical education. Many studies, however, report that self-assessment does not correlate with actual clinical competence. Medical schools should identify which factors influence students to over- or underestimate their performance because these factors impede student ability to identify areas of learning. Despite the yearly increase in female matriculants to medical schools, female medical students tend to underestimate their academic performance compared to male students.

OBJECTIVE

This study uses retrospective data to determine gender differences in medical student self-assessment during the inpatient pediatrics clerkship.

METHODS

De-identified mid-clerkship evaluation forms were obtained from the Office of Medical Student Education for academic years 2011-2016. On these forms, third-year medical students ranked themselves on a linear scale from “unacceptable” to “outstanding” for seven competency domains in inpatient pediatrics: History & Physical, Academic Resources, Patient-Physician Relationship, Verbal Reports, Attitude and Professionalism, Synthesis of Information and Differential Diagnosis, and Treatment Plan and Follow Up. A faculty preceptor evaluated the student on the same scale. To account for variation in competency as a student progresses through clinical training, only students who had pediatrics as their first clerkship in the academic year were included in the study. A total of 110 students’ evaluations (56 female, 54 male) were analyzed. Comparisons between student versus faculty ranking were recorded as underestimated, same, or overestimated ranking. Statistical analysis with Fisher exact test was performed for each competency area.

RESULTS/DISCUSSION

In six out of seven competency domains, female students were more likely to underestimate their performance compared to male students. The domain with the highest degree of female student underestimation (78.6%) was “Treatment Plan and Follow Up”. Male students had a higher percentage of overestimated or same-as-faculty ratings compared to females in most categories. However, these findings were only statistically significant ($p < 0.05$) for the “History & Physical” and “Treatment Plan and Follow Up” competency domains. The results suggest that gender may influence student self-assessments of performance during third-year clerkships. Medical schools should address this influence in order to improve learning during clinical training.

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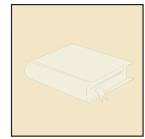
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Effect of Active Learning on Student Performance in Psychiatry

Note: This is not a formal abstract since results have yet to be collected.

The behavioral health pre-clinical education at the George Washington University has changed over the past 3 years as part of a new curricular drive to integrate teaching within a larger systems block. The course has had two different directors with different approaches to active learning and lecture format standardization. This provides a unique opportunity to evaluate the effectiveness of lecture format standardization and active learning on students' subjective satisfaction scores and subject-specific exam performance, including the USMLE.

Lectures and case reviews were standardized for academic year 2017-2018 behavioral health sessions. Each psychiatry session in the Brain & Behavior block was audited on several criteria, including the coverage of assigned learning objectives and readings. Strategies for active student participation using Poll Everywhere questions were also determined. These methods of standardization were suggested to the psychiatry department faculty and were incorporated to varying degree.

Brain & Behavior post-block class reviews, subjective exam scores, and subjective USMLE scores from 2015 to 2018 will be analyzed to determine if the standardization methods will yield higher satisfaction, block exam, and USMLE scores compared to those of students who have had more passive learning and unstandardized lecture formats.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Feasibility and Usability of Tele-Interview for Medical Residency Interview

Every year in the United States, medical students and residency programs dedicate millions of dollars to the residency matching process. On-site interviews for training positions involve tremendous financial investment, and time spent detracts from educational pursuits and clinical responsibilities. Students are usually required to fund their own travel and accommodations, adding additional financial burdens to an already costly medical education. Similarly, residency programs allocate considerable funds to interview-day meals, tours, staffing, and social events. With the rapid onslaught of innovations and advancements in the field of telecommunication, technology has become ubiquitous in the practice of medicine. Internet applications have aided our ability to deliver appropriate, evidence-based care at speeds previously unimagined. Wearable medical tech allows physicians to monitor patients from afar, and telemedicine has emerged as an economical means by which to provide care to all corners of the world. It is against this backdrop that we consider the integration of technology into the residency application process. This article aims to assess the implementation of technology in the form of web-based interviewing as a viable means by which to reduce the costs and productivity losses associated with traditional in-person interview days.

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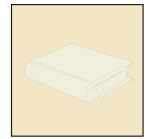
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Creating a Checklist Tool for Teaching the Focused Abdominal Sonography in Trauma (FAST) Exam

The Focused Abdominal Sonography in Trauma (FAST) exam is recommended by the American College of Emergency Physicians (ACEP) and American Academy of Pediatrics (AAP) for training. Education regarding point-of-care ultrasound is becoming more important in emergency medicine, particularly at the resident level. However, evidence-based methods for evaluating competency has not been established.

Researchers from George Washington University Hospital (GWUH) and Children's National Medical Center (CNMC), led by Justin Moher, created a checklist that contained the necessary tasks required for completion of an adequate FAST exam. The checklist was created using the Quality of US Imaging and Competency (QUICK) Score assessment tool, which was then expanded upon by expert sonographers at CNMC and GWUH. The checklist contained 47 items, 31 of which came from the QUICK assessment tool and 16 of which came from expert opinion. Using that 47-item checklist, we observed medical providers performing the FAST exam to identify the most commonly forgotten tasks. Initial results found that 33 of the 47 items on the checklist were missed at least once, nine items on the checklist were missed 18% or more of the time, and four items were missed more than 30% of the time. The research team concluded that the initial results supported the hypothesis that vital items of the FAST examination are frequently missed by novice sonographers. This suggested that an effective checklist tool for the FAST exam is needed.

The research team subsequently identified the nine most frequently missed items from the checklist for creation of a more precise and efficient checklist tool. This 9-point checklist tool is the basis for phase two of the study which is currently underway. During the second phase of the study, we will investigate the checklist tool's utility via comparison of performance of novice sonographers randomized to use the checklist to those randomized to not use the checklist. Both groups will be observed performing FAST exams and will be scored based on the QUICK assessment.

The successful creation of an effective checklist tool will be beneficial for all novice sonographers who are learning the FAST exam for the first time, and could advance the performance of previously trained sonographers. The result of this effort is a possibly innovative discovery that can be applied to all incoming novice bedside sonographer trainees at CNMC and GWUH, and eventually to an even broader population of healthcare providers in ER settings around the country.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

synDRME: A Synthesis of Digital Resources for Medical Education

BACKGROUND

In many developing countries, there is a critical shortage of physicians. Compounding this problem is that medical schools in these countries are unable to train future physicians due to a lack of faculty. Despite efforts, such as those by the Global Health Service Partnership of the Peace Corps, to increase faculty in African medical schools, it has become apparent that many schools will not in fact have adequate faculty numbers for generations to come. However, with markedly improved internet technology, e-learning is becoming a reality in making it possible to deliver quality content to medical students who need supplementary materials in their medical training. Moreover, e-learning can be cost-effective, which overcomes one of the greatest barriers in finding potential solutions to this problem.

OBJECTIVE

synDRME is a website that was created by a team based at George Washington University School of Medicine and Health Sciences to provide students with free electronic resources that have been reviewed and graded on a rubric to help guide users. With the vision to create a complete curriculum that medical students are able to use, synDRME was still lacking in coursework relating to public health and community-based medicine. The team identified this as a major weakness of the project, as these topics are often the cornerstone in practicing medicine in developing countries.

METHODS

Over the past summer, progress was made in identifying, reviewing, and rating resources relating to public health and community-based medicine. Over one hundred different online resources were reviewed, and the team identified the resources it thought would be most valuable to medical students. Additionally, more resources were identified outside of the public health/community-based medicine domains.

RESULTS

The recently identified resources are not yet live on the website, as this is a work-in-progress, but the goal is to have the resources posted as soon as possible. Additionally, the team worked together to identify areas of improvement within the website, take down outdated links, and note areas where more resources should be added. Once complete, the team will look to market synDRME as an educational resource to faculty and administrators in African medical schools, as well as to the students themselves.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Enriching the Medical Student Radiology Clerkship: Simulating the Radiologist's Experience

BACKGROUND

Current radiology training in medical schools is still predominantly limited to passively observing the radiologist at the workstation and through lectures, textbooks and online sources. Evaluation is also mainly limited on still image interpretation or knowledge-based multiple-choice questions. Furthermore, students may have specific interests based on their choice of residency. In order to create a tailored and active learning experience, and to evaluate students' ability in image interpretation, we utilized an open-source web-based Picture archiving and communication system (PACS) named "Weasis" and integrated a report system.

METHOD

We establish a new PACS teaching system by utilizing the open-source PACS system "dcm4chee" and integrating Weasis as imaging viewing browser, MySQL as database and JBOSS as application server. The developmental environment is MyEclipse, developmental language is JAVA. We use WADO (Web Access to Digital Imaging and Communications in Medicine (DICOM) Object) to achieve web-client DICOM images access. Java applets are used via a browser to serve as a DICOM viewer without special software required, and all functions (window width and level, zoom, measurement, etc.) are provided as controls within the server application. Thus we built a reporting system using the same method for student reporting and preceptor commenting and grading. Following the establishing and implementation of a reporting system using the same way as a plug-in, students can write up very brief reports in the form of impression points.

RESULT

Attending radiologists can send desired anonymized studies from hospital PACS during read-out to a shared secure server on the hospital network. Cases can then be immediately accessed by trainees on any computer in the hospital. Students, even simultaneously, can simulate being a radiologist and independently formulate an opinion and write up a brief report, without the need for occupying an expensive PACS workstation. The cases can be categorized into different subspecialties, difficulty levels, and imaging modalities. In addition, this can be also used for examination purposes, both for radiology rotation evaluation of medical students and as part of the pre-call Objective Structured Clinical Examinations (OSCEs) of first year residents.

CONCLUSION

By implementing Weasis and add-on reporting system, a real-time, easy-access, sophisticated Image Database can be established for learning, didactic and evaluation purposes. Teaching cases can easily accumulate, thus to provide a new opportunity for both versatile training and evaluation purposes for radiology programs.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluation of the Current Level of Incorporation of an Integrative Medicine Curriculum into National Physical Medicine & Rehabilitation Residency Training

The most recently released American College of Physicians (ACP) guidelines on treatment of acute, subacute, and chronic low back pain (LBP) suggest a departure from standard medical therapy and an emphasis on integrative medicine (IM) modalities. The guidelines state that non-drug therapies should be used by physicians and patients for acute and subacute LBP. This includes superficial heat, massage, acupuncture, and spinal manipulation. For chronic LBP, the ACP recommends supplementation of non-drug therapy with exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based exercise, tai chi, yoga, and more. The object of this study is to determine if and how integrative medicine modalities are being incorporated into Physical Medicine & Rehabilitation (PM&R) residency training across the country. Data was gathered through email-based outreach to the eighty-seven accredited PM&R residency programs as listed on the AMA FREIDA database. At this point in the research, responses have been obtained from just over 50% of the programs. A preliminary grading system has been established in an attempt to standardize the responses. A grade of "3" was given to programs in which residents receive non-voluntary, organized exposure to IM. A grade of "2" was given to programs in which residents receive voluntary and/or informal exposure to IM, and a grade of "1" was given to programs in which residents receive no official exposure to IM but faculty practice may include some IM modalities. Of the responses received to date, the average grade across all eighty-seven residency programs was found to be roughly 2.04, excluding several entries that must be reevaluated after more data is received. At this point only nine programs have received a grade of 3. Additional work is in progress to create a more specific grading system and to maximize response rate. Future goals also include submission for IRB approval. This research will be an important analysis for medical students with an interest in IM who are pursuing a career in PM&R, and for PM&R residency programs who wish to incorporate IM modalities into graduate medical education in accordance with the most recent ACP guidelines.

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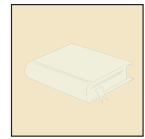
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Exploring Standardized Patients' Perspectives on Working with Medical Students

Little is known about how working with emerging medical professionals affects Standardized Patients' (SPs') professional identities, yet understanding the SP-medical student interaction could be useful for screening SPs, supporting SP professional identity formation, and bridging the SP and medical student cultures. This project provides the unique perspective of SPs involved in the growth of medical students into physicians.

Qualitative methods were used to understand the SPs' perspectives. Two researchers, without evaluative relationships with the SPs, conducted 2 one-hour focus group interviews (n=3; n=9) using a semi-structured interview protocol. Interviews were audio-recorded and transcribed verbatim. Three researchers independently analyzed the transcripts to identify clusters of meaning and codes. Codes identified by consensus and analysis continued until saturation was reached, followed by identification of categories and themes. To ensure credibility and trustworthiness of the results, investigators used triangulation of methods and researchers, prolonged engagement with the data, and presentation of thick rich descriptions as evidence of each theme.

A number of themes were identified in these focus group interviews. SPs experienced a transformation of purpose and the emergence of a new professional identity, including genuine professional, guide, teacher, counselor and surrogate parent. They discovered personal meaning and mutuality in their relationships with students, like the satisfaction of helping others, benefiting society, and growing personally. SPs found themselves reacting to student behaviors in a variety of ways including admiration, dislike, surprise, and discomfort. Finally, SPs confronted challenges in moving between their simulated and real selves.

This analysis provided insights into transformations SPs underwent as a result their work. It revealed a self-actualization process in which SPs experienced an emergence of new roles and a discovery of new meaning in their relationships similar to the professional identity formation process of students. Understanding this process may prove useful to SP educators in knowing how to best nurture identity, train SPS, reinforce job meaningfulness and increase SP recruitment and retention. SP perspectives about their students' behaviors may be useful to SP educators in acclimatizing them to the simulation process.

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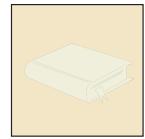
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Review of Social Mission Requirements Across Health Professions Education Accreditation Standards, 2017

BACKGROUND

A number of new trends in health professions education have emerged over the last decade, including the idea of social mission at an institutional and accreditational level. Nevertheless, these ideas lie along a wide spectrum of implementation through written requirements.

RATIONALE

To identify trends in implementation of selected aspects of social mission across health professions education accrediting bodies. We hypothesized that explicit requirement for local community involvement, which is one of the more recently proposed aspects of social mission, is less explicitly addressed than the other aspects.

METHODS

Data were analyzed from the latest editions of public-domain documents as of August 2017. There may be additional private-domain documents which were not included in this analysis.

- MD programs: Liaison Committee on Medical Education (LCME)
- DO programs: AOA Commission on Osteopathic College Accreditation (COCA)
- DMD programs: Commission on Dental Accreditation (CODA)
- Baccalaureate Nursing programs, with scores averaged across the three bodies:
 - Commission on Collegiate Nursing Education (CCNE)
 - Accreditation Commission for Education in Nursing (ACEN)
 - National League for Nursing Commission for Nursing Education Accreditation (CNEA)

Each of the four selected categories, listed below, was assessed by two main questions. Scoring was conducted on a scale of 0 to 2.

- Cultural Competency
- Service Learning
- Local Community Involvement
- Student Teamwork and Diversity

RESULTS

With a maximum score of 16 per category, we observed overall scores of 7 for Cultural Competency, 5 2/3 for Service Learning, 2 for Local Community Involvement, and 9 1/3 for Student Teamwork and Diversity. There were also several implied standards among accreditation bodies for Cultural Competency, Service Learning, and Local Community Involvement.

CONCLUSIONS

Explicit accreditation requirements for institutional involvement in local communities lags far behind the rest of the selected aspects of social mission. In contrast, there is popular emphasis on requiring a certain degree of diversity within student bodies. Based on these findings, the absence of explicitly written requirements for institutional involvement in local communities warrants further study and discussion regarding what local community involvement means to an educational institution's likelihood of inspiring social accountability in its future professionals.

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Occupational exposure to Organophosphate Pesticides and its Effects on Human Sperm Parameters: A Systematic Review

BACKGROUND

Previous research has indicated there is a decrease in sperm quality in the last 40 years. There have been a few reports that have associated occupational exposure to Organophosphate pesticides with a decrease in sperm count, abnormalities in the head or tail, and motility leading to infertility over time. Organophosphates are the most common pesticides used in the United States and have been classified as toxic to bees, wildlife, and humans by the EPA even at low exposures. Furthermore, Organophosphates are considered endocrine disrupting chemicals altering the normal function of the endocrine system. This occurs by interfering with the natural hormones the body produces due to their strong bind to estrogen and androgen receptors.

OBJECTIVE

This systematic review sought to identify relevant studies evaluating the relationship of occupational exposure to Organophosphate pesticides and the decrease of sperm parameters in agriculture workers, pesticide sprayers, and farm workers worldwide.

METHODS

PubMed, Scopus, Himmelfarb, and Agriculture Environmental Science databases were searched for all studies in English. Peer-reviewed articles were selected between the years of 2008 and 2016. Risk of bias was assessed according to the Navigation Guide a Systematic Review Methodology. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was utilized to rate the quality of evidence of each study.

RESULTS

Five studies were identified, reviewed, and analyzed according to inclusion criteria. Selected studies were rated “low, probably low, not applicable, probably high risk, and high risk” for risk of bias. Studies were assigned a “low quality” rating for strength of evidence. Grey literature was excluded.

CONCLUSION

There is sufficient evidence that supports a positive association between occupational Organophosphate exposure and a decrease of sperm parameters in agriculture workers, pesticide sprayers, and farm workers worldwide. Sperm analysis demonstrated a decrease in sperm volume, motility, quality of sperm, and DNA damage, however, future studies are needed to explore this association further.

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Neighborhood Scale Health Impacts from PM2.5 in Four United States Metropolitan Areas

BACKGROUND

Several large cohort studies have found associations between long-term exposure to fine particulate matter (PM2.5) and increased mortality as well as associations between short-term PM2.5 and asthma exacerbation. Findings from these epidemiological studies have been used to quantify health impacts due to PM2.5 and other air pollutants in the United States. Health impact assessments of PM2.5 in the United States have primarily utilized population and baseline incidence information on the county level.

OBJECTIVE

The objective of this study is to evaluate health impacts of PM2.5 at a finer spatial resolution than has previously been estimated (0.01x0.01-degree, approximately 1km x 1km), utilizing tract level disease rates and high resolution exposure estimates in four major US metro areas: Boston, Los Angeles, New York, and Washington, DC.

METHODS

We estimated PM2.5-related asthma emergency room visits and cause specific mortality for stroke, lung cancer, and COPD using epidemiologically-derived health impact functions. We first derived census tract level disease- and age-specific baseline incidence rates by using tract-level to city-level disease rate ratio scaling. Census tract surveillance information was obtained through the CDC's 500 Cities Project and age-stratified mortality rates were obtained from the CDC's WONDER database. Relative risk estimates linking PM2.5 with health outcomes are drawn from a recent American Cancer Society study. The estimated health impacts are calculated using the environmental Benefits Mapping and Analysis Program-Community Edition version 1.3 (BenMAP-CE 1.3). We used tract-level population information from the US Census Bureau. High resolution (0.01x0.01-degree) PM2.5 concentrations are from a global dataset integrating satellite remote sensing with chemical transport modeling and in situ observations.

RESULTS

The results of this analysis show the computed asthma emergency room visits and cause-specific mortality attributable to PM2.5 on 0.01x0.01-degree grid in four major US cities. PM2.5-attributable health impacts vary considerably between tracts within these metropolitan areas. Estimated PM2.5-attributable health impacts will be compared to previous estimates using coarser scale exposure and baseline incidence datasets.

DISCUSSION

We estimated PM2.5-attributable health impacts on a finer spatial resolution than has typically been used, highlighting which neighborhoods within these cities may be experiencing particularly large health impacts from PM2.5 exposure.

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Community Odor Exposure and its Association with Stress and Respiratory Symptoms

BACKGROUND

Odors from industrial facilities are typically characterized as nuisances, however researchers are increasingly studying the potential adverse health effects of community odor exposure. Chronic low-level odor exposure to non-toxic compounds can lead to irritation and physical symptoms.

OBJECTIVE

The objective of this review is to examine whether there is an association between odor exposure and respiratory symptoms or stress in communities that are located near industrial facilities.

METHODS

Using the Navigation Guide systematic review methodology, risk of bias and quality of evidence was assessed for each study. These measures were used to evaluate the overall strength of evidence for an association.

RESULTS

Six studies met the inclusion criteria and were rated from “low” to “high” for risk of bias and “low” to “moderate” for quality of evidence. Overall, the body of evidence had “limited” strength due to imprecision and because bias and confounding could not be completely ruled out.

CONCLUSIONS

There is limited evidence to support an association between industrial odor exposure and respiratory symptoms or stress. More rigorously designed odor assessment studies are needed before a recommendation can be made regarding industrial odor exposure.

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Impact of Water, Sanitation, and Hygiene Interventions on Environmental Enteric Dysfunction in Children in Developing Countries: A Systematic Literature Review

Environmental Enteric Dysfunction (EED) is a global disturbance of intestinal structure and function that has its origin in environmental factors (Owino et al. 2016). As a response to prolonged and persistent inflammation, the intestine morphology is altered. EED is an important contributor to poor child cognitive development, child stunting, poor oral vaccine response, acute infections, and childhood mortality globally (Trehan et al. 2016) in developing countries.

We hypothesized that WASH interventions could reduce the risk of EED, thereby positively impacting children's overall health. The Navigation Guide review methodology and the Grading of Recommendations Assessment and Evaluation (GRADE) were followed to conduct this systematic review. Protocol, including exclusion and inclusion criteria, was developed prior to the review to maintain the transparency of the systematic review. PubMed and Scopus were used to search for studies. Lastly, a qualitative analysis was conducted to evaluate the qualifying studies.

Four studies met our inclusion criteria. Interventions were: Safe disposal of child feces; household environmental cleanliness; household fecal sludge management; and sanitation (presence of toilets). The studies assessed EED by a laboratory diagnostic. All four studies found a significant reduction of EED in the intervention group compared to the control group.

Findings of these studies suggest that WASH could be an effective tool in preventing EED. As prevention is seen to be the only alternative to overcome EED in children, these results also show the need for additional research to determine the most effective WASH intervention.

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The Connection Between Chronic Trichloroethylene Vapor Inhalation and Neurotoxicity

BACKGROUND AND OBJECTIVES

Trichloroethylene (TCE) is a prevalent environmental contaminant with known neurotoxic effects. TCE vapors migrate through soils and building foundations to impact residents via inhalation. This study aims to find literature addressing TCE inhalation effects on the central nervous system (CNS).

METHODS

Based on the Navigation Guide, a systematic review of literature available on PubMed, SCOPUS, and ToxLine was performed using search terms relevant to the following PECO (population, exposure, control, outcome) statement: Does chronic vapor inhalation of TCE have neurotoxic effects on the CNS of adult humans? Article titles, abstracts, and full texts were subsequently reviewed to identify articles that answered the PECO statement. Each article, along with relevant references, was qualitatively analyzed according to risk of bias and quality and strength of evidence criteria adapted from the Navigation Guide. The results of each article were summarized according to the effects they found.

RESULTS

Five articles that meet the criteria were found. Four out of five articles found by the search demonstrated a connection between chronic TCE inhalation exposure and neurotoxic effects, such as decreased coordination and balance. The fifth study failed to find any connection between chronic TCE inhalation exposure and neurotoxicity.

DISCUSSION

Neurotoxic effects on the CNS, including changes in mood, lack of hand-eye coordination, and cognition, may be among early signs of TCE exposure. The inequity of exposure to TCE by lower socio-economic status populations may serve to worsen existing social gaps. Targeted human studies are necessary to inform effective regulations. However, most studies failed to exclude other forms and sources of exposure.

CONCLUSIONS

Although evidence suggests that TCE relates to neurotoxicity, further research is needed to effectively isolate TCE inhalation as the cause of the adverse outcomes. Future studies need to isolate inhalation as the sole source of exposure, develop a consistent method of measuring both exposure and neurotoxicity, and adequately isolate TCE exposure from exposure to organic solvents.

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Attributing Human Health Outcomes to Climate Change: A Systematic Review

OBJECTIVE

A systematic review to examine the attribution of negative health outcomes to extreme weather events caused by climate change.

BACKGROUND

Humans have experienced, and survived, extreme weather events for as long as they have walked on Earth. Over the last few decades, those events have become more frequent and more severe; this increase in intensity is due largely in part to anthropogenic climate change. Although climate scientists were previously unable to attribute any single weather event directly to climate change, this is no longer the case as the scientific evidence has continued to expand. Now, quantitative statements about how human-induced climate change has impacted the frequency and severity of extreme weather events are possible, and the field of studying the effects is known as “attribution science.”

METHODS

We followed the Navigation Guide systematic review method and Johnson et al. (2014) protocol to investigate attribution. We included articles published within the last 10 years directly addressing attribution of human health outcomes to climate change. We evaluated the strength of evidence provided in each selected study and analyzed potential risk biases based on the Navigation Guide’s recommended scale.

RESULTS TO DATE

Four studies met our predetermined inclusion criteria during the preliminary search. We concluded that, although the bias domains were dissimilar from those in Johnson et al. (2014), the overall risk of bias across studies was low, and there is ample evidence to support action.

CONCLUSION

The findings of these studies indicate that anthropogenic climate change has led to increased mortality during extreme weather events, particularly extreme heat events. More studies, and standardized methods, are needed to address attributable mortality for other extreme weather events.

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Occupational Exposure to Solvents and Risk of Neurotoxicity in Construction Painters: A Systematic Review

BACKGROUND

Existing evidence suggests that occupational exposure to solvents can have devastating and adverse effects on cognitive function. Individuals in the construction industry, specifically construction painters, often come in contact with these harmful chemicals on a regular basis. A solvent is a liquid that can dissolve, suspend, or extract other materials without chemical change to the solvent itself. They are present in a wide range of industries and can be used for extraction of fats and oils, degreasing, or manufacturing of paints and plastics. Their main routes of exposure are through inhalation and skin absorption, and they have a tendency to accumulate in lipid-rich tissues like the brain. It is estimated that 49 million metric tons of solvents are produced every year in the United States, and approximately 10 million people are exposed daily. Many solvents used in occupational settings have been shown to adversely affect the central nervous system (CNS), causing a wide range of neurotoxic effects. Symptoms can range from mild nausea, dizziness, and irritability to more serious cases of impaired memory and behavior or alterations to the nervous system. A systematic review was conducted to assess the evidence of occupational solvent exposure and associated symptoms of neurotoxicity in construction painters.

METHODS

A systematic search of the literature was conducted in PubMed and SCOPUS using the Navigation Guide methodology. Titles and abstracts were screened for relevance to the review topic, and appropriate records were chosen based on the specified inclusion criteria. Each record was assessed for risk of bias, and quality and strength of evidence were rated across the body of evidence.

RESULTS/DISCUSSION

A total of seven records were included in this review. Risk of bias was generally low, and quality of evidence was rated moderate. The overall strength of evidence was rated sufficient, as findings from each study suggested that solvent exposure was associated with symptoms of neurotoxicity. Future research should focus on identifying other vulnerable populations with past and current solvent exposure to better understand their toxic effects. Conducting cohort studies with large sample sizes and appropriate, robust exposure assessments is key to confirming associations over a longer period of time.

CONCLUSION

There is sufficient evidence supporting the association between occupational exposure to solvents and neurotoxicity in construction painters. It is crucial we take action to protect workers by reducing or eliminating exposure to ultimately prevent the onset of neurotoxicity and other adverse health outcomes.

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Disparities in Diabetes Rates and Quality of Care within Immigrants in the USA

Immigrants to the USA present an interesting opportunity to test the classical public health question of the impact of place on a health outcome. Diabetes is a prevalent disease in the USA which is slated to rise in rate in the future. Currently, 9.4% of the country is diabetic, and another 28% of the country is prediabetic. We posed the question - is this impact felt disproportionately by immigrants as they live in the US for a decade or more? Our preliminary literature search indicated that this has not been studied extensively, although the impact of American fast food on foreign rates of diabetes has been explored recently.

Using the CDC National Health and Nutrition Examination Survey (NHANES) public dataset, we performed preliminary analysis on the association between the variables measuring how long individuals had lived in the USA and whether or not they had ever been told by a doctor that they have diabetes (either type I or II). Our analysis indicated a statistically significant difference between rates of diabetes in immigrants who had lived in America for less than 10 years and more than 10 years after controlling for age, gender, and education. Based on these preliminary results, we will be building a stronger set of tests by controlling for any other potential confounders we discover from a literature search. The endpoint of such a project is to develop a dose-response or similar model connecting time spent in USA to risk of diabetes.

We also will use the NHANES variables which measured patient satisfaction, insurance rate, and hospital utilization to assess whether diabetic immigrants are receiving an adequate standard of care compared with the general population. Through these two analysis, we hope to illuminate areas for policy change or programmatic activity which can lead to reductions in diabetes rates and prediabetes rates.

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Environmental Degradation in Baía de Todos os Santos, Brazil: A Review of the Evidence

The communities living in Baía de Todos os Santos (BTS) has been subjected to toxicants released into the environment by the growing petrochemical industry surrounding the area. Community members are concerned about the effects that these chemicals have on the health and wellbeing of the people, as well as the natural environment. Many of the communities are artisanal fishers and rely on the fish and shellfish produced by the bay for a living.

Working in collaboration with the Movement of Artisanal Fisher People (MPP), this research aims to summarize previous research conducted in the BTS. The research describes the environmental quality of the Bay and exposures to humans and animals living in the bay. A target systematic review was conducted to identify peer reviewed literature meeting the search criteria. This study reviews twenty five scientific papers that monitor and evaluate the environmental conditions in BTS. The research found strong data that proves the environmental degradation occurring in BTS has a toxic effect on the air, sediment, and water quality in the area. Also, studies that analyze the biota living in the Bay indicated excess stress in the organisms due to the surrounding petrochemical plants that leak pollutants into the water. The chemicals found in all four categories: sediment, water, air, and biota were then scanned for possible carcinogenic effects, as well as the chronic and acute exposure effects on humans. The health impacts of these unregulated petrochemical plants on the residents of BTS have not been quantified. The summary was developed to be a foundation for potential change in policy or regulation of toxic chemicals in Baía de Todos os Santos.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Dangers of DEET in Pregnancy

Infections in pregnancy are leading causes of severe neonatal morbidity and mortality. According to the World Health Organization (WHO), infections account for 36% of neonatal deaths worldwide (WHO, 2017). Expecting mothers are screened for several pathogens, such as Pertussis, Influenza, Hepatitis B, Measles, Mumps, Rubella, Tetanus, Diphtheria, and Varicella, in order to prevent fetal and neonatal infection (Swamy & Heine, 2015). Fortunately, antibiotic treatment or vaccination is available to prevent or ameliorate infections. However, new infections, such as the Zika virus (ZIKV), are particularly threatening for neonates as there is currently no effective vaccine or treatment. On February 1, 2016, the WHO declared ZIKV a public health emergency of international concern. ZIKV particularly threatens reproductive aged patients as the virus can cause devastating effects on their developing fetus, such as microcephaly and miscarriage. The lack of ZIKV treatment requires that health care providers be able to provide accurate information about preventative ZIKV measures. The goal of this paper is to explore the safety and efficacy of N,N-diethyl-meta-toluamide (DEET), an insect repellent, so that more specific and well-informed recommendations can be made by health care providers to their patients, specifically pregnant women.

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How Climate Effects the Tick Vector of Lyme Disease: A Critical and Systematic Review of the Literature

BACKGROUND

Lyme disease (LD) is a common vector-borne disease in North America. Understanding the causes behind inter-annual fluctuations of LD incidence can help warn healthcare providers of upcoming outbreaks.

OBJECTIVE

Identifying what specific climate variables affects the vector, *Ixodes scapularis ticks*, and ultimately LD incidence.

METHODS

A systematic review was carried out to understand how climate variables affect the tick population variables that are related to LD.

RESULTS

Twenty-one studies met the inclusion criteria. Risk of bias was generally rated “low” or “probably low” and quality of evidence was rated “moderate”. Strength of evidence was assessed for tick abundance, a proxy for LD. The relationship with climatic moisture was rated as “sufficient”, but was rated “inadequate” for temperature and temperature+moisture. A positive, moderate-strong relationship between prior climatic moisture and tick abundance ($r=0.82$; $r^2=0.56-0.64$) was observed in 50% of studies. The relationship was observed in 75% of nymph-only abundance studies. While relationships were observed between tick abundance and temperature (70% of studies, $r=(-0.89)-0.93$; $r^2=(-0.56)-0.34$) and temperature+moisture (38% of studies, 75% negative relationships), direction and magnitude could not be determined.

CONCLUSION

Higher climatic moisture (yearly or 0.5–2 years prior) increases tick abundance and, by proxy, LD incidence. Nymph-only abundance studies, a more accurate proxy, was more likely to show this relationship. Climate change is predicted to increase precipitation in Northeast US/ Canada, which appears likely to increase LD incidence.

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Assessing Urban Tree Canopy and Vegetation in Mitigating Urban Heat Island Effects and Heat-Related Mortality Rates: A Systematic Review

BACKGROUND

Extreme heat events are increasing in frequency, duration, and severity in many parts of the world due to climate change. Certain vulnerable urban populations are disproportionately impacted by such EH events, which are exacerbated by the urban heat island effect. Mitigation and adaptation strategies including urban greening are a growing trend in many cities, but there is variability in this intervention's effectiveness, dependent on the area of study.

OBJECTIVES

Based on the Navigation Guide by Johnson et al., we conducted a systematic review of the literature to determine the effectiveness of urban tree canopy (UTC) and vegetation in mitigating urban heat island effects and reducing heat-related mortality rates in the Northeastern and Midwestern US.

METHODS

In applying the Navigation Guide methodology, we followed the three step framework: 1) we identified our study question, 2) we systematically researched and chose our evidence, and 3) we rated the quality and evidence of our selected studies. We developed specific criteria to select and rate the body of literature included in this systematic review.

RESULTS

Our research resulted in the inclusion of 6 studies based on our criteria. We established the risk of bias across all studies to be fair and determined the overall quality of evidence to be moderate.

CONCLUSION

We modified the Navigation Guide framework to better fit the studies assessed. We determined that there was limited evidence of effectiveness of UTC and vegetation in lowering air and land surface temperatures and reducing heat-related mortality rates in Midwestern and Northeastern US cities.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Assessing Psychophysiological Effects of Malodorous Pollutants in Residents of Leandrinho, Bahia, Brazil: A Pilot Study Using a WhatsApp-Based Questionnaire

BACKGROUND

Leandrinho is located in a region that is home to the largest industrial chemical complex in the southern hemisphere that covers approximately 49 km². Leandrinho residents have reported experiencing adverse health effects that co-occur during periods of malodor emitted by the petrochemical industry. However, there is currently no tool for the residents to systematically record incidents of malodor. This pilot study assessed the feasibility of using a questionnaire designed through Whatsapp, a text-messaging application commonly used among residents.

METHOD

Leandrinho residents were randomly recruited to complete a daily questionnaire using either paper (n=24) or Whatsapp (n=24) over the course of 49 days. All study participants (n=42) spent most of their days in the town. The age for inclusion ranged from 18 to 50. The questionnaire comprised of six questions that asked when and where odor was detected, as well as the level of odor intensity and symptoms experienced.

RESULTS

Preliminary analysis shows that of the 24 participants randomized into the paper group, only two participants recorded using the paper forms, citing WhatsApp was easier and more convenient. Of the 42 participants, only 30 sent at least one reply over the course of the study. The average number of replies per day was 5.5, and the highest number of responses received on a single day was 12. Only 6 of the 30 participants sent replies on at least 50% of the days. Odor was reported on 24 study days; however, 16 of those days were reported only by one person. Given the low response rate, determining the days when an odor occurred was difficult to determine.

CONCLUSION

Evaluating the feasibility of a data collecting tool that is widely available and user-friendly is important for addressing the environmental concerns experienced by Leandrinho and for highlighting the need for such tool to be further developed. Further development could result in a more accurate representation of the experiences of Leandrinho and other communities alike.

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JOINT PA/MPH PROGRAM

The Silent Souvenir—Are Travelers at Increased Risk of Antibiotic Resistant *Enterobacteriaceae* (ARE) Colonization?: A Systematic Review

BACKGROUND

With the recent introduction of mobilized resistance genes and the growing public health concern for antibiotic resistance, the role of tourism in the global spread of superbugs has not been well established.

OBJECTIVES

The primary objective of this review was to determine the association between foreign travel and risk of gut-colonization by antimicrobial-resistant *Enterobacteriaceae* (ARE).

METHODS

A thorough systematic literature review was conducted on the existing body of evidence. A total of 18 prospective cohort studies were analyzed using the Navigation Guide methodology. Included studies analyzed either fecal samples and/or rectal swabs both pre- and post-travel to determine incidence of colonization with antimicrobial-resistant *Enterobacteriaceae*. Questionnaires were obtained to determine travel behaviors and identify risk factors for acquisition.

DISCUSSION

Key risk factors for colonization included travel to the Indian Subcontinent and Asia, as well as traveler's diarrhea and antibiotic use during travel. The prevalence of bacteria with mobilized colistin resistance found in healthy travelers was profound, given that this gene was discovered just 2 years prior to this review.

CONCLUSION

Overall, increased acquisition rates of antimicrobial-resistant *Enterobacteriaceae* among healthy travelers were noted in this review. Larger, more homogenous studies need to be performed in order to influence key antibiotic use policy reform on a global scale.

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Phthalate Exposure and Risk of Bacterial Vaginosis Among U.S. Reproductive-Aged Women, NHANES 2001--2004

INTRODUCTION

Consumer product chemicals, such as phthalates, that are found in feminine products may affect the vaginal microbiota and the etiology of bacterial vaginosis (BV). Our objective was to estimate the association between phthalate exposure and BV in a cross-sectional, population-based sample of reproductive-aged women.

METHODS

We used data on 940 women aged 18-49 in the National Health and Nutrition Examination Survey, 2001-2004. Phthalate metabolites were measured in urine and include mono-ethyl phthalate (MEP), mono-n-butyl phthalate (MnBP), and metabolites of di (2-ethylhexyl) phthalate (DEHP). To control for measurement error from urinary diluteness, we used covariate-adjusted standardization with inclusion of urinary creatinine concentration as a covariate. BV was assessed using Nugent's Gram stain score, categorized as no BV (score 0-3), intermediate (4-6) and Nugent-score BV (7-10). We used survey-weighted multinomial logistic regression to model the Nugent-score categories, adjusting for age, race/ethnicity, BMI, education, and past six-month vaginal douching.

RESULTS

In unadjusted models, MnBP (Q4 RR 3.12, 95% CI 1.79, 5.41, p trend <0.001), and Σ DEHP metabolites (Q4 RR 2.43, 95% CI 1.43, 4.12, p trend=0.04) were associated with BV. The association of MnBP with BV persisted after adjustment for confounders (Q4 RR 2.25, 95% CI 1.24, 4.20, p trend=0.02). However, associations for MnBP and Σ DEHP were attenuated after creatinine adjustment (MnBP Q4 RR 1.11, 95% CI 0.63, 1.96, p trend = 0.55; Σ DEHP Q4 0.72, 95% CI 0.37, 1.39, p trend=0.35).

CONCLUSION

Elevated urinary concentrations of phthalates were observed among women with Nugent-score BV. Associations were attenuated after creatinine adjustment; however, this adjustment may not be optimal as urinary diluteness may be physiologically related to BV. We recommend further investigation of environmental chemicals and BV using novel methods for direct assessment of intravaginal exposure.

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JOINT PA/MPH PROGRAM

The Effect of Occupational Exposures to Animals on the Prevalence and Evidence of Leptospirosis

BACKGROUND

The disease leptospirosis is one of the deadliest zoonotic illnesses worldwide and has been understudied in occupational populations who regularly work with animals. Previous studies have focused on weather and climate related exposures, neglecting this working population.

OBJECTIVE

The Navigation Guide methodology was used to conduct a systematic literature review to determine if there is increased prevalence of leptospirosis or seroprevalence indicating previous infection in occupationally exposed animal professions.

METHODS

By following the Navigation Guide procedures, we identified a specific study question and systematically evaluated the literature for inclusion in the final review. The 14 studies that were included subsequently underwent evaluation for risk of bias, quality, and strength of the evidence.

DISCUSSION

Due to issues with non-uniform presentation of the results among the included studies, cross study comparisons were made sparingly. Factors influencing the odds of contracting Leptospirosis included; smoking OR 14.4 (1.39, 134.74), consuming a liquid while working OR 5.1 (1.04, 24.30), washing hands after work OR 0.2 (0.03, 0.81), and using protective aprons OR 0.4 (0.2, 0.7). The annual prevalence of Leptospirosis ranged from 0.07-1.6 per 100,000 individuals. Occupation as the source of infection ranged from 30% to 88%. Studies had similar outcomes indicating increased prevalence/evidence of leptospirosis in occupational groups but these measures were not presented in an overly convincing manner.

CONCLUSION

The quality of evidence was deemed moderate among the included studies and there was only "limited evidence" of an association between the occupationally exposed to animals population and increased prevalence of leptospirosis or leptospira antibody seropositivity. However, several factors were identified as either being protective or increasing the odds of contracting leptospirosis within this working population, and can subsequently serve as short term areas of intervention while more rigorous prospective research is conducted in the future.

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The Contribution of Foodborne *Escherichia coli* to Pediatric Urinary Tract Infections in the District of Columbia

BACKGROUND

Escherichia coli is a common contaminant of retail poultry and the leading cause of human urinary tract infections. Young children are at excess risk for urinary tract infections and long-term kidney damage as compared to adult populations. The objective of this study was to characterize *E. coli* isolates collected from retail poultry and pediatric urinary tract infections (UTIs) to assess their genetic similarity.

METHODS

E. coli isolates were collected from raw retail poultry purchased from Washington, DC grocery stores during 2013 and from positive, standard of care urine cultures collected at Children's National Medical Center between October 2013 and February 2014. Isolates were subjected to whole genome sequencing (WGS) and relationships among isolates were assessed with multi-locus sequence typing (MLST) and WGS phylogenetic analyses. Genomes were also screened for avian-associated ColV plasmids. *E. coli* carrying ColV plasmids were defined here as being of poultry origin.

RESULTS

In total, 108 isolates—52 UTI and 56 poultry—were subjected to WGS. Fifty-six different MLST sequence types (STs) were detected. There were 39 STs identified among poultry isolates and 21 STs identified among UTI isolates. Five STs—ST10, ST38, ST69, ST117, and ST13—contained both poultry and UTI isolates. WGS-based phylogenetic analyses revealed close relationships among poultry and UTI isolates. Eleven out of fifty-two clinical *E. coli* isolates carried avian-adaptive ColV plasmids. Approximately 21% of the UTI isolates shared a common ancestor with poultry isolates and/or carried ColV plasmids.

CONCLUSIONS

Our data suggest that a substantial portion of pediatric UTIs are caused by *E. coli* of poultry origin and that reducing the prevalence of pathogenic *E. coli* strains in the food supply may be a strategy for reducing UTI in children.

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Dirty Cotton: Occupational Pesticide Exposure and Elevated Suicide Risk Among Male Cotton Farmers in India

PURPOSE

The aim of this critical analysis was to examine the association (or lack thereof) of occupational pesticide exposure and elevated suicide risk among male cotton farmers in India.

METHODS

A literature review was performed using *Scopus*, *PubMed*, and *Google Scholar* databases. The review included documents published before and after year 2002. Children were excluded from the search as well as women, with exception to research on gender differences in suicide.

RESULTS

Studies outside India show a positive correlation between work-related pesticide exposure and suicide. Animal studies have shown that pesticides, as organophosphates, are toxic, producing neurobehavioral effects that include mood disorders and depression—a primary risk factor for suicide mortality. Since the introduction of genetically modified (GM) cotton to India, pesticide consumption (and suicide) has increased among the Indian farmer population. Conventional cotton practices, involving agricultural biotechnology and high-priced agricultural inputs (e.g., pesticides), trap low-income and often poorly educated farmers into massive debt; their response can be tragic. While pesticide poisoning is the most common suicide method in India, it sends a particularly loud message from the farmer community. Although this community is inclusive of women agricultural laborers, male cotton farmers have higher suicide rates compared to their female counterparts.

CONCLUSIONS

India's farmer suicide epidemic can be stopped. Pesticide-free farming practices are available. Health information dissemination and less toxic pesticides may additionally work to mitigate the adverse effects of pesticide exposure. Research about the pesticide-suicide link in India is encouraged for improved health outcomes, especially among the male cotton farmer population.

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Recycled Tire Crumb Rubber Playgrounds or Athletic Fields and Air Pollution Hazards to Children: A Systematic Review

BACKGROUND

All around the world tire disposal is becoming a greater environmental problem. The installment of recycled tire crumb rubber fields and playgrounds are one way communities have decided to relieve the issue of end-of-life tire disposal. Many laboratory toxicology studies have identified hazardous chemicals within these shredded tires to include polycyclic aromatic hydrocarbons (PAH), volatile organic compounds (VOC), semi-volatile organic compounds (SVOC), and as well as heavy metals such as lead and fine particulate matter.

OBJECTIVE

This paper aims to systematically review the current literature on the association between exposure to tire crumb rubber playgrounds or fields and the air pollution health risk to children worldwide.

METHODS

Databases were searched using inclusion and exclusion criteria. A PRISMA flow diagram was used to display search steps during a systematic literature review database search. The search was limited to the English language and studies published in last twenty years or after 1996. Search terms were created for each database and repeated among all databases then individualized due to poor search results. The Navigation Guide systematic approach was used to rate risk of bias, overall quality, and overall strength of the studies included.

RESULTS

10 studies and reports met the inclusion criteria. The studies on average were rated “probably low” to “probably high risk” of bias. Selection bias was rated at “probably high risk” in 60% of the studies due to the voluntary nature of the selection process. The overall quality across all studies as were rated “low” quality with “limited” evidence for association of tire crumb rubber exposure and air pollution health hazards to children.

CONCLUSION

There was limited evidence supporting the association between exposure to outdoor tire crumb rubber playgrounds or athletic fields and the air pollution health hazards to children. Limitations included poor recruitment of playgrounds and fields for sampling, large number of confounders either not accounted for or unable to control for, and unknown information of many of the volatile and organic compounds found within crumb rubber tires. The question “Does exposure to tire crumb rubber present an air pollution hazard to children worldwide?” requires additional studies to evaluate larger sample of crumb rubber playgrounds and fields along with use of biomarkers and personal air monitors.

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Climate-Driven Models of Valley Fever: A Systematic Review

BACKGROUND

Valley Fever incidence has risen dramatically in the Southwest United States over the past two decades. Current hypotheses of Valley Fever infection implicate dust as a vector and climate as an influencing factor on seasonal and annual disease incidence. Climate-driven models have aided the understanding of other infectious disease such as meningococcal meningitis and Rift Valley Fever.

OBJECTIVES

To evaluate model design of climate-driven models predicting Valley Fever incidence by through the framework of a systematic review.

METHODS

We conducted a systematic literature review using both the PRISMA and Navigation guides. Web of Science, Pubmed, Embase, ProQuest, and Scopus were searched for all articles published in English after 1997 pertaining to climate and Valley Fever. Only studies utilizing county, state, and national level exposure and case information from the Southwest United States were included in this review.

RESULTS

Eight studies modeling Valley Fever incidence by climate variables were identified and reviewed. Exploratory analysis revealed bimodal peaks in both incidence and precipitation throughout the study areas. Adjusting for disease incubation and grouping incident cases by season provided the best estimate of a case's exposure window. Detrending annual incident case data increases model sensitivity as recent linear increases in incidence cannot be explained solely by climate. Seasonal incidence terms and seasonal climate parameters provided the most accurate and precise model results, with a maximum full model R^2 of 0.8.

DISCUSSION

Application of climate-driven Valley Fever models in public health can enhance preventative and diagnostic measures. Use of large exposure windows or seasons improves model accuracy and accounts for the varied nature of disease report dates.

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The Occurrence of Zoonotic Tuberculosis Among People with Livestock Exposure in Low- and Middle-Income Countries: A Systematic Review

Zoonotic tuberculosis (zTB) makes up an estimated 1.4% of the global tuberculosis burden. Cases are largely underreported and misdiagnosed because the largest burden of disease is in low and middle income countries (LMICs). Populations in LMICs are at increased risk of zTB due to livestock rearing practices and raw dairy consumption. This systematic review of the literature investigates the risk of human zoonotic tuberculosis in LMICs based on exposure to livestock and livestock products.

Utilizing the Navigation Guide, the study question was identified, peer-reviewed literature databases (Scopus, PubMed, and Web of Science) were searched, and studies were selected and evaluated for risk of bias and quality of evidence. Fifteen studies in LMICs were included in the final evaluation that used laboratory diagnostics to determine the species of *Mycobacterium*. Overall there was probably low risk of bias and low quality of the evidence. Prevalence of zTB reported in the observational studies ranged from 0% to 28%, with cattle and raw dairy being the primary exposure. All confirmed cases of zTB in these studies were *Mycobacterium bovis*.

Four of six WHO regions were represented: Africa (n=9), the Americas (n=3), Southeast Asia (n=2), and the Eastern Mediterranean region (n=1). Several studies looking at pastoralist communities found low to zero prevalence of zTB in humans. Eight of the 15 studies included livestock sampling for zTB during a similar timeframe as human sampling, finding prevalence rates ranging from 0-23% in sampled livestock, which were predominantly cattle. One study found TB lesions in goats and camels at slaughter as well. There are several concerns with the body of evidence: variability and reliability of laboratory diagnostics, small sample sizes, differential risk of zTB based on livestock breed and production setting, and the need for global dairy pasteurization.

Large scale studies that pair livestock and human data are greatly needed to fill knowledge gaps. More emphasis must be placed on livestock TB surveillance and control programs and safe dairy consumption, such as pasteurization and boiling. Future paired studies will allow better characterization of the high zTB transmission areas for targeted control and prevention programs.

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Active Commuting as a Predictor of Physical Activity and BMI Among Children, Adolescents and Adults: A Systematic Review

BACKGROUND

Physical activity is declining worldwide, and reliance on passive commuting is increasing. Physical inactivity is a leading cause of reduced health and increased obesity and mortality. Active commuting is an alternative to passive commuting, providing an environmentally friendly mode of transportation and potential health benefits. We conducted a systematic review to assess the benefits of active commuting among children, adolescents and adults.

OBJECTIVES

Apply the Navigation Guide systematic review methodology to answer the question: “does active commuting increase physical activity and decrease BMI among children, adolescents and adults?”

METHODS

This article presents the results of a systematic review of the association between active commuting and outcomes of physical activity and BMI among youth, adolescents and adults.

RESULTS

Strong associations were found in active commuters and increased physical activity among children and adolescents. Active commuting from youth through adulthood positively predicted physical activity in adulthood. Mixed results were found for the association of active commuting and BMI among children and adolescents as well as adults.

CONCLUSIONS

Interventional studies and prospective cohort studies are needed to help determine causation regarding active commuting and physical activity as well as active commuting and BMI among youth, adolescents and adults.

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Characterizing the Exposome: Critical Analysis of Exposome-Wide Association Studies

PURPOSE

The exposome is a conceptual framework of all exposures encountered by an individual in his or her lifetime. Studying the exposome is thereby a monumental feat that may require extensive research, conceptualization, and proof-of-concept analyses. Researchers have begun studying the exposome by developing exposome- and environment-wide association studies (EWAS). Since EWAS is such a novel technique, this critical analysis of existing EWAS in the literature sought to determine whether the studies utilized common research methods, how the data were analyzed, and whether the analyses were similar. The analysis also sought to explore ways in which these studies could inform study of the exposome.

METHODS

The ProQuest Environmental Science Collection was queried for articles conducting exposome-wide association studies and environment-wide association studies. Only research articles were accepted for further analysis. These articles were examined following epidemiological study critical analysis guidelines.

RESULTS

Five research articles were returned through literature review. Methods analysis determined that the studies conducted similar regression analyses of extensive exposure variables with a single health outcome as the dependent variable. One study utilized an animal model and primarily studied metabolites, thereby supporting the concept that metabolomics may play a supporting role in study of the exposome. All studies utilized validation procedures and examined results using a false discovery rate.

CONCLUSIONS

The EWAS articles examined in this critical analysis conducted extensive validation procedures to successfully demonstrate the statistical significance of large-scale linear and logistic regression. These procedures will likely make EWAS a valuable resource in future exposome studies.

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Occupational Lung Disease: Coal Workers' Pneumoconiosis

OBJECTIVE

The aim of this literature review is to investigate the effectiveness of the Federal Coal Mine Health and Safety Act of 1969 with regards to coal dust exposure limits, whether the regulatory policy reduced the prevalence of coal workers' pneumoconiosis (CWP) among coal miners who began work after it the policy was implemented in 1970, in comparison to coal miners who worked prior to the passage and implementation of the policy.

METHODS

Scopus, pubmed and wed of science search engines were search for literature published in English that deals with pre-and post-1970 implementation of the Federal Coal Mine Health and Safety Act of 1969, and the prevalence of CWP. Literatures were screened for human studies.

DISCUSSION

Four studies were analyzed with the use of navigation guide. Of the four studies, two concentrated specifically on the effectiveness of the prevalence of CWP pre-and post-1970 implementation of the Federal Coal Mine Health and Safety Act of 1969. While the other two included how other factors, such as mine size and lower seam heights in mines adds to the prevalence of coal worker pneumoconiosis. The study found that the dust rule was effective in reducing the prevalence of CWP, but lack of enforcements of the dust rule and increased work hours in recent years could have added to the recent prevalence in CWP.

CONCLUSION

These studies have shown that with proper enforcement of the dust rule, especially in small mines, the prevalence of CWP could be reduced, and with the increase in work hours in recent decades, there's a probable increase in cumulative exposure levels of coal dust. A further reduction of the permissible exposure limit of coal dust should be considered, especially because of the increase work hours.

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Evaluation of PM Emissions of a Diesel Engine Fueled with Waste Cooking Oil Biodiesel: A Systematic Review

BACKGROUND

The Navigation Guide developed by Johnson et al was used to conduct a robust systematic review of six experimental intervention studies looking at particulate matter (PM) emissions from conventional petroleum diesel and a biodiesel alternative utilizing waste cooking oil in heavy-duty petroleum diesel engines. Waste cooking oil biodiesel is thought to be a more sustainably sourced alternative to its fossil fuel counterpart.

OBJECTIVES

Application of the Navigation Guide systematic review methodology to answer the question: Does the replacement of petroleum diesel with waste cooking oil biodiesel reduce hazardous PM emissions?

METHODS

The study question was specified, evidence was selected and the quality and strength of the overall evidence was assessed both for the individual studies and across the body of studies identified. Precise criteria and protocols were developed and followed throughout the process of the review to ensure that a thorough evaluation of all data was completed.

DISCUSSION

Six investigative experimental studies were identified that met the inclusion criteria. All studies utilized six-cylinder direct injection engines. Although the PM emissions were measured differently across the exposure continuum, there was an overall PM emission reduction of 28% across the studies when petroleum diesel was substituted with waste cooking oil biodiesel. The overall risk of bias was determined to be 'low'.

CONCLUSION

Based on the application of the Navigation guide methodology, it was found that the strength of the evidence provided was 'sufficient' to suggest an association between waste cooking oil biodiesel and PM emission reductions.

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Tracking *Escherichia coli* on Retail Meat Sold in California and Implications for Human Health

OBJECTIVE

Our research aims to study how production methods of retail poultry can lead to antimicrobial resistant urinary tract infections (UTIs) caused by foodborne *Escherichia coli* (*E. coli*) as opposed to UTIs caused by commensal *E. coli* associated with the host.

BACKGROUND

Compelling research has been conducted that suggests the poultry industry's supplementation of antibiotics into animal food and water is contributing to antimicrobial resistant *E. coli* in human populations. Due to the mutable nature of pathogens such as *E. coli*, the continual exposure to antimicrobials via poultry production methods allows ample opportunity for selection pressures to opt for more antibiotic resistant strains of *E. coli*. These resistant strains can then be introduced into the human population through direct or indirect exposure of retail poultry meat. Although most associate *E. coli* with gastrointestinal tract illnesses, extraintestinal pathogenic *E. coli* (ExPEC) is the most common uropathogen, responsible for the majority of UTI cases worldwide. Strains of ExPEC are frequently commensal organisms as part of the normal gut flora of the human body and are capable of causing disease under certain circumstances. UTIs were once easily treatable with antibiotics; however, growing rates of drug-resistant strains of ExPEC have been observed. Understanding that an infection can spread from the urinary tract to other vital organs, it is imperative to 1. understand the origin of drug-resistant UTIs and prevent their proliferation and 2. understand the delineation of foodborne and commensal UTIs caused by *E. coli* in order the better address the source of these potentially life-threatening infections.

METHODS

Packaged poultry meat, sourced from California, was processed every week. Collection sizes ranged from 30-70 samples. *E. coli* was selected and isolated from the meat. Using DNA in a real-time PCR, the presence of *E. coli* was confirmed. Positive samples were then subjected to antibiotic susceptibility testing, evaluated, and stored systematically for future analyses involving comparison of genetic fingerprints of clinical samples also from California.

RESULTS

E. coli was found on 73.6% (436/592) of samples. Resistance was detected in 10 of 12 antibiotics with elevated resistance rates noted for the following antibiotics: Ampicillin, Gentamicin, and Tetracycline.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Predicting Oxidative Stress Potential Through Spectroscopic Methods

Rational design of safer chemicals is of the upmost importance. The potential of chemicals to cause oxidative stress, the generation of free radicals, must be investigated. Oxidative stress is chosen as the ultimate endpoint because it encompasses critical toxicological pathways for many environmentally adverse chemicals and has been linked to cancer, cardiovascular disease, Alzheimer's disease, and AIDS. In response to high levels of free radicals, the Nrf2 pathway will signal the release of glutathione to react with the radical species. It is understood that chemicals which react with a glutathione model likely cause oxidative stress. The glutathione model is the molecule 5-(Dimethylamino)-N-(2-mercaptoethyl)naphthalene-1-sulfonamide (DCYA). The glutathione model will be synthesized using a procedure found in *Chemical Research in Toxicology* (Chittiboyina, et al). Chemicals with mutagenic properties will be reacted with DYCA to probe oxidative stress potential. The reaction will be monitored by NMR spectroscopy to quantify the depletion of the chemical. NMR spectroscopy provides information on the reactivity of the chemicals and the quantifies the structure of the final adduct.

Multiple chemicals have been successfully tested with the model thiol. The products of the reaction have been monitored and structurally investigated through NMR spectroscopy. The above procedure has yielded an efficient method to determine the oxidative stress potential of chemicals.

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Implications of Foodborne Bacteria on Human Health: Isolation and Antibiotic Resistance of *Salmonella enterica* and *Campylobacter spp.* on Retail Chicken Sold in California

Overuse of antibiotics contributes to antimicrobial resistance (AMR), which continues to be a growing threat to human health. In the United States, industrial food animal production (IFAP) is a formidable driver for antibiotic use. Prior work has focused on the link between antimicrobial use in poultry and human AMR infections. Common foodborne pathogens such as *Salmonella enterica* (*S. enterica*) along with *Campylobacter coli* (*C. coli*) and *Campylobacter jejuni* (*C. jejuni*) are commonly associated with human gastroenteritis. However, it has been shown that these pathogens are capable of causing disease outside of the gastrointestinal tract, specifically urinary tract infections (UTIs). Due to their ubiquitous nature on raw and undercooked poultry, these pathogens serve as an overlooked source of UTIs for individuals with exposure to retail poultry. AMR has become a major public health concern and predicted to cause more than 10 million AMR related deaths.

In 2015, California passed senate bill 27 (SB-27), the first bill of its kind to restrict the use of antimicrobial drugs in the poultry industry. Implemented on January 1, 2018, the legislation places poultry farmers' ability to administer "medically important antimicrobial drugs" to their livestock under the discretionary supervision of licensed veterinarians. The legislation is intended to reduce antibiotic usage in the poultry industry for non-therapeutic purposes such as preventative measures, promoting weight gain, or improving feed efficiency.

This study, therefore, examined the relationship between the implementation of SB-27 and rates of AMR in *Salmonella* and *Campylobacter* species present on retail chicken produced and sold in California. Samples were collected weekly from September 2017 through April 2018. Collection sizes ranged from 30-70 samples. *S. enterica*, *C. coli*, and *C. jejuni* were selected and isolated from the meat. Confirmed isolates were then subjected to AMR testing. *S. enterica* was found on 15.2% of samples and *Campylobacter spp.* on 28.0% of samples. Resistance was found in 14 of 15 antibiotics tested on *Salmonella* positive samples. Resistance was found on 7 of 7 antibiotics tested on *Campylobacter* positive samples. In future analyses, the AMR profiles of the retail poultry isolates will be compared to those of clinical isolates from UTI patients diagnosed in proximity to the outlets from which poultry samples were collected. This comparison probes the validity of the foodborne urinary tract infection (FUTI) paradigm for *Salmonella* and *Campylobacter*, which posits the significance of foodborne reservoirs of pathogenic bacteria leading to the acquisition of urinary tract infection.

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Human Evidence for Parental Glyphosate Exposure on Developmental Malformations and Neurodevelopmental Effects: Systematic Literature Review via the Navigation Guide Methodology

BACKGROUND

Glyphosate is one of the most widely used pesticides on a global scale. Toxicity potential has been a controversial topic with regards to glyphosate, however some links have shown mechanistic plausibility between glyphosate and offspring defects.

OBJECTIVES

Applied the Navigation Guide methodology for a systematic literature review to assess the current the literature as a means to answer if an association can be seen between glyphosate exposure from parental pesticide applicators and developmental malformations (DM)/ neurodevelopmental effects (NE) in infants.

METHODS

A comprehensive search of the literature through PubMed and SCOPUS was conducted, using a set of inclusion and exclusion criteria. Risk of bias, quality of evidence and the strength of evidence were assessed for each included study.

DISCUSSION

Six studies were ultimately included, 3 of which assessed NE as the outcome and 4 studies assessed DM as the outcome (1 study overlap). The quality of evidence was rated as "Moderate" for NE and "Low" for DM studies. Limited evidence of a statistically significant result was seen for the NE association, while a consistent statistically insignificant result was seen for the DM association.

CONCLUSION

This Navigation Guide based systematic literature review illustrated a "limited evidence of human toxicity" for the NE outcome and glyphosate while "insufficient evidence of human toxicity" was assessed for glyphosate and the DM outcome.

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Specific Amplification of *Escherichia Coli* Genomic Regions for Eventual Use in Targeted Amplicon Sequencing

BACKGROUND

Laboratory identification of *Escherichia coli* sequence types (STs) in a mixed sample remains a challenge, as commonly used genome sequencing regions do not provide enough resolution to characterize communities beyond the genus or species level. Multilocus sequence typing (MLST) is a robust method of strain typing for *E. coli*, but requires isolation of each sub-species. The importance of identifying particular *E. coli* sub-species is increasingly being recognized, and a need exists for a culture-independent laboratory assay capable of distinguishing the sub-species present within bacterial communities.

METHODS

Candidate 500 base pair genomic loci were identified based on single nucleotide polymorphism (SNP) diversity and the number of clusters of genomes formed when each locus was evaluated against 5,000 *E. coli* genomes *in silico*. 20 initial loci were selected based on the feasibility of designing primers of an appropriate annealing temperature and with limited degeneracy at the 3' end. These loci were screened using the polymerase chain reaction (PCR) and gel electrophoresis, to evaluate amplification of 12 non-*E. coli* *Enterobacteriaceae* species. To reduce non-specific amplification, a touch-down PCR protocol was developed and used for additional analysis of the 2 highest-performing loci (82752 and 143365). The DNA from 31 *E. coli* STs was quantified by qPCR, normalized to a starting input of 100,000 genomes, and serially diluted. Diluted *E. coli* DNA was then used to estimate limit of detection and confirm amplification of a range of diverse *E. coli* sub-species.

RESULTS

On the initial tests of loci 82752 and 143365, visible bands were observed for only 2 non-*E. coli* organisms, but amplification of *E. coli* controls was sub-optimal. With lower annealing temperatures and lengthened cycles, all *E. coli* controls were amplified, but specificity to the *E. coli* genome was lost. Using touch down PCR, all *E. coli* controls were detected and non-specific amplification was minimized to 2-3 species/locus. Diversity panel testing indicated that both loci could be used to effectively amplify 31 *E. coli* STs. Preliminary limit of detection analysis showed visible bands for the 4 STs tested at a starting value of 1,000 genomes.

CONCLUSIONS

These results indicate the feasibility of selective amplification of a 500 bp region of the *E. coli* genome by touch down PCR, with minimal non-specific amplification of related organisms. Additional experimentation will focus on developing a targeted amplicon sequencing method specific to one of these *E. coli* loci.

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Bioavailability of Heavy Metals in Coal Ash: A Systematic Review

BACKGROUND

Coal ash is the second largest industrial waste stream in the U.S., after mining wastes. In the United States, coal power plants produce 140 million tons of coal ash each year (Sierra Club 2017). Coal ash, the waste by product of burning coal, contains several toxic chemicals including arsenic, chromium, mercury, lead, selenium and other heavy metals. These toxic chemicals can cause several types of health impacts, including cardiovascular diseases, respiratory diseases, cancer, and neurodevelopmental disorders. For years' coal burning power plants have been disposing the coal ash into coal ash sites; impoundments; nearby water sources; or landfills, increasing exposure to heavy metals and health risk to those communities living nearby.

OBJECTIVES

Given the limited health studies on coal ash exposure, our objective was to apply the Navigation Guide systematic review methodology to answer the question: What is the heavy metals bioavailability of coal ash in water? Bioavailability is the proportion of total metals that are available for incorporation into biota (bioaccumulation), or the ability to be absorbed by an organism. This systematic literature review focuses on the pathway of heavy metals from coal ash particles by studying the bioavailability and leaching of heavy metals in water to address the potential human health impacts through ingestion.

METHODS

The literature review was conducted using the Navigation Guide, in which we specified the study question, select the evidence, evaluated the risk of bias of individual studies, and evaluated the overall quality and strength of the evidence.

RESULTS

Our search retrieved a total of 36 unique records, of which 7 included the inclusion criteria. We concluded that the risk of bias was high across studies, and assigned a "low" quality rating to the overall body of evidence. We identified recruitment strategy, confounding, and other bias as the most common risk of bias. Comparing the evidence and results of the studies was challenging, but in several of them, studies found a significant concentration of heavy metals after sequential extraction tests.

DISCUSSION

Results from the studies demonstrate evaluating the bioavailability and leaching factors of heavy metals in coal ash is complex and depends on several factors, including chemical speciation, pH, absorption, particulate size, temperature, and the surrounding environment.

CONCLUSION

We concluded that there was "limited evidence of toxicity" to determine the bioavailability of heavy metals from coal ash in surface water.

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Breastfeeding as a Predictor of Serum Concentrations of Per- and Polyfluorinated Alkyl Substances in Reproductive-Aged Women and Young Children: A Rapid Systematic Review

PURPOSE OF REVIEW

Per- and polyfluorinated alkyl substances (PFASs) are synthetic chemicals widely detected in human serum, and at low levels in breast milk. We conducted a rapid systematic review on breastfeeding practices and serum concentrations of PFASs—specifically PFOS and PFOA - among reproductive-aged women and young children using the Navigation Guide systematic review methodology.

RECENT FINDINGS

We included 14 studies examining associations between breastfeeding and PFASs in infants/toddlers or pregnant/postnatal women. Breastfeeding was significantly associated with lower PFASs exposure among women and higher PFASs exposure among children.

SUMMARY

We concluded there was “sufficient” evidence supporting an association between breastfeeding and serum PFASs concentrations among women, and “limited” evidence of an association among children due to issues with sample size, confounding, and exposure assessment. These findings reinforce that lactation is an important excretion route of PFASs for women, and that breast milk may be an important exposure pathway for young children.

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Indoor Air Quality and Asthma in School Children

Asthma is a chronic respiratory disease that puts a strain on lung function and breathing. It is the leading cause of school absenteeism and hospitalization for American children. Genetics play a major role in allergy related disease development such as asthma, but environmental exposures are proving to be a potential contributor to childhood asthma. Despite the sufficient data regarding air pollution, there is a huge knowledge gap regarding indoor air quality and its relationship with health outcomes such as asthma. Many of the studies available only look at outdoor air pollution levels, while children spend the majority of their time indoors. The majority of studies focus on particles smaller than $10\ \mu\text{m}$ (Pm_{10}). Studies show that the smaller particles ($\text{PM}_{2.5}$, PM_1) are more dangerous than larger ones however, because they can penetrate deeper in the lungs and are not as easily expelled at the nasal/ oral level. The health effects of $\text{PM}_{2.5}$ exposure in schools still being explored and the ability to monitor these smaller particles is advancing only as fast as the detection technology. Children are a vulnerable population and are at a disadvantage in managing their own circumstance since they are told where to be and how long to be there, i.e. school and home. Research in this field needs to be drastically increased in order to better understand the relationship between schoolchildren's respiratory health and their indoor environments.

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Latino Communities, Diesel Exhaust and Environmental Justice in the United States: A Systematic Review of the Literature

Diesel particulates are an environmental contaminant that is associated with illnesses that affect the respiratory, cardiovascular and reproductive systems. People of color are disproportionately affected by environmental exposures, but the issue of diesel particulate exposure among Latino populations in the United States has not been investigated in the literature.

This review investigates how diesel exposure in the United States affects Latino communities. We studied US Latino communities living in areas with measured heavy diesel pollution and compared them to communities in areas with lowered measured diesel pollution levels. The objective was to compare the incidences of respiratory, cardiovascular, or reproductive diseases.

I searched articles published up to 3 October 2017, and included original studies that measured diesel particulate exposures, demographic data on race, and health status of the community. Nine studies met the inclusion criteria. Every study found that people of color were most likely to be exposed to diesel, usually by way of highways. Two studies found that Latinos were more likely to be exposed to diesel than any other population and as a result had higher rates of asthma. Another two studies had similar findings for heart diseases and cardiovascular mortality. Two others found associations between diesel exposure and low birthweight.

In areas where diesel exhaust is present, Latino communities are 50% more likely to get lung cancer than Anglo-Saxons. 68% of those in the highest quartile of cancer risk are people of color, while only 32% are Anglo; the risk of a POC living in a high cancer-risk neighborhood in Southern CA is 1-in-3, and the risk of an Anglo-Saxon living in a high-risk neighborhood is 1-in-7. A 92% increase in frequent asthma symptoms was observed among those in high traffic, low-income neighborhoods and a 50% increase among those in medium traffic density compared to those who experience less exposure. There are approximately ten times as many Latino children living near high-traffic, low-income groups statewide than Caucasian children, which suggests that this is a vulnerable population. Census data found that families and children of color were overall three times more likely to live in high traffic areas than white children.

Based on the review of these articles, we concluded there was sufficient evidence supporting an association between diesel exposure and respiratory, cardiovascular and reproductive illnesses among Latino populations in the United States. Further research must be done to fully substantiate this link, especially longitudinal and cohort studies.

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Does Increasing Exposure to Swine Increase Influenza Antibodies in Swine Workers? A Systematic Literature Review

BACKGROUND

Workers who have an occupational exposure to swine may have an increased risk of influenza infection.

OBJECTIVE

We conducted a systematic review regarding occupational exposure to swine and influenza infection in humans.

METHODS

We searched articles published within the past ten years at the time of writing, and included original studies that quantified exposures to swine and resulting influenza infections in swine farm workers, including veterinarians. We evaluated the risk of bias of individual studies and the overall quality and strength of the evidence according to the Navigation Guide systematic review methodology. Twelve studies met the inclusion criteria. We rated studies “low”, “probably low”, “probably high”, and “high” risk of bias and rated the overall body of evidence as “moderate” quality with “sufficient” evidence for an association between occupational swine exposure and risk of influenza.

DISCUSSION

Understanding the risk factors for possible spillover and species jump of influenza is critical to preventing not only illnesses, but also epidemics. Our review found “sufficient evidence” of an association between occupational exposure to swine and increased influenza antibodies, or increased influenza infection. Our results that occupational exposure to swine is associated with an increase in influenza exposure were generally consistent across all twelve studies, except for one.

CONCLUSIONS

We concluded there was sufficient evidence supporting an association between occupational exposure to live swine and increased influenza antibodies and/or infections. Preventing on-farm influenza exposures may reduce the risk for novel viruses entering the broader human population.

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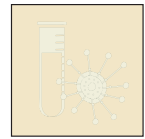
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A Qualitative Analysis of Structural Barriers in HIV Prevention Services

BACKGROUND

Black men who have sex with men (MSM) are not only disproportionately burdened by HIV rates, but also by structural level barriers that impede their access and engagement with prevention services. An exploration of how different social influences affect Black MSM and what solutions are available to overcome these dynamics in prevention services are not conclusively understood.

METHODS

A descriptive qualitative analysis of Black MSM aged 18 and older was conducted to identify structural factors experienced while accessing prevention and general healthcare services in the District of Columbia. Thirty semi-structured interviews were transcribed, reframed into a thematic codebook, and evaluated to characterize how different social influences acted as barriers and facilitators in the HIV prevention continuum.

RESULTS

Participant interviews identified multiple structural barriers and revealed unique themes along provider, individual, and infrastructural levels of influences. The interviews also identified facilitators to prevention services and explored potential opportunities to overcome barriers to HIV testing, retention services, and adherence support.

CONCLUSIONS

Black MSM report facing a variety of complex barriers in general healthcare and along the HIV prevention continuum. The provision of HIV services must account for the impact of structural barriers and take advantage of opportunities to overcome their influence on key populations. This study recommends that culturally suitable and population guided policies are among ways to improve the uptake of HIV services by Black MSM.

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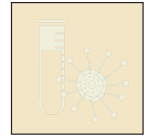
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Role of Blimp-1 in CD4 T Cell Exhaustion in Cancer

Cancer is the second leading cause of death (8.8 million) globally according to the data published by World Health Organization (WHO) in 2015. Although treatments including surgery, radiotherapy and chemotherapy have been used clinically, these methods still have huge limitations in either curing the disease or prolonging patients' life with good quality. Recently, highly promising therapies targeting immune checkpoint inhibitors such as programmed cell death protein 1 (PD1) pathway blockade have been brought forward. Nevertheless, with an increasing number of resistance from these therapies that have been observed, treatments do not work as effective as they should be in theory. Thus, it is important to have a closer look on the exact inhibitory mechanisms in tumor microenvironment. CD4 and CD8 T lymphocyte cells play critical roles in human cell-mediated immune response to cancer. However, due to over expression of inhibitory receptors, T cells ultimately lose their functionality which is manifested by decrease in their cytokine producing ability and other effector mechanisms. This stage is referred to as "state of T cell exhaustion", and it results in the decreased host ability to prevent tumor growth, which leads to the failure of cancer elimination. In a melanoma cancer model, in depth analysis by 12-color flow cytometry showed increased expression of inhibitory markers PD1, 2B4, Tim3, and LAG3 on T cells in tumor bearing mice. However, the level of inhibitory marker expression was different between CD8 and CD4 T cells. Similarly, cells from lymph nodes (LNs) and tumor-infiltrating lymphocytes (TILs) exhibited different inhibitory receptor expression pattern. By gating on antigen specific CD8 T cells using a surrogate marker strategy, CD44^{hi}CD11a^{hi} CD8 from TILs showed higher expression of all inhibitory markers as compared to the cells from LNs. Furthermore, SPICE analysis revealed that a greater proportion of TILs exhibited concomitant expression of three or more inhibitory markers when compared to CD8 T cells from the LNs. Antigen specific CD4 TILs (CD11a^{hi}CD49d^{hi}) exhibited a prominent increase in PD1 and LAG3 expression compared to LNs, but interestingly, 2B4 and Tim3 expression were similar to antigen specific CD4 T cells from the LNs. The expression of Blimp-1, a transcription factor associated with T cell exhaustion, was elevated in T cells that have the most concomitant increased expressions of several inhibitory markers. This is an agreement with published results from our laboratory which showed that high expression of Blimp-1 by CD4 T cells leads to their dysfunction during chronic toxoplasmosis.

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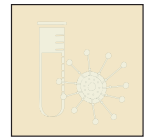
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Changes in Levels of Matrix Metalloproteinases and Tissue Inhibitors of Metalloproteinases in Women Following Recent Sexual Violence

BACKGROUND

In the HIV/AIDS pandemic, women comprise almost half of the infected population and make up the fastest growing group of new cases. A critical contributor to this trend is violence against women. The WHO estimates that more than 30% of women have experienced physical or sexual partner violence in their lifetime. Abrasions, lacerations and inflammation all enhance the risk of HIV acquisition in the female genital tract (FGT). Yet, the immune microenvironment of the FGT following sexual violence, and its role in HIV infection and transmission, is not well understood. A family of enzymes, the matrix-metalloproteinases (MMPs) and their inhibitors, tissue inhibitors of metalloproteinases (TIMPs), both initiate and terminate important inflammatory processes at barrier surfaces and contribute to tissue repair. Interestingly, MMPs have also been implicated in physiological stress and depressive disorders. This project aims to assess the levels of these immune mediators in women who have recently experienced vaginal sexual violence and whether hormonal changes during menopause affects the FGT immune microenvironment. We hypothesize that cases will have higher levels of MMPs and TIMPs than controls, and that there will be differences between premenopausal and postmenopausal samples. In addition, we aim to determine if there are differences in MMP/TIMP between plasma and cervical-vaginal lavage (CVL) samples.

METHODS

Plasma and CVL samples were obtained from women aged 21–45 and >50 recruited from the community. Cases experienced sexual violence in the prior 12 weeks, and controls have never experienced sexual violence. To determine the effects of hormonal changes in the FGT immune microenvironment, some participants were followed through their menstrual cycle, and samples were collected over 8 weeks. As comparison, samples were collected from some postmenopausal women, over multiple visits. To measure soluble immune factors solid-phase ELISA for MMP7, 9, TIMP-1 and TIMP-2 was used. Statistical analysis was performed in GraphPad Prism and R Studio.

RESULTS

For all markers measured, levels in the plasma were significantly higher than levels in the CVL. When comparing cases and controls, we found that cases had greater levels of TIMP-1 in plasma than controls. When comparing by menopausal status, we found that MMP-7, MMP-9 and TIMP-1 varied between premenopausal and postmenopausal status in either plasma or CVL.

CONCLUSION

This data suggests that MMP and TIMP expression are affected by recent sexual violence and menopausal status in women. Further studies are needed to determine their role in HIV transmission and acquisition.

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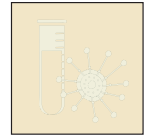
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Impact of Chronic Sexual Violence on Genital Tract Matrix Metalloproteinase (MMP) and Tissue Inhibitor of Metalloproteinase (TIMP) Expression in HIV Infected and Uninfected Women

PROBLEM

Matrix metalloproteinases (MMPs) and tissue inhibitors of matrix metalloproteinases (TIMPs) are important proteases/antiproteases whose levels within the body have important implications for physical and mental health. Dysregulation of these biomarkers during pregnancy or wound healing is well characterized and has been shown to result in complications. Dysregulation of MMPs and TIMPs in the blood has also been found to be associated with a myriad of health complications including heart disease, cancer, depression, and cognitive functions. Currently, a gap in the literature exists as to the effects of sexual violence, depression and HIV status on MMP and TIMP expression.

METHODS OF STUDY

Using the Women's Interagency HIV Study (WIHS) repository, we identified 4 groups of HIV infected and 4 groups of HIV uninfected women (8-11 per group) representing life-long (chronic) sexual abuse exposure and depression (CES-D score > 16). Groups were defined as follows: 1) no history of sexual abuse at baseline or depression (Control); 2) no history of sexual abuse at baseline but current depression (Depression); 3) chronic sexual abuse but no depression (Abuse); 4) chronic sexual abuse with current depression (Abuse+Depression). MMPs (MMP1, MMP2, MMP7, MMP8, MMP9) and their inhibitors (TIMP1 and TIMP2), were analyzed in plasma and cervical vaginal lavage (CVL) samples using ELISA. Linear regression was used to model levels of biomarkers with both depression and abuse as predictors. Models were run separately for HIV infected and HIV uninfected women, with CD4 counts and viral load as covariates for HIV infected group.

RESULTS

For HIV uninfected individuals, we found significantly higher levels of MMP1 in CVL of Abuse+Depression group when compared to Controls. However, levels of MMP7 was significantly lower in Depression and Abuse groups when compared to Controls. In plasma, levels of MMP2 was significantly lower in Abuse and Abuse+Depression groups when compared to Controls.

For HIV infected individuals, significantly higher levels of MMP2 and significantly lower levels of MMP1 was noted in Abuse+Depression groups compared to Controls. No significant changes by Abuse or Depression status was observed in plasma.

CONCLUSIONS

Our data suggests MMP/TIMP expression in plasma and CVL can be affected by Abuse, Depression, as well as HIV status.

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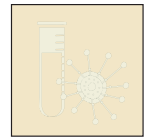
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Comparison of Existing Methods for Algorithmic Classification of Dementia in the Health and Retirement Study

BACKGROUND

Dementia ascertainment is difficult and costly, hindering the use of large, representative studies such as the Health and Retirement Study (HRS) to monitor trends or disparities in dementia. To address this issue, multiple groups of researchers have developed algorithms to classify dementia status in HRS participants using data from HRS and the Aging, Demographics, and Memory Study (ADAMS), an HRS sub-study that systematically ascertained dementia status. However, the relative performance of each algorithm has not been systematically evaluated.

OBJECTIVE

To compare the performance of five existing algorithms, overall and by sociodemographic subgroups.

METHODS

We created two standardized datasets: (a) training data (N=786, i.e. ADAMS Wave A and corresponding HRS data, which was used previously to create the algorithms) and (b) validation data (N=530, i.e. ADAMS Waves B, C, and D and corresponding HRS data which was not used previously to create the algorithms). In both, we used each algorithm to classify HRS participants as demented or not demented and compared the algorithmic diagnoses to the ADAMS diagnoses.

RESULTS

In the training data, overall classification accuracies ranged from 80% to 87%, sensitivity ranged from 53% to 90%, and specificity ranged from 79% to 96% across the five algorithms. Though overall classification accuracy was similar in the validation data (range: 79% to 88%), sensitivity was much lower (range: 17% to 61%), while specificity was higher (range: 82% to 98%) compared to the training data. Classification accuracy was generally worse in non-Hispanic blacks (range: 68% to 85%) and Hispanics (range: 65% to 88%), compared to non-Hispanic whites (range: 79% to 88%). Across datasets, sensitivity was generally higher for proxy-respondents, while specificity (and overall accuracy) was higher for self-respondents.

CONCLUSIONS

Worse sensitivity in the validation dataset may suggest either overfitting or that the algorithms are better at identifying prevalent versus incident dementia, while differences in performance across algorithms suggest that the usefulness of each will vary depending on the user's purpose. Further planned work will evaluate algorithm performance in external validation datasets.

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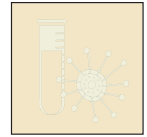
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Characterization of ERV9 Elements within the Human Genome

Human Endogenous Retroviruses (HERVs) are the genomic remains of ancient retroviruses that infected vertebrate genomes millions of years ago. Over evolutionary time, these proviruses have lost their infectious capacity due to an accumulation of mutations in the coding regions and long terminal repeats (LTRs), and most are believed to be transcriptionally silent in normal human tissue. However, recent evidence has shown several mechanisms by which HERV expression can influence homeostatic processes, including alternative enhancers for protein coding genes, activation of non-coding genomic regions, and expression of retroviral transcripts or proteins. The HERV9 family of endogenous retroviruses is of particular interest because it represents one of the more recent endogenization events, and is thus expected to retain more of its functional capacity than older HERV families. Despite this relatively young evolutionary age, HERV9 has been given relatively little attention compared to other HERV families such as HERV-W and HERV-K (HML-2). Finally, HERV9 and its long terminal repeat, LTR12, has been shown to regulate the activity of certain proapoptotic genes involved in prevention of cancer, specifically TP63 and TNFRSF10B in testicular cancer(1). In the present work, we identified and detailed the location and genomic context of 190 HERV9 elements in humans. This bioinformatic analysis has led to a characterization of all near-complete HERV9 elements in the human reference genome (hg38), with a report on the genomic and epigenomic context of their insertions throughout the genome and a phylogenetic classification of HERV9 subfamilies. Our exploratory analyses show dynamic connectivities within the HERV9 families. This body of work illustrates the importance of HERV9 elements and possible contributions to human homeostasis and pathogenesis. The goal of our study is to provide an exhaustive reference library for HERV9 to be used in understanding its role in both pathology and cooption throughout human evolution.

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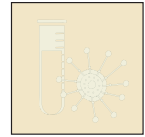
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Cross Sectional Analyses of HIV-1 Drug Resistance Mutations and Transmission Networks Present in People Living with HIV-1 in Washington, DC by Next Generation Sequencing: Comparison of Drug Resistance Mutation Reports Generated using a Publicly-Available Pipeline to that of a Commercial Pipeline

BACKGROUND

Detecting clinically relevant drug resistance mutations (DRMs), especially those conferring “high-level” resistance is important when making treatment decisions for people living with HIV (PLWH) and for public health surveillance efforts alike. Next Generation Sequencing (NGS) platforms are making possible detection of lower frequency DRMs that are not detectable using Sanger-based sequencing platforms. Study objectives included: 1) Describe our NGS approach using publicly-available software for data analysis and compare these results to those obtained using a commercial pipeline, 2) Determine what impact the selection in frequency cutoffs has on the number of DRMs detected for protease, reverse transcriptase (RT) and integrase gene targets from NGS data, and 3) Generate transmission networks to better understand potential linkages among an urban cohort of viremic PLWH.

METHODS

Plasma from 79 viremic participants was extracted and used to generate libraries for targeted NGS using Illumina® MiSeq platform. Sequences were uploaded into HyDRA Web developed by the Public Health Agency of Canada where minimum amino acid frequency cutoffs of $\geq 20\%$, $\geq 15\%$, $\geq 10\%$ and $\geq 1\%$ were selected to create separate DRM reports employing both the publicly available pipeline and SmartGene IDNS 5 for HIV-1 Deep-Sequencing, along with the Stanford HIV Drug Resistance Database using the Genotypic Resistance Interpretation Algorithm. Consensus RT sequences at 20% were used to generate transmission networks using HIV-TRACE software developed by UCSD and Temple University.

RESULTS

There was 99.5% agreement (2172/2184 data points) seen between the DRM frequency reports obtained using the publicly-available pipeline and those obtained using the commercial pipeline. Highest rates of DRMs among these participants were seen for RT Inhibitors, with the next highest being for Integrase Strand Transfer Inhibitors. In all, 40% of DRMs conferring “high-level” resistance would have been missed had a $>20\%$ cutoff been used rather than a $>1\%$ cutoff. Transmission networks were constructed in 14.1% (11/78) of participants; most were Non-Hispanic Black males who reported being MSM or high-risk heterosexuals.

CONCLUSIONS

DRM reports generated from NGS data analyzed using publicly-available software was validated against a commercial pipeline from SmartGene®. There is a risk-benefit issue in detecting low frequency DRMs; they may be an early indicator of emerging resistance leading to virologic failure, or they may not be clinically relevant. Future longitudinal studies are needed to assess this.

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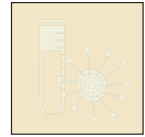
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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Differences in Psychosocial and Behavioral Risk Profiles of Cigarette Smokers and E-cigarette Users Among Minnesota Adolescents: 2016

BACKGROUND/OBJECTIVES

Rates of cigarette smoking among adolescents have been trending downward, however rates of adolescent e-cigarette use rates are now twice those of adolescent cigarette smoking nationally. The objective of this study was to examine the association of demographic, socioeconomic, psychosocial and health behavioral factors as surveyed by the Minnesota Student Survey with cigarette smoking and e-cigarette use among Minnesota adolescents.

METHODS

This study analyzed the 2016 Minnesota Student Survey (MSS), an anonymous, school-based, cross-sectional survey of students in grades five, eight, nine and eleven. The 2016 MSS contains a total of 168,733 records, 118,198 of which were analyzed for this study. Frequency analysis, Chi-square, and logistic regression models were used to assess for association of demographic, psychosocial and behavioral factors with student cigarette smoking and e-cigarette use.

RESULTS

A total of 17,917 students reported using cigarettes or e-cigarettes in the past 30 days. Of these, 67.5% reported smoking e-cigarettes and 32.5% reported smoked cigarettes, while 22.5% (4015 students) reporting smoking both cigarettes and e-cigarettes. Students identifying as bisexual were over four times as likely (AOR=4.40 [95% CI 4.01, 4.82]) versus heterosexual-identified students to smoke cigarettes but only twice as likely (AOR=2.24 [95% CI 2.06, 2.43]) to use e-cigarettes, while students identifying as gay or lesbian were 2.75 times as likely (AOR 2.75 [95% CI 2.27, 3.34]) to smoke cigarettes and only 1.5 times as likely (AOR=1.50 [95% CI 1.24, 1.76]) to use e-cigarettes. Students receiving free/reduced lunch were nearly twice as likely (AOR=1.92 [95% CI 1.80, 2.05]) to smoke cigarettes versus students not receiving free/reduced lunch, but only 1.33 times as likely (AOR=1.33 [95% CI 1.27, 1.39]) to use e-cigarettes. Students reporting skipping meals due to family economic hardship were over 3.5 times as likely (AOR 3.63 [95% CI 3.33, 3.95]) to smoke cigarettes but only 2.79 times as likely (AOR=2.79 [95% CI 2.59, 2.99]) to use e-cigarettes. Both increasing levels of alcohol usage and decreasing levels of reported academic performance are linearly associated with increasing likelihood of both cigarette smoking and e-cigarette use, but in both cases more steeply with cigarette smoking versus e-cigarette use.

CONCLUSION

Results of this study expand on existing research demonstrating differences in the psychosocial and behavioral risk profiles for adolescent cigarette smokers versus e-cigarette users. Further understanding of these predictors is critical to informing comprehensive public health strategies targeting prevention and reduction of youth tobacco and nicotine use.

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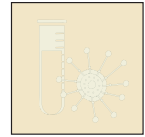
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Impact of Sexual Violence on Plasma and Cervico-Vaginal C-Reactive Protein Levels

The dual pandemics of violence against women and HIV/AIDS are still on going, and women who experience sexual violence are at greater risk of HIV acquisition. Though many studies have been conducted on the behavioral risks, less is known regarding immunological changes in the female reproductive tract (FRT) that may influence the risk of HIV acquisition. Our study investigates immunological changes in plasma and FRT in women exposed to sexual trauma. We hypothesize that inflammatory biomarkers can be upregulated following sexual trauma, which can facilitate HIV entry and infection. For this analysis, we investigated C-reactive protein (CRP), a well-characterized clinical marker for systemic inflammation. CRP has not previously been characterized as a marker for mucosal inflammation.

Cases defined as women who had experienced non-consensual vaginal intercourse in the last 3 months (n=42 visits) and Controls, defined as women who had no history of sexual violence, were recruited from the local Washington DC community (n=63 visits). Plasma and Cervical-vaginal lavage (CVL) samples were collected from each woman. To investigate whether changes in systemic or mucosal biomarkers following sexual trauma are affected by the menstrual cycle, premenopausal women were asked to return 4 more times over a 2-month time period. Post-menopausal women were also asked to return in order to compare data to the premenopausal women. Samples were analyzed by standard Enzyme Linked Immunosorbent Assay (ELISA) (R&D Systems) for CRP according to manufacturer's protocol. In-vitro HIV inhibitory activity in CVL were determined using TZM-bl indicator cells. Data was analyzed using RStudio.

CRP levels in plasma did not predict levels in CVL either by linear modeling or Spearman correlation coefficients. When compared by Case/Control status, plasma, but not CVL CRP levels were significantly lower among Controls compared to Cases ($p=0.03$). When compared by menopausal status, CVL CRP levels were significantly lower in premenopausal women ($p = 0.0002$) but plasma CRP levels were not significantly different. Step-wise linear regression was used to determine whether plasma or CVL CRP predicted HIV inhibition. After adjusting for clinical and demographic factors, plasma CRP showed a negative association with HIV Inhibition ($p < 0.001$), whereas CVL CRP was not a predictor.

Our results demonstrate that CRP can be measured in CVL but the lack of correlation between CVL and plasma levels indicate that CRP is not a good indicator of inflammation in the FRT. However, higher plasma CVL in Cases indicate increased systemic inflammation in this population.

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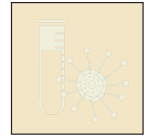
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Factors Associated with Delayed HIV Diagnoses in Washington, DC, 2006–2016

BACKGROUND

Delayed diagnosis of HIV is a critical indicator on the HIV care continuum. Washington DC has a high burden of HIV disease and the DC Department of Health (DOH) has implemented various public health strategies to increase routine opt-out HIV testing since the number of new infections peaked in 2007. We examined delayed HIV diagnosis in DC over 11 years, the association with demographic and transmission risk factors, and clinical indicators at time of diagnosis.

METHOD

Reports of HIV cases diagnosed in DC residents 13 and older between January 1, 2006, and December 31, 2016, were extracted from the DC DOH Enhanced HIV/AIDS Reporting System. Cases were matched to CD4 and viral load labs to determine median CD4 at diagnosis, linkage to care, and delayed diagnosis status. For regression analysis, cases were excluded if AIDS diagnosis date or CD4 count were missing or unreported. Delayed diagnosis was defined as stage 3 diagnosis within 90 days of the HIV diagnosis. Covariates assessed were year of diagnosis, gender, race/ethnicity, mode of transmission and age at diagnosis. Cochran-Armitage/Cuzick's test of trend and Chi-square were used for univariate analyses. The multivariable log-binomial regression was modeled, and we reported adjusted prevalence ratios (aPR).

RESULTS

8518 DC residents were diagnosed with HIV between 2006 and 2016. Age at diagnosis and proportion of delayed diagnoses significantly decreased over time while there were increasing trends in median CD4 count and proportion of cases linked to care within 30/90 days. In the regression analysis, 581 were excluded due to missing data, resulting in 7937 eligible for analysis. 2198 (27.7%) had a delayed diagnosis and it declined from 2006 (36.5%) to 2016 (25.5%). Black or Hispanic/Latino (vs. White, aPR 1.36 and 1.42, respectively) and persons with other/unknown mode of transmission (vs. heterosexual, 1.17) increased the prevalence of delayed diagnosis. Female (vs. male, aPR 0.81), MSM (vs heterosexual, aPR 0.80), ages 13-39 at diagnosis (vs. ages 60 and older, aPR range 0.43 to 0.83), and later year of HIV diagnosis (aPR for each 1 year increase beyond 2006 was 0.97) were less likely to have delayed diagnosis.

CONCLUSION

Delayed HIV diagnoses decreased from 2006 to 2016 after adjusting for demographic factors, indicating that over the analysis time period, people were diagnosed with HIV earlier in the disease course. The results suggest a need for better risk assessment and more targeted HIV testing among the populations identified to optimize health outcomes.

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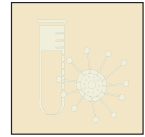
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Shigellosis and Giardiasis Among People Living with HIV in Washington, DC, 2012-2016

BACKGROUND

Shigellosis and giardiasis are transmitted via food, water, and fecal-oral contact. CDC has recently reported increased shigellosis among men who have sex with men (MSM) and among people living with HIV (PLWH), particularly stage 3. Our goal was to characterize the incidence and risk factors associated with shigellosis and giardiasis among PLWH in Washington, DC, in an era of robust availability of antiretroviral treatment.

METHODS

We conducted a retrospective analysis of HIV, shigellosis and giardiasis cases reported to the District of Columbia Department of Health from 2012 to 2016. We used LinkPlus to probabilistically match individuals with reported HIV and *Shigella* or *Giardia*. We conducted bivariate analysis on gender, race/ethnicity, and age for Shigella-HIV, Giardia-HIV and HIV alone. Among men, we conducted bivariate analysis for HIV transmission risk factors. Among those with Shigella-HIV or Giardia-HIV, we compared CD4 cell count, HIV stage, HIV viral load, and viral suppression (VS) using laboratory data within 8 weeks before or after the incident enteric infection. We compared the incidence of shigellosis and giardiasis in the general population versus among those living with HIV in 2016.

RESULTS

During 2012-2016, 250 DC residents were reported with shigellosis (2.1 per 100,000 in 2016) and 412 with giardiasis (7.3 per 100,000 in 2016). The proportion with HIV coinfection was 20.4% for shigellosis and 10.6% for giardiasis. Incidence rate ratio (PLWH versus general population) was 25.8 for shigellosis and 9.6 for giardiasis. 40.9% of coinfection cases, versus 15.9% HIV alone, were ages 25-34 at the end of 2016 ($p < 0.0001$). White race was more common among Shigella-HIV (19.6%) and Giardia-HIV (27.3%) versus HIV alone (15.9%) ($p < 0.0001$). Nearly all (97.8%) coinfection cases occurred in men. MSM was the most common HIV risk factor among men with Shigella-HIV (80%) and Giardia-HIV (64.3%) compared to HIV without enteric disease (60.4%). Rates of stage 3 HIV and VS were similar between Shigella-HIV (stage 3 HIV 25%, VS 40%) and Giardia-HIV (stage 3 HIV 34.3%, VS 40%).

CONCLUSIONS

PLWH in DC disproportionately acquired shigellosis and giardiasis in 2012-2016. Factors associated with shigellosis and giardiasis among PLWH include male gender, white race, being in the 25-34 age group, and MSM. Among the Shigella-HIV and Giardia-HIV cases, most did not have stage 3 HIV, but we found low viral suppression rates. Our data supports the need for obtaining a thorough sexual history, focused HIV prevention and antiretroviral adherence counseling, and provides information to target high risk groups in DC.

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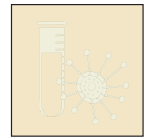
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Reframing Discourse: Using BRFSS Data to Deconstruct Influences of Parenthood on Depression and LGBTQ+ Mental Health

INTRODUCTION

Rates of depression contribute to the mental health epidemic, with parents in the United States considered a population at greater risk. Framing of mental health and depression has remained centered on cisgender, heterosexual identities (cis-heteronormative) despite diversity in family constellations. This presentation looks to reframe and expand the discussion on LGBTQ+ parents, depression, and mental health. The hypotheses tested look first at the differences in depression diagnosis. Second, the number of poor mental health days per month are examined for differences between the subsamples.

METHODS

The study reviewed data from the 2014-2016 BRFSS surveys (n=371,268) focused on parents as compared to non-parents. Analysis used Sexual Orientation and Gender Identity (SOGI) measures alongside self-reported mental health status and depression diagnosis. The results controlled for socioeconomic variations, case demographics, and SOGI data using a pair of regression models (one linear regression model and one binary logistic model). Interaction terms included in the models were constructed between SOGI data and parenthood status.

RESULTS

Protective factors against depression were more evident within the models. All parents are approximately 12% more likely to receive a diagnosis of depression, despite reporting fewer poor mental health days. Expounding on findings related to the SOGI data, the gender and sexual orientation show significant variety. Outcomes support existing research as it pertains to cisgender women being twice as likely as cisgender men to receive a depression diagnosis - however, evidence supports that certain LGBTQ+ populations, when combined with parenthood, show significant reductions in depression diagnosis or self-reported poor mental health days.

DISCUSSION

The interaction between parenthood and LGBTQ+ identities appear protective against depression for some when compared to the reference group (cisgender woman). As such, results encourage a discussion on the mental health benefits of stepping away from the cis-heteronormative framing and approaches toward parenthood narratives. Evidence as it pertains to mental health outcomes bolster existing ethnographic research with quantitative analysis. Taking an intersectional approach to analysis, details on the interaction between identity factors and structural influences can help improve both occurrences of bias and efforts towards preventative mental health program planning. Results encourage a discussion on the mental health benefits of stepping away from the cis-heteronormative framing and approaches toward how social norms perceive and define parenthood.

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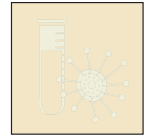
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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Hidradenitis Suppurativa Disease Activity and Marijuana Use

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, recurrent, inflammatory disease of the apocrine sweat glands. The disease affects approximately 1-4% of the population and there is currently no known cure. Smoking is a known risk factor of development of HS and HS disease activity strongly correlates with tobacco smoking exposure.

Marijuana (MJ) is psychoactive drug recently legalized in several states for chronic pain management. Pain control is a common problem for HS patients; however, the implications of Marijuana exposure in HS are unknown. The purpose of this study is to investigate the impact of Marijuana exposure on disease activity scores in HS patients.

METHODS

This research was conducted through the Wound Etiology and Healing Study (WE-HEAL Study), a biospecimen and data repository approved by The George Washington University IRB (041408). At the time of data lock, data from 86 HS patients were available for analysis. HS disease activity scores used in this analysis included Hurley Stage, Hidradenitis Sartorius Score (HSS) and active nodule (AN) count.

RESULTS

Of the 86 HS subjects, 14 were self-reported MJ users and 72 were non users. The mean (SD) age of MJ users was 34.3 ± 12.9 years compared to 40.3 ± 13.0 years in the non-MJ users ($p=0.159$). Patients were 72% female, and 59.3% were African American, with no differences in demographics between the MJ users compared to non-users. Baseline body mass index was similar in the MJ users and non-users ($p=0.59$). At the time of enrollment, there was no significant difference in Hurley stage ($p=0.07$), HSS ($p=0.69$) or AN count ($p=0.48$) in the MJ users compared to non-users.

A limitation of this study was the small sample size, as well as the patients self-reporting marijuana use.

CONCLUSION

In this small pilot study, we were unable to show a correlation between HS disease activity and MJ exposure. However, the relationship between HS disease activity and MJ use merits further study.

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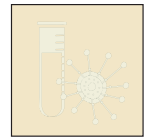
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A One Health Approach to Leptospirosis Serogroups and their Distributions in Humans and Animal Species within Rio Grande do Sul, Brazil 2013-2015

BACKGROUND

Leptospirosis is a global zoonotic bacterial disease widespread throughout the state of Rio Grande do Sul, Brazil. Human infections arise mainly from contact with infected urine or contaminated environment where rodents, domestic animals, and livestock may act as reservoirs for specific leptospirosis serogroups.

METHODS AND PRELIMINARY RESULTS

A descriptive analysis was conducted of leptospirosis human cases with laboratory confirmation from the surveillance data (SINAM/Ministry of Health of Brazil) and animal leptospirosis cases from the surveillance laboratory of the State Agriculture Secretary, from 2013-2015. Predominant serogroups in both human and various animal species were identified. Among the 107 reported human cases that were considered positive with MAT, 18 were classified with their serogroup undetermined, the other 90 had Icterohaemorrhagiae (n=18) as the most prevalent serogroup, followed by Australis (n=12), and Sejroe (n=9). Of the total 443 animal cases, the most common serogroup was Sejroe (n=186), with 76% of those cases observed in bovines, followed by Celledoni (n=23), which was almost evenly distributed between equine, bovine, and canine species. Current ongoing analysis includes species-specific maps describing the spatial distribution of the various serogroups from both human and animal species, to analyze the public health implications for their location and potential overlap within municipalities of Rio Grande do Sul, Brazil.

DISCUSSION

This study further increases the awareness of this neglected zoonotic disease and provides an initial outlook of the situation of the distribution of leptospirosis serogroups in both human and animal cases within the state of Rio Grande do Sul, Brazil. By determining the predominant presumptive infecting serogroups and their distribution within the state, it will aid in guiding public health policy within the One Health framework to implement control and prevention efforts, advance the research to reduce the gaps in mapping leptospirosis serogroups in Brazil, and further the need for developing a human vaccine for high-risk populations.

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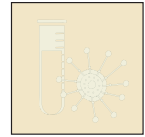
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Development of an Evaluation System for Immunological Tolerance in Sickle Cell Disease HSC Transplanted Patients with Stable Mixed Chimerism

Research in transplantation tolerance is robust; yet, tolerance induction remains elusive. Previously, we reported that the immunosuppressive drug sirolimus allowed long-term, stable mixed chimerism between donor and recipient cells in adult sickle cell disease (SCD) patients who underwent matched-sibling hematopoietic transplantation. Moreover, this state was maintained without graft rejection or graft-versus-host-disease even after withdrawal of the drug, suggesting tolerance. Here, we developed a novel assay using lymphocyte proliferation to evaluate tolerance in this unique patient population.

METHODS

Since we cannot separate donor cells from recipient cells in mixed chimeric patients, we developed a two-way mixed-lymphocyte reaction (MLR) using normal healthy donors to determine if proliferation could be measured when both cell populations are present within the same sample. As patients experience varying levels of donor chimerism, the proportion of one healthy donor to another spanned a full range of 1:9 to 9:1.

Next, to ensure that sirolimus would not impede *in vitro* proliferation, we challenged lymphocytes with sirolimus and measured proliferation over a 12 day course.

Finally, lymphocytes from 18 transplanted patients at various time points post-transplantation were split into two groups: on sirolimus—those who required continued immunosuppression per protocol—and off sirolimus—those who displayed tolerance—and evaluated proliferation.

RESULTS

Using the two-way MLR, lymphocyte proliferation from both healthy donors was able to be measured at each proportion tested, suggesting patient chimerism could be evaluated in both directions.

Sirolimus strongly inhibited lymphocyte proliferation *in vitro* during the first 6 days, but did not inhibit proliferation after 12 days, validating applicability in patients on sirolimus therapy.

Finally, patients on sirolimus were found to have on average 3-fold higher proliferation than an unstimulated control ($p < 0.01$) and 1.8-fold higher proliferation than patients off sirolimus ($p < 0.05$), while proliferation in patients off sirolimus did not differ from an unstimulated control (n.s.), reflecting tolerance. Patients with high levels of proliferation were predominately within the first year post-transplantation and had donor lymphocyte chimerism lower than 50%.

CONCLUSION

Using this assay, lymphocyte proliferation in transplanted SCD patients was found to decrease to near normal levels after one year post-transplantation, suggesting tolerance occurs early during recovery. Further study of lymphocyte activity during this first year may reveal mechanisms leading to tolerance and enable patients to be weaned off of chronic immunosuppression without risk of rejection.

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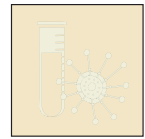
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Comparison of Serological and Symptomatic Diagnosis of Zika Virus Infection Using the Reporter Virus Particle (RVP) Neutralization Assay on Samples from Atlántico, Colombia

BACKGROUND

Zika virus associated morbidities have prompted a global response to Zika infection detection. Recommended serological tests make diagnostics difficult because of cross-reactivity to other flaviviruses and restriction to laboratory availability. In resource-limited settings where Zika is endemic, it is necessary to assess the utility of clinical symptoms as a standard diagnostic strategy for Zika. This study uses a reporter virus particle (RVP) neutralizing antibody assay to evaluate symptomatic clinical diagnosis of Zika virus.

METHODS

Serum and plasma samples collected from patients from Atlántico, Colombia who reported clinically defined symptoms of Zika between October 2015 and June 2016 were tested for neutralizing antibodies to Zika virus H/PF/2013 and dengue-II using RVPs. Standard curves against known antibody concentrations were generated to determine specificity of RVPs for analysis. A result was positive if the Zika antibody inhibitory concentration (IC) to 50% of the RVPs was two-fold greater than corresponding dengue IC 50%. Positive predictive value of symptomatic diagnosis was determined. Prevalence odds ratio was used to compare RVP assay determined Zika infection status to patient symptoms, number of symptoms, and time since infection. Regression analysis was used to assess changes in IC titers due to symptoms. Statistical analysis was conducted using SAS (9.4).

RESULTS

The RVP analysis was specific for Zika H/PF/2013 and dengue-II virus antibodies. Among the 77 patient specimens analyzed, 53 were Zika positive through RVP analysis, 19 negative, and 4 demonstrated an indeterminate result. The average number of days between symptoms and collection date was 37 days. Patients were on average 44 years old, and more than half were female (69.14%). Half of all patients had 6-8 symptoms. The positive predictive value of symptomatic diagnosis was 69%. Of the eight symptoms assessed symptom type, number of symptoms, collection time, and age had no significant correlation with a positive result compared to negative cases. Neither collection time since symptoms nor age had a significant impact on Zika infection status. Increases in IC 50% for Zika or for dengue-II did not relate to number or type of symptoms. Presence of skin rash was positively associated with a 90% IC antibody titer to dengue-II ($p < 0.05$).

DISCUSSION

Symptomatic diagnosis of Zika virus in Colombia may be not useful in the absence of laboratory capacity, and may not be enough to rule out other arboviral diseases. Further study is needed to assess the impact of previous flavivirus history on RVP positivity results.

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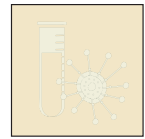
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Perceived Risk of HIV, PrEP Eligibility, and PrEP Use Among Young Men Who Have Sex with Men in Washington, DC

BACKGROUND

In 2014, the CDC issued guidelines recommending pre-exposure prophylaxis (PrEP) for people at high risk of HIV infection. Recent studies indicate that low HIV risk perception may be a barrier to PrEP use among high-risk men who have sex with men (MSM). With efforts to increase awareness and uptake of PrEP, this analysis aimed to examine relationships between HIV risk perception, PrEP eligibility, and PrEP use specifically among young MSM, who accounted for an estimated 22% of new HIV diagnoses in 2015.

METHODS

We analyzed cross-sectional survey data collected from MSM ages 16-25 in the Washington, DC metro area. The Perceived Risk of HIV Scale, a validated eight-item Likert scale, was adapted to measure risk perception (low or moderate/high). PrEP eligibility was determined using the MSM Risk Index, a six-item sexual risk behavior tool included in the 2014 CDC Clinical Providers' Supplement. Participants reported their willingness to use PrEP and whether they currently used PrEP. Chi-square and Fisher's exact tests were used to assess differences in PrEP eligibility by risk perception categories. Adjusted odds ratios (aOR) were calculated using multivariable logistic regression to evaluate the associations between risk perception and PrEP willingness and use among PrEP-eligible participants.

RESULTS

Of 188 participants with self-reported HIV-negative or HIV-unknown status, 149 (79.3%) had moderate/high perceived risk and 115 (61.2%) met index criteria for PrEP eligibility. A higher proportion of PrEP-eligible participants had moderate/high risk perception compared to those not considered eligible (86.1% vs. 68.5%, $p=0.004$). Among participants who were PrEP-eligible, 75.7% reported that they were willing to use PrEP. PrEP-eligible participants with moderate/high perceived risk had greater odds of willingness to take PrEP compared to those with low perceived risk (aOR 4.3, 95% CI: 1.4-13.8). Current PrEP use was reported by only 9.6% of PrEP-eligible participants and was not significantly associated with risk perception (aOR 1.7, 95% CI: 0.2-14.1).

CONCLUSION

HIV risk perception and willingness to use PrEP were both high among young MSM who met criteria for PrEP eligibility, yet few of these participants reported currently taking PrEP. Those who perceived their risk of HIV infection to be moderate or high were significantly more likely to be willing to take PrEP. These findings suggest the importance of risk perception as a correlate of PrEP acceptance and indicate that public health interventions to increase PrEP uptake may benefit from the inclusion of risk-related messaging tailored specifically to the young MSM population.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Physical Activity and Goals

INTRODUCTION

Regular physical activity (PA) is essential for a healthy lifestyle, yet many US adults fail to get the recommended amount of PA. While initiating improvements in PA is an important first step, sustaining PA is essential to experience the health benefits of PA. Hence, there remains a critical need to identify approaches to get individuals to initiate and sustain PA. Existing reports that the type of PA goal an individual pursues is related to sustained PA whereby individuals with PA goals focused on personal growth or interest are associated with higher levels of sustained PA than individuals with goals focused on outcomes of PA such as weight loss or appearance. However, there are several gaps in the existing literature. One is that the literature on goals and PA has focused almost exclusively on white, female subjects. A second gap is that studies utilize assessments of PA goals that are most relevant to younger, healthier subjects (i.e., undergraduate students), and fail to reflect PA goals relevant to adults in a primary care clinic setting.

OBJECTIVE

The objective of the present study was to examine whether physical activity goals of individuals in a primary health care setting were related to whether or not they met PA guidelines established by the Centers for Disease Control.

METHODS

Six hundred and twenty six adults (41.1% African American, 40.6% White, 6.4% Asian, 4.9% Other, 3.8% Hispanic, 1 % Native American) were recruited from the waiting room of a primary care clinic over a 30-day span. Participants completed a 1-page questionnaire about PA and goals.

RESULTS

The most commonly mentioned PA goals included: Weight maintenance, overall health benefits, stress reduction, weight loss, tone/shape of body, sense of well-being, cardiovascular health, and energy level. Logistic regression analyses showed that African Americans were more likely to report weight loss and weight maintenance as one of their most important PA goals than were Whites. Furthermore, Whites were more likely than African Americans to adopt overall health as a PA goal. These results held even after controlling for self-reported overall health.

CONCLUSIONS

African American subjects were more likely than were White subjects to endorse PA goals that past literature has found to be unrelated, or negatively related, to sustained PA. In contrast, White subjects were more likely than African American subjects to report holding a goal that is a positive predictor of sustained PA. Implications of these findings are discussed.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

SWEET MAPS: Conceptualization of Low-Calorie Sweetener Consumption Among Young Adults

BACKGROUND

Over 40% of adults and 25% of children report consuming low-calorie sweeteners (LCS) daily, yet whether LCS are beneficial for weight management and metabolic health is unclear. Epidemiologic studies demonstrate that LCS promote weight gain and development of chronic disease, yet human intervention studies suggest replacement of added sugars with LCS may be beneficial. Discrepancies in findings of observational compared to interventional studies suggest the effects of LCS may be largely dependent on the context in which they are used. The purpose of this study was to develop a conceptual framework using a mixed-method, applied social research methodology called concept mapping to understand the determinants of LCS consumption among young adults (18-35 years old) reporting habitual LCS consumption.

METHOD

Concept mapping engages participants in a step-wise series of tasks (i.e., brainstorming, sorting, rating), which was conducted in two phases. In phase one, participants (n = 68) were asked to brainstorm as many reasons for their LCS use as possible, responding to the prompt, *I consume low-calorie sweeteners and/or products labeled 'diet,' 'sugar-free' or 'no sugar added' because.* Once a saturation of ideas was reached, idea synthesis identified a discrete list of LCS determinants that was representative of all brainstormed ideas. In phase two, participants (n = 93) were asked to sort the LCS determinants based on their meaning and rate (n = 97) each determinant on how true it was to their own consumption of LCS. All activities were completed using an online platform.

RESULTS

Idea synthesis identified 38 determinants of LCS consumption. Similarity matrices, multidimensional scaling, and hierarchical cluster analysis with a two-dimensional solution produced a series of maps (i.e., SWEET MAPS) spatially representing young adults LCS consumption within 8 overarching factors (i.e., *Taste Preference, Sweetness, Don't Like Water, Dependence, Health Benefits & Performance, Weight Management, Habitual Influence, and Cost & Availability*). Among these factors, *Weight Management, Taste Preference, Sweetness, and Habitual Influences* were rated the highest.

DISCUSSION

Although weight management was among the highest rated factors for LCS consumption, our findings demonstrate that LCS are consumed for numerous reasons. These results will aid in the design of subsequent studies to investigate LCS health effects in a manner that best reflects 'real-life' consumption and accounts for contextual factors that may influence LCS effects. Furthermore, these findings call attention to the many challenges in extrapolating findings reported in highly controlled rodent models into the complex framework of human behavior.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Evaluation of Group Movement Programs (PLIÉ and Paired PLIÉ) for People with Memory Loss, Alzheimer’s Disease or Dementia

Today, one in ten people ages 65 and older have Alzheimer’s dementia. This serious condition often causes great suffering among affected individuals and their families, and there are no medications that stop or slow the disease. It is therefore important to evaluate alternative interventions that may benefit both patients and their care partners. Preventing Loss of Independence through Exercise (PLIÉ) and Paired PLIÉ are group movement programs that combine neuroscience and integrative medicine for individuals with dementia. We analyzed data from [N=39] anonymous evaluation surveys performed as part of two ongoing randomized control trials. Survey data included general questions on how the intervention affected care partners and their loved ones. Written responses were classified as either positive or negative. Word cloud was then used to identify the most common themes. Most common themes among the positive feedback were health, enjoyment, social cohesion and reduced caregiver stress/burden. Common themes among negative feedback were time constraint, no change, accessibility, and increased responsibility. Outcomes in each category were counted for a final sample of 71 responses. One-sample test of proportions using STATA compared over-all ratio of positive feedback to the null ($H_0: p = 0.5$). Results show PLIÉ was beneficial for individuals with dementia and their care partners (Z-score = 2.02 | P-value = 0.0216).

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Evaluating Methods for Utilizing Time-Loss Data in Sports Settings Using a Sample of U.S. Collegiate Soccer-Related Injury Observations

BACKGROUND

Time loss has featured heavily in assessments of sports-related injury severity. Typically, it is measured as a count of days lost to injury and analyzed using ordinal cut points. We argue that a refinement of methods for the analysis of time loss which acknowledges the role of severity, is advantageous. We propose to instead model time loss with count or survival regression and adopt the view that it is a manifestation of injury severity, which is a latent variable. Inclusion of a random intercept in the model enables representation of latent injury severity as an unobservable predictor of time loss and admits an interesting, clinically relevant interpretation of observable covariate effects as being ‘severity-adjusted.’

METHODS

Using a sample of U.S. collegiate soccer-related injury observations, we fit random effects Poisson and Weibull Regression models to perform ‘severity-adjusted’ evaluations of time loss.

RESULTS

Injury site, injury mechanism and injury history emerged as the strongest predictors in our sample. In comparing random effects and fixed effects models, we noted that the incorporation of the random effect attenuated associations between most observed covariates and time loss, and model fit statistics revealed that the random effects models improved model fit over the fixed effects models.

CONCLUSIONS

Our analyses serve as a useful starting point for modeling how time loss may actually occur when a player is injured, and suggest that random effects or frailty based approaches can help isolate the effect of potential determinants of time loss.

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The Joint Associations of Weight Status and Physical Activity with Mobility Disability in Older People: The NIH-AARP Diet and Health Study

BACKGROUND

The purpose of this study was to determine the joint associations of weight status and physical activity with mobility disability in older men and women.

METHODS

We analyzed prospective data from 135,220 participants in the NIH-AARP Diet and Health Study between 1995-1996 and 2004-2005. Height and weight, as well as light- and moderate-to-vigorous-intensity physical activity typical of the past 10 years (h/week) were self-reported at baseline, and body mass index (BMI: kg/m^2) was categorized into normal weight (BMI 18- $<25 \text{ kg}/\text{m}^2$); overweight (BMI 25- $<30 \text{ kg}/\text{m}^2$); and obese (BMI $\geq 30 \text{ kg}/\text{m}^2$). Mobility disability at follow-up was defined as being "unable to walk" or having an "easy usual walking pace ($<2 \text{ mph}$)". Multivariable logistic regression determined the independent and joint associations of weight status and total physical activity with the odds of mobility disability.

RESULTS

We observed a curvilinear dose-response association between increasing categories of weight status and mobility disability within each tertile of physical activity, with the highest odds experienced by men and women with overweight (OR=2.40; 95%CI 2.20, 2.61 for men and OR=3.0; 95%CI: 2.75, 3.19 for women) and obesity (OR=3.90; 95%CI: 3.54, 4.28 for men and OR=5.05; 95%CI: 4.63, 5.52 for women) in combination with low physical activity. Moreover, among those reporting $\leq 7 \text{ h}/\text{week}$ of total physical activity, being of normal body weight did not eliminate the excess odds of mobility disability.

CONCLUSIONS

These findings highlight the combined importance of obesity prevention and physical activity promotion to mobility in older age.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Investigating Effects of Low-Calorie Sweetener Consumption on Metabolic Dysregulation

BACKGROUND

Consumption of low-calorie sweeteners (LCS)—including acesulfame-potassium, aspartame, saccharin and sucralose—has increased in the US over the past decade, mainly through LCS containing beverages. Recent studies have reported 25% of adolescents and 30% of adults consume LCS daily. This increase in LCS consumption is likely to continue, as foods and beverages containing LCS are advertised as healthier alternatives to products high in sugar. Prior studies have shown that when rodents are exposed to LCS for a prolonged time period, they develop metabolic abnormalities. However the majority of human studies have only looked at the effects of single-dose LCS ingestion on metabolic parameters. The goal of this study is to investigate the LCS-induced changes in at-risk adolescents and young adults under conditions that reflect real life LCS consumption.

METHODS

Ten females between the ages of 18 and 25, who were overweight or had mild to moderate obesity (a BMI between 25 and 35 kg/m²) were enrolled in a longitudinal study design. Individuals were selected to represent a population that is already metabolically vulnerable and likely to use LCS for weight loss. Participants served as their own controls and the following were measured using fasted blood samples collected before and after 8 weeks of three times daily diet soda (containing sucralose and acesulfame-potassium) consumption: fasting glucose levels, HOMA-IR, Leptin, Adiponectin, TNF-alpha, hs-CRP, triglyceride and HDL levels. Anthropometric and dietary data were also collected.

RESULTS

Eight participants completed the eight week study. Given our small sample size, there were no statistically significant differences in any of the metabolic or inflammatory biomarkers measured when comparing baseline and post-intervention values. However, there was a trend towards increased HOMA-IR and leptin, driven largely by changes observed for a single participant. Observed changes in biomarker profiles before and after the intervention were highly variable across study participants.

CONCLUSIONS

Given the massive variability in responses across study participants, comparing average values for all eight participants before or after the intervention is likely inaccurate for describing LCS effects. Further analyses to evaluate potential factors associated with 'responders' and 'non-responders' are warranted to determine whether some individuals may be more susceptible to LCS-induced metabolic effects. Our results also highlight the urgent need for future studies testing a larger sample of metabolically at-risk individuals.

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Effects of Prolonged Low-calorie Sweetener Consumption on Calorie and Macronutrient Intake in Female College Students

BACKGROUND

Low-calorie sweeteners (LCS) provide individuals with alternatives to added sugars and provide the desired sweet taste without calories. LCS are found in foods and beverages labeled 'sugar-free', 'no-sugar added', and 'light'. The consumption of LCS in the U.S. has increased in the last decade, with 25% of adolescents and 40% of adults consuming LCS daily. However, their effects on the human health and metabolism are not fully understood and it has been hypothesized that LCS may paradoxically promote sugar and calorie intake, leading to weight gain. The purpose of this study is to investigate how eight weeks of LCS consumption impacts caloric and macronutrient intake in female college students.

METHODS

Participants were eight healthy, non-smoking, non-pregnant females between 18-25 years of age, who did not report regular LCS consumption and who were classified as overweight or obese according to BMI (body mass index) ($25 \leq \text{BMI} < 35 \text{ kg/m}^2$). Participants were screened over the phone to determine their eligibility. Participants who consumed foods or beverages containing LCS more than once per week were excluded. After the in-person screening and baseline visit, participants were instructed to drink the diet sodas, three times per day for eight weeks. Dietary recalls were conducted over the phone three times a week, based on the participants' availability. Dietary recall data was compiled to study changes in calorie, macronutrient, and sugar intake over the course of the study.

RESULTS

Eight participants completed the study and provided plausible dietary intake data. One participant was excluded due to consistently reporting implausible energy intake (<600 kcal per day). Overall, mean caloric intake among the seven remaining participants increased between the start of the study and their follow-up visit after drinking diet soda for eight weeks. Six of the seven participants reported an increase in carbohydrate consumption. Similarly, six participants reported increased sugar intake after the intervention period compared to baseline.

DISCUSSION

Our results suggest that consistent with data in rodent models, chronic LCS intake may promote rather than reduce calorie, carbohydrate, and sugar intake. This is in direct opposition to the intended benefits of using LCS as a replacement for added sugars. Given our small sample size, future studies with more participants are necessary to confirm these findings and assess potential differences in the relationship between LCS and dietary intake across sociodemographic and weight status subgroups.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Cardiovascular Health is Associated with Disability Among Older Community Dwelling Men and Women

BACKGROUND

Disability is a public health concern affecting the quality of life among the elderly. Our study investigated whether an index of overall cardiovascular health (CVH) based on American Heart Association guidelines is associated with disability in older individuals.

METHODS

Data from the InCHIANTI study were used to assess the associations between CVH and disability among 925 cohort participants (≥ 65 years, 55% women) with median follow-up 9-years. CVH score, ranging from 0-12 (maximum possible score of 14), was operationalized using adherence to ideal levels for health behaviors including smoking status, physical activity, body mass index, and diet quality; and health factors including blood pressure, plasma cholesterol, fasting blood glucose, with higher scores indicating better CVH. Disability was examined using Instrumental Activities of Daily Living (IADL) and Activities of Daily Living (ADL) questionnaires. If a participant indicated that they were unable to accomplish a task, they were considered to have a disability. Generalized estimating equations (GEE) models assessed the relationship between baseline CVH with ADL and IADL disability and worsening over 9-years. Cox proportional hazard models examined associations between baseline CVH and disability in participants without disability at baseline.

RESULTS

For GEE models, a 1-point increase in the CVH score was associated with 23% and 17% of lower odds of ADL (odds ratio [OR]=0.77, 95% confidence interval (CI): [0.69-0.86], $p < 0.001$) and IADL (OR=0.83, 95% CI: [0.77-0.89], $p < 0.001$) disability. Higher CVH scores were also protective of worsening of disability over 9-years. Additionally, Cox models demonstrated that a 1-point increase in CVH score was associated with lower hazards of both ADL (hazard ratio [HR]=0.86, 95% CI: [0.77-0.95], $p = 0.005$) and IADL (HR=0.91, 95% CI: [0.86-0.98], $p = 0.007$) disability.

CONCLUSIONS

In this cohort of older individuals, better CVH was associated with lower risk of ADL and IADL disability and worsening over 9-years.

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Greater Participation in the Produce Plus Healthy Food Incentive Program Supports Food Security

INTRODUCTION

The Produce Plus Program (PPP), a farmers' market-based healthy food incentive program, provides income qualified Washington, DC residents with vouchers worth \$10/market/day for fruit and vegetable (F&V) purchases. This study evaluated whether frequency of PPP participation is associated with changes in food security status (FSS) and F&V intake.

METHODS

PPP participants were invited to complete a survey which included the NCI Fruit and Vegetable Screener and a modified 6 question USDA Household Food Security Module at markets during the PPP-season (June-September 2016) and again by mail during the off-season (March-April 2017). Chi-square and paired t-tests were used to compare FSS and F&V intake between seasons by high vs low frequency of participation, dichotomized by mean number of vouchers received during the PPP-season among all participants (mean=14).

RESULTS

Eighty-nine PPP participants completed the survey during both seasons. Among the 59 survey participants who received ≥ 14 vouchers during the PPP-season, those reporting being food secure decreased from 32(54.2%) during the PPP-season to 19(32.2%) during the off-season ($p=0.04$). Among the 30 survey participants who received < 14 vouchers during the PPP-season, with those reporting being food secure decreasing from 17(56.7%) during the PPP-season to 11(36.67%) during the off-season ($p=0.86$). Among the 59 survey participants who received ≥ 14 vouchers during the PPP-season, mean reported daily F&V intake decreased from 5.1 servings per day during the PPP-season to 4.19 servings per day during the off-season ($p=0.12$). Among the 30 survey participants who received < 14 vouchers during the PPP-season, mean reported daily F&V intake decreased from 5.9 servings per day during the PPP-season to 4.4 servings per day during the off-season ($p=0.34$).

DISCUSSION

Greater participation in the PPP appears to support FSS, but does not alter F&V intake. Lack of change in F&V intake may be because the program attracts participants who already prefer F&V, consistent with our previous findings that PPP participants reported higher median F&V intake compared with local Behavioral Risk Factor Surveillance Survey respondents with similar incomes.

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Novel Use of Respiratory Conditioning Masks During High-Intensity Interval Training to Improve Respiratory Function in Healthy Adults

PURPOSE

Respiratory conditioning masks (RCMs, also known as altitude masks) have become increasingly popular for use in aerobic exercise training. Thus far, evidence for RCM effectiveness is somewhat ambiguous. Previous studies typically utilize RCMs during the exertional period of exercise training. The purpose of this study was to examine the effects of RCMs on lung function when used only during the low-intensity recovery intervals of high-intensity interval training (HIIT).

METHODS

A group of recreationally active healthy adults performed a 6-week HIIT protocol where half of the participants were randomly assigned to wear an RCM during the low-intensity rest intervals (Mask Group), or no mask (Control). Participants performed three HIIT bouts per week, where each bout included eight high-intensity intervals of 60s exercise performed within 10 beats of maximal heart rate for each subject obtained from a baseline graded exercise test to volitional exhaustion. Each high-intensity interval was immediately followed by a 90s low-intensity recovery interval at a work rate corresponding to 10% VO_{2max} for each participant at baseline. Pulmonary function testing was also performed at baseline and following a six week intervention period.

RESULTS

12 subjects (7 women, ages: 25.5 ± 4.55 yrs, BMI: 23.6 ± 1.5 kg/m²) to date completed the study. Expiratory reserve volume was significantly larger in the mask group compared to the control group after training (1.5 ± 0.5 vs. 0.8 ± 0.4 L, $p=0.02$). Resting VE/VO_2 (41.8 ± 6.9 vs. 28.3 ± 2.7 , $p=0.001$) and VE/VCO_2 (47.3 ± 11.6 vs. 35.8 ± 3.9 , $p=0.04$) increased in the mask group compared to controls. In the mask group alone, at peak exercise VE/VCO_2 significantly increased at isowork rates (31.5 ± 2.3 to 34.3 ± 3.6 , $p=0.02$) while the respiratory exchange ratio decreased (1.22 ± 0.11 vs. 1.14 ± 0.08 , $p=0.02$). Resting $PETO_2$ significantly increased in the mask group alone after exercise training (111.7 ± 6.5 vs. 115.5 ± 6.1 mmHg, $p=0.02$). No other changes were observed in forced vital capacity, total lung volume, or maximal inspiratory/ expiratory pressures for both groups.

CONCLUSIONS

RCMs worn only during the low-intensity recovery intervals in a 6 week HIIT protocol appear to have a significant effect on select measures of respiratory and ventilatory function. VE/VCO_2 is an indicator of ventilatory drive, and changes in VE/VCO_2 have been shown to have prognostic significance for several clinical populations. Using RCMs in this novel fashion may play a role in modifying ventilatory drive.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Urinary Sucralose Concentrations Before and After 8 Weeks of Diet Soda Ingestion

BACKGROUND

Products containing low-calorie sweeteners (LCS), including acesulfame-potassium, aspartame, saccharine, and sucralose are frequently promoted as healthier alternatives to sugar-laden foods and beverages. The effects of LCS on metabolic health, however, remains controversial. In this study, we aimed to assess the changes in urinary LCS concentrations after 8 weeks of three times daily diet soda consumption.

METHODS

Urine samples were collected from 8 females, 18-25 years of age, with overweight and mild to moderate obesity at baseline and after the eight-week intervention. We specifically enrolled individuals who did not habitually consume LCS, based on self-report. During the intervention, study participants consumed diet soda containing sucralose and acesulfame-potassium for eight weeks, three times daily (dose of approximately 3 mg/kg/day sucralose and 1.75 mg/kg/day acesulfame-potassium for average 70kg adult). They were instructed not to change their normal eating habits, and to maintain their weight throughout the study. Compliance was evaluated by collecting empty soda cans from participants and measuring urinary LCS concentrations from urine samples collected at the baseline and post-intervention visits.

RESULTS

With the exception of one participant who had trace urinary LCS concentrations at baseline, neither sucralose nor acesulfame-potassium were detected in the remaining seven urine samples prior to the intervention. Following eight weeks of diet soda consumption, urinary LCS concentrations increased dramatically in seven of the eight individuals. Peak sucralose and acesulfame-potassium concentrations ranged from 2,941–5,010 ng/mL and 22,869–55,204 ng/mL, respectively. Despite the large variability in concentrations measured, individuals with the highest urinary sucralose concentrations also had the highest acesulfame-potassium concentrations. Self-reported compliance with diet soda consumption instructions was similar across the study participants.

CONCLUSIONS

While LCS concentrations in urine varied greatly across individuals, seven of the eight post-intervention urine samples contained significantly elevated concentrations of both sucralose and acesulfame-potassium, as expected. Our data therefore suggest that participants did indeed ingest diet soda in accordance with study instructions. However, the marked inter-individual differences in LCS concentrations suggests that there may be differences in absorption, distribution, or clearance of LCS based on demographic, genetic, or metabolic characteristics, which requires further study.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Is Using a Bicycle as Method for Transportation Contributing to Your Mental Health?

PURPOSE

Depression and anxiety are on the rise and have become two of the most common mental health diseases in society. Both linked to poor quality of life, missed time from work and disability. Traditional treatments are depressive and anxiolytic drugs that sometimes produce uncomfortable side effects. The purpose of this critical review is to recommend an alternative approach to depression and anxiety in the form of cycling used as a method for transportation.

METHODS

Literature review of research performed through Scopus and Google Scholar. The review has neither date nor country limitations. However, papers written in English were only considered.

RESULTS

Studies agree that, despite unclear mechanisms, physical exercise can alleviate depressive and anxiety symptoms. Most studies refer to aerobic exercise as the most effective form. Environment where exercise is conducted can vary in benefits. Outdoors is the ideal environment for better healing results. Cycling was found to not only improve the condition of depressive patients, but also to increase quality of life. Benefits of active commuting were evaluated and finding that it contributes to better health status by reducing the risk of cardiovascular diseases, cancer and death along with helping to acquire better mood and reduce stress levels.

CONCLUSION

Given the satisfactory results of an outdoor environment and cycling as contributors to reduce depression and/or anxiety symptoms along with active commuting as a potential health and mood improver. There is a need for further research on how active commuting on bicycle could affect individuals suffering from depression and anxiety.

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A Novel Application of Altitude Training Masks and High-Intensity Interval Training to Improve Exercise Performance

INTRODUCTION

Altitude training masks (ATM, also known as respiratory fitness masks) have been widely implemented by recreational and professional athletes during high-intensity interval training (HIIT) and other forms of exercise training in an effort to improve performance by purportedly inducing a hypoxic physiologic state. However, previous research on high altitude exercise training demonstrates that training at low altitudes elicits a greater training adaptation as participants can achieve higher work rates when compared to high altitude training. **PURPOSE:** To examine the effects of ATMs used solely during recovery periods (low intensity intervals) during HIIT.

METHODS

Participants underwent six weeks of HIIT (3 sessions per week) with each exercise bout consisting of eight, 60-second high-intensity intervals interspersed with eight, 90-second low-intensity recovery intervals. Workloads for the high-intensity intervals were individualized to elicit heart rates within 10 bpm of each participant's maximal heart rate as assessed during a baseline graded exercise test. The low-intensity recovery intervals were prescribed at a fixed workload corresponding to approximately 10% of each participant's baseline maximal oxygen consumption (VO₂max). Participants were assigned via block randomization to either a control group (CG) or a training mask group (TMG) that only wore the ATM during the low-intensity recovery bouts of the HIIT intervention. Participants performed a graded exercise test to volitional exhaustion at both baseline and following the HIIT intervention as well as a vascular occlusion test to assess the tissue saturation index nadir (TSIN) of the gastrocnemius. Outcomes were VO₂max, oxygen consumption at anaerobic threshold (AT), and TSIN.

RESULTS

Twelve participants (7 women; 25.5±4.5 years; BMI: 23.6±1.5 kg/m²) have completed the study to date. VO₂max increased significantly in the TMG group (40.5±3.6 to 44.5±5.4 ml/kg/min, p=0.03) but not in the CG. TSIN was significantly greater in the TMG group (-17.8±7.3 to -28.3±7.3% from baseline, p=0.05) with no significant change in the CG. No change in AT was observed in either group.

CONCLUSION

Implementing ATMs only during the low-intensity recovery intervals of HIIT training appears to improve key components of cardiorespiratory function not observed in the standard HIIT training group. These findings demonstrate a novel use of ATMs that has potential to change how ATMs are used by recreational and professional athletes. These results also have implications for the use of ATMs as potential adjunctive modalities for enhancing training effects in rehabilitative settings where improvements in short time periods are desirable.

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EXERCISE AND NUTRITION SCIENCES



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Low Calorie Sweeteners and Weight Management in Children and Adolescents

BACKGROUND

Excessive sugar intake contributes to weight gain and obesity, as well as a variety of other adverse health consequences. Sugar is found in many foods and beverages, and is most often consumed in the form of sugar-sweetened beverages (SSB). SSB include many types of drinks such as sodas, sports drinks, flavored juice drinks, coffee drinks, and energy drinks. Given the well-established link between excess sugar intake and weight gain, consumption of diet beverages sweetened with low-calorie sweeteners (LCS) instead of sugar has been increasing among children and adolescents. This raises the question as whether the LCS are effective for weight management, which has remained a topic of considerable controversy over the past several decades. The purpose of this review is to summarize the existing evidence in order to determine whether the consumption of LCS has beneficial, harmful, or neutral effects on weight among children and adolescents.

METHODS

The PubMed database was used to search for previously conducted studies investigating LCS consumption in relation to body weight among children and adolescents. Keywords used to search the database included artificial sweeteners, nonnutritive sweeteners, diet beverages, children, adolescents, and weight management. A total of nineteen sources were included, comprising both observational and interventional studies.

RESULTS

The majority of observational studies reported that LCS consumption was associated with increased body weight, BMI, and adiposity. In contrast, the majority of interventional studies found that LCS were helpful for weight management.

DISCUSSION

Our results demonstrate that whether LCS is helpful or harmful for weight management among children and adolescents differs depending on the type of study performed. As observational studies suggested potentially detrimental effects while interventional trials demonstrated benefits of LCS use, it is likely the LCS effects on weight may vary based on how and by whom they are used. Due to these discrepant, further research should be conducted with careful consideration of the study design and individuals enrolled.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Impact of Polymorphisms in PTK2 on Intrinsic Muscle Strength

Recent studies have begun to search for correlations between genetic variations and muscle strength. One such study by Stebbings et al. examined two single nucleotide polymorphisms (SNPs)—rs7843014 and rs7460—on the PTK2 gene. The study found that genetic variation in the PTK2 gene impacts muscle-specific force, which is the force generated per unit of cross-sectional area of muscle. Muscle-specific force ultimately represents the intrinsic strength of a muscle and is a key determinant of functional capacity and mobility. This study sought to expand on prior research by looking for associations between genetic variants of PTK2 and measures of grip strength, as well as general anthropomorphic measures, in a cohort of healthy young adults.

Our study assessed phenotypes for height, weight, VO₂ max, max grip strength, and body mass index (BMI) using the Assessing Inherited Markers of Metabolic Syndrome in the Young (AIMMY) University of Calgary subset of 190 healthy, primarily Caucasian, individuals between the ages of 18 and 35. DNA samples were genotyped using ThermoFisher Taqman SNP genotype assays, and underwent the Applied Biosystems 7900HT real-time polymerase chain reaction (PCR) process. Analysis of covariance (ANCOVA) models were used to perform statistical analysis to look for genotype-phenotype associations.

Unlike the findings by Stebbings et al. an association between the PTK2 genotypes and grip strength was not found. This could be due to the lower statistical power in the grip strength test, thus potentially indicating that grip strength and muscle-specific force do not measure similar parameters of muscle strength. Genetic variation in PTK2 has also been previously associated with VO₂ max, but no association was found in the current study.

Positive associations were found between genetic variants rs7843014 and rs7460 in PTK2 and BMI, and between genetic variant rs7843014 and height. High levels of functioning PTK2 have been found to have increased strength due to increased costamere density, resulting in more muscle myofibrils, and therein larger, presumably heavier muscles. However, this finding was only observed in males, and could be attributed to differential acquisition and maintenance of muscle mass based on sex.

We identified a potentially novel association between genetic variants in PTK2 and anthropomorphic phenotypes. However, we were unable to confirm the effects of genetic variants on measures of intrinsic muscle strength, namely max grip strength or VO₂ max in terms of functional capacity. Further research is needed to confirm this newly identified role for PTK2.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Survey of Language Diversity and Communication in Indian Academic Emergency Departments

BACKGROUND

Communication in the Emergency Department (ED) is particularly important given the acuity of patients and lack of prior medical history. In India, patient care is further complicated by the many spoken languages, the regional differentiation in language and the fact that medical training is primarily delivered in English. Our objective was to document language diversity among clinicians in Indian EDs linked to an international training program and explore issues related to clinician-clinician and clinician-patient communication.

METHODOLOGY

A cross-sectional survey of ED clinicians was conducted from May to July 2017. Survey participants were recruited via convenience sampling by a researcher at 6 ED training sites in Kerala and Karnataka. Doctors were also sent an email link to the survey. ANOVA and binary logistic regression were used to perform subgroup analysis.

RESULTS

106 clinicians completed the survey including 42 doctors (9 consultants and 33 residents), 45 nurses and 19 paramedics. On average, clinicians spoke 3.75 languages. Fluency in the majority language at the hospital was reported by 93% of doctors, 84% of nurses and 95% of paramedics. Fluency in English was reported by 100% of doctors, 71% of nurses and 63% of paramedics. Type of clinician, age, gender, and time in clinical practice did not predict number of languages spoken or fluency in the majority language. Doctors were more likely to report fluency in English, compared to other providers ($p < 0.003$).

70% of clinicians reported that they used a non-English language to speak to their fellow providers most of the time. 64% felt that information was lost or changed when English medical knowledge was explained in a different language. 53% reported at least one critical incident over the last year where poor communication played a part. Time constraints, language and differences in medical knowledge were the most frequently identified barriers in these incidents.

CONCLUSIONS

Our study is the first to document language diversity in Indian EDs. Important findings include the common use of non-English language in clinician-clinician communication and the frequent perceived loss of information in clinician-patient communication. The reported rates of critical incidents linked to poor communication are higher than reported in comparable studies and warrant further research and action.

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Enhanced Visual-Based Cervical Cancer Screening in Kenya

Cervical cancer is the leading cause of cancer related death for women in low-resource settings. In many developing nations, cervical cancer screening suffers from a lack of infrastructure, such as lack of national cancer registries, and inconsistencies in operational and policy decision making by hospitals, aid organizations and national governments. In much of the developing world there is a lack of access to Pap and HPV testing. Cervical cancer screening is typically done by visual inspection with acetic acid (VIA). There is great variability in VIA outcomes owing to provider experience. An enhanced visual assessment (EVA) System was developed to improve infrastructure and decision making in low resource settings. The EVA System consists of a mobile colposcope that attaches to any smartphone, and a cloud-based app for uploading pictures to a portal. This image portal is viewable by registered physicians and lab technicians who are experts in identifying suspicious lesions. Smartphones allow for collecting statistics on user behavior in the app, tabulating statistics on imaging-related activities in cervical-cancer clinics and provides insight into operational decision making. As a community outreach effort, several aid organizations used the EVA System at cervical screening camps in Kenya. Over one week, 1058 women were screened with enhanced visual assessment and 94 women were treated with cryotherapy for dysplasia. Results were able to be viewed in real time by licensed practitioners in the United States who were able to assist in decision making. The ability to eliminate delay in treatment by getting immediate feedback from medical experts and increase treatment rates holds promise for broader use in screening programs in low-resource settings.

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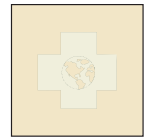
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Developing the Health Profile for Female Children Formerly Associated with Armed Forces and Armed Groups in the Reintegration Processes

BACKGROUND

Although twenty years since the Cape Town Principles, armed groups continue to actively target children, including young girls. Girls within armed forces fulfill roles ranging from cooks or caretakers, to wives or active combatants. These young women are often called female children associated with armed groups and armed forces (CAAFAG), with the term 'association' capturing the varied roles they assume within armed forces. Despite recognition of their presence, little is known about the health impacts of association with armed groups on girls, and consequently their unique health needs during reintegration into communities. This research aims to understand the health consequences of association on female CAAFAG, and articulate their health priorities upon reintegration.

METHODS

The research utilized two methodologies to develop the health profile: (1) systematic literature review; (2) analysis of Survey of War Affected Youth (SWAY) data.

The systematic literature review, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards, searched six databases and yielded 735 studies. Following eligibility review, 56 (7.8%) studies were included for final analysis.

STATA was used to analyze the SWAY data, examining the impacts of association with armed forces on the health of female youth. The SWAY, funded by UNICEF, was administered in 2007 to 1,044 female youth in Northern Uganda, including female CAAFAG.

Criteria were then applied to the health profile, identifying health priorities for female CAAFAG.

RESULTS

Three themes emerged in the health profile: psychological, physical, and reproductive health. Findings suggests that CAAFAG face greater psychological consequences than other war affected youth (ex. PTSD), and several studies found that female CAAFAG are at increased risk for depression. SWAY data analysis supports these conclusions, and through multiple regression, demonstrates that exposure to violence often mediates the relationship between psychological distress and abduction status.

Beyond mental health, data analysis reveals that abducted girls are younger at age of first birth ($p < .001$), which may explain some of the reproductive health concerns expressed in the qualitative literature. Additionally, female CAAFAG were more likely than girls never abducted to have been beaten in the past 2 months, and have physical injuries ($p < .001$).

SIGNIFICANCE

This research is evidence for a stronger health presence during reintegration. The sparsity of literature on the impacts of association beyond psychological requires further attention. The next phase of this investigation will build off these findings, using the profile to identify where health needs remain unmet for female CAAFAG.

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JOINT PA/MPH PROGRAM

Effect of Elevated CO₂ Levels on Zinc Concentrations in Rice: A Systematic Review

BACKGROUND

The direct and indirect effects of climate change are adversely affecting human health in a variety of ways through changes in weather patterns, increasing temperatures, and rapidly increasing carbon dioxide. Changes in crop yields or crop quality may be expected from these changes in climate. However, it is unknown at this point to what extent elevated carbon dioxide (e[CO₂]) is impacting grains. These effects have the potential to exacerbate micronutrient deficiencies in vulnerable populations around the world which are reliant on specific grains as staple food crops and important sources of daily micronutrient needs.

OBJECTIVE

We used Navigation Guide methods for this systematic literature in order to evaluate if predicted future environmental conditions, such as e[CO₂], are associated with changes in zinc (Zn) levels in rice.

METHODS

According to Navigation Guide methodology, we specified the study question, selected evidence according to a priori exclusion and inclusion criteria, and evaluated the literature. Three studies met the criteria and were included in the final comparative analysis.

DISCUSSION

The evidence was inadequate to determine whether e[CO₂] alters Zn levels in rice. Lack of research investigating this specific association, varying study designs, and use of different rice cultivars are likely to have played a role in variability across studies.

CONCLUSION

Confidence in the evidence of an association between e[CO₂] and decreased Zn levels in rice was low due to inconsistencies among included study results. The suggestive, but lacking research about this specific potential association warrants more research.

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Reliability Testing of the Star Rating for Schools (SR4S) Mobile Application: Results from a Pilot Study

Globally, approximately 3500 individuals are killed due to a road traffic injury each day, equating to nearly 1.3 million deaths each year and more than a million children are either killed by, or sustain serious injury, from road traffic incidents. School zones are locations where there may be high concentrations of children at certain hours of the day, thereby increasing their exposure to road and pedestrian injuries. The International Road Assessment Programme (iRAP), an NGO established in 2006, developed the Star Ratings measurement system, which is used globally to provide simple, comparable and objective measurements of the built-in safety of road segments for road users. These ratings are given to governments and other users to inform infrastructure and other road safety programs. Recently, the Star Rating methodology has been adapted for the Star Rating for Schools (SR4S) mobile application (an app), which is designed to measure and communicate road and pedestrian safety risks that children and adolescents are exposed to on their journey to and from school. iRAP has brought together several organizations, including Safe Kids Worldwide (SKW), from around the globe to pilot test the SR4S app.

This project, in collaboration with SKW, aims to test the reliability of the SR4S app to answer the following questions: 1) Does the SR4S app produce consistent Star Ratings for the same road segments across multiple users? 2) Does training app users increase the reliability of the SR4S app to assess road and pedestrian safety in local school zones?

Data collection took place during a two-day workshop in Washington, D.C., where 9 child injury experts with experience working in pedestrian safety advocacy (i.e. Safe Kids Coordinators) conducted multiple safety assessments using the SR4S app at a local elementary school at 10 road segments and received training on how to use the app. Data was collected once before training, and twice post-training. This data is currently being analyzed for inter-rater reliability and test-retest reliability. Preliminary results: only 5 of 9 users fully collected the required data and this greatly reduced the reliability of the app. The results of the reliability analysis will be presented to iRAP and the SR4S app developers to inform the development of improved versions of the app which will eventually be rolled out for worldwide use.

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Replacing Sugary Drinks with Water among Young Latino Children and their Parents

OBJECTIVES

Test the preliminary effects and provide proof of concept of a newly-created, theory-based intervention that was designed using a community-participatory approach to increase plain water consumption (mostly from tap) and reduce sugary drink intake among Latino children and their mothers. The 12-week intervention addresses sociocultural (via a curriculum) and physical (via water filters) barriers to drinking tap water and sugar sweetened beverage (SSB) in this predominantly Central American immigrant, low-income community. The primary hypothesis is that the intervention will increase overall plain water consumption and decrease sugary drink intake among parents and their children. We also examine 100% fruit juice intake, as our community partners are concerned about excess drinking of this beverage.

METHODS

This is a pre and post evaluation study. The intervention was integrated into an existing home visiting program of two partner Early Head Start (EHS) centers in the Washington DC metropolitan area. All children are from families living below the poverty guidelines. EHS home visitors were trained to deliver the intervention during 3, 2-hour training sessions. We intended to recruit and retain 50 Latino families. The Beverage Intake Questionnaires (for preschoolers, as parent-reported, and for adults) were cognitively tested for our population and administered to determine SSB (a sum of sweetened fruit drinks, soda, flavored milk, sport drinks and sweetened coffee/tea), 100% fruit juice and water intake. A survey assessed knowledge and attitudes. Data were analyzed using paired t-tests.

RESULTS

We were able to recruit 45 parents, of which 86.67% completed the 12-week program (others moved out of the EHS network during the program). Preliminary data indicate that among children there was an average increase of 15.32 oz in water/day and a 6.07 oz/day decrease in SSB+100% fruit juice. Among parents, there was an average increase of 1.75 oz/day of water and a decrease of 4.95 oz/day of SSB+100% fruit juice intake.

CONCLUSION

Preliminary findings are encouraging results, and suggest the 12-week intervention is effective in both increasing water and decrease SSB intake among primary caregiver and their children.

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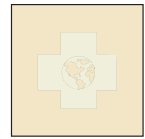
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Gender Perceptions and Attitudes among Adolescents in India: A Critical Time for Change

Secondary education is linked to better health outcomes for women and girls. When a community invests in a girl, she marries later, experiences less violence, and has healthier children. Women completing their secondary education are 40% less likely to report spousal violence and half as likely to have stunted children, and children of literate mothers have a 50% better chance of surviving past age five. In India, gender stereotypes prevent adolescent girls from achieving a secondary education-- 41.34% of girls do not make it to Class 8, and 9 out of 10 girls do not complete secondary school. Construction of gender attitudes and socialization occurs during this period making adolescence a critical time to alter gender perceptions. Our study aimed to better understand the differences in gender perceptions among adolescents in Delhi, Punjab, and Rajasthan, India.

We conducted a cross-sectional study of 1,693 adolescent students, 895 girls and 798 boys, from 25 schools and one community center in grades 5 through 9 in three states. We collected quantitative data on mobile tablets, allowing for audio capabilities and self-administration. Survey questions assessed gender perceptions and attitudes, including gender roles/privileges/restrictions, attributes, and violence.

The results showed a significant difference between the gender perceptions of girls and boys. Boys had significantly less gender equitable perceptions in comparison to girls ($p < .001$). Compared to 5th graders, 7th, 8th, and 9th graders had greater gender equal perceptions ($p < .001$). A greater number of children per household correlated with a decrease in gender-equal perceptions ($p < .05$). Compared to Delhi, there was a negative relationship with Amritsar, Ludhiana, Sangrur, and Jodhpur, with Jodhpur representing the highest gender inequality ($p < .001$).

This study will provide meaningful knowledge and fill gaps in the evidence base for gender sensitization interventions to improve the health and well-being of women and girls throughout their life course.

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Utilization of and Attitudes towards Free Open Access Medical Education Resources and Social Media among Emergency Medicine Physicians in India

BACKGROUND

Emergency Medicine (EM) is still in its early development in much of the world, including India. Educational tools such as Free Open Access Medical Education (FOAMed) resources and social media are being used to augment learning and aid in clinical decision making in EM settings including the United States. However the utility in other settings is less well understood. The aim of the study was to characterize current usage and attitudes toward FOAMed and social media among EM physicians in India.

METHODS

We used an online survey and in-person semi-structured interviews to collect data regarding attitudes toward and usage of FOAMed and social media. Survey invitations were sent via email to current residents and faculty. Semi-structured interviews were conducted in-person with a convenience sample of faculty and residents. Survey data was analyzed using STATA 11.0 to calculate mean responses with 95% confidence intervals (CI). Interview content was analyzed using rapid assessment methodology.

RESULTS

91 respondents completed the survey. The most commonly used resources for medical education were YouTube (70.3%, 95% CI 60.8-79.9%), WhatsApp (59.3% 95% CI 49.1-69.6%), and Facebook (36.3% (95% CI 26.2-46.3%). These resources are reportedly used at least daily or numerous times per week by almost half of all respondents. Approximately 70% of respondents reported at least one barrier to the usage of FOAMed or social media, including cost (28.6% [95%CI 19.1-38.0%]), blocked websites (19.8% [95%CI 11.4-28.1%]) and internet connectivity (18.7% [95% CI 10.5-26.8%]).

103 interviews were conducted. Common themes included the ease of sharing knowledge and clinical information via social media. Many respondents reported using WhatsApp to expedite patient care when consultants were not readily available, and to answer clinical questions in real time. Respondents also described using social media to expand learning in unusual cases. Advanced residents and consultants were more likely to describe importance of FOAMed resources as adjuncts to basic learning tool such as textbooks.

CONCLUSIONS

Most EM trainees and faculty in India are aware that Free Open Access Medical Education resources exist, though familiarity with the term was variable. Trainees expressed a need for resources specifically focused on India or Low and Middle Income Countries (LMICs).

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Cross-Sectional Comparison of Behavioral Risk Factors for HIV/HCV in People Who Inject Drugs in Egypt

BACKGROUND

Egypt has the greatest HCV prevalence worldwide at 15% and a concentrated HIV epidemic in male people who inject drugs (PWID) at 6.8%, who are at a high risk for HCV infection as well. Injection drug use is criminalized in Egypt, and there is limited availability of harm reduction programs. Drug-use and sexual risk behaviors between PWID and the general population have not been studied there.

METHODS

To address this gap, a cross-sectional HIV/HCV epidemiological study of 632 consenting injection drug users in Cairo and Alexandria was conducted. Bivariate logistic regression analysis was done to evaluate the associations between HIV/HCV and needle sharing or sexual practices using SAS 9.4.

RESULTS

10.6% (63/604) of the study population tested positive for HIV and 61.5% (384/624) tested positive for HCV. Sharing needles with more than 10 people was associated with HIV and HCV infection (OR=3.65, p-val=0.001; OR=2.05, p-val=0.02, respectively). Age was associated with both HIV and HCV (p-val=0.03 and <0.001, respectively). Duration of injection drug use, measured in years, was associated with HCV (p-val=0.001). 80% of the HIV cases in Eastern Europe and Central Asia. In response to the epidemic, even more punitive laws and regulations were introduced in Russia, and their HIV prevalence has seen a 49% increase between 2005 and 2015. A similar trajectory can be expected for Egypt if preventative measures are not taken. Common-sense harm reduction programs like clean needle exchanges and decriminalization of injection drug use should be part of a comprehensive plan to control the spread of HIV and HCV in Egypt.

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Dengue Infection in Costa Rica from 2012-2016

Dengue virus is a mosquito-borne viral illness that is endemic to more than 100 countries across the globe. While the virus causes flu-like symptoms in its mildest form, more severe cases may progress to shock and, ultimately, death. Costa Rica is one country that experiences significant morbidity and mortality from Dengue, having the 2nd and 11th highest caseload in Central America and worldwide, respectively. Given the significant burden that dengue places on a country's health and economic prosperity, it is important to track the disease carefully. This project aimed to document trends in the number of cases of dengue from 2012-2017. Data from the Ministerio de Salud in Costa Rica was used to analyze the rates of dengue infection across the country and in each of Costa Rica's seven provinces. Country-wide caseload was found to have increased since 2014, though the individual provinces showed varying trends. Dengue control is an ongoing challenge that Costa Rica must continue to address.

El dengue es una enfermedad viral transmitida por un mosquito, la cual es endémica en más de 100 países en el mundo. El virus causa síntomas similares a los de la gripe común en su forma más leve, sin embargo los casos graves pueden progresar a shock y a un desenlace fatal. Costa Rica es un país que tiene una significativa morbilidad y mortalidad por el dengue; tiene el 2 y el 11 mayoría de casos en America Central y en el mundo, respectivamente. Dada la carga importante que el dengue impone a la salud y a la prosperidad económica de un país, es importante dar un seguimiento cuidadoso a esta patología. Este proyecto tuvo como objetivo documentar las tendencias en el número de casos del dengue entre 2014-2017. Los datos del Ministro de Salud en Costa Rica se utilizaron para analizar las tasas de infección por el dengue en todo el país y en cada una de las siete provincias de Costa Rica. Los casos en todo el país parecían en aumento desde 2014, aunque las provincias mostraron tendencias diferentes. El control del dengue es un desafío continuo que Costa Rica deberá seguir abordando.

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Hookworm Vaccine Phase I Clinical Trial, Americaninhas, Brazil: The Faces Behind the Data

Hookworm is a parasitic worm that is in the category of neglected tropical diseases (NTDs) by the WHO. The parasite thrives in impoverished areas of the world which lack proper sanitation. While hookworm's mortality figures do not compare to other diseases such as malaria, hookworm is a chronic infection that affects up to 740 million people in developing nations of the tropics, including tropical regions of the Americas such as Americaninhas, Brazil. As hookworm attaches to the mucosa of the small intestine, it causes blood loss and can cause iron deficiency anemia in hosts burdened by the infection. Children and pregnant women are particularly vulnerable to the effects of hookworm infection. The Sabin Vaccine Institute in Washington, DC created a vaccine against the hookworm parasite in an attempt to combat these detrimental effects: the Na-GST-1/Alhydrogel® and Na-APR-1 (M74)/Alhydrogel® vaccines. The vaccine is now in a Phase I clinical trial in Americaninhas, Brazil through a collaboration between the Sabin Vaccine Institute and the Centro de Pesquisas René Rachou (CPqRR) of Brazil.

My summer project began with a thorough investigation of the various components of the hookworm vaccine clinical trial in Americaninhas, Brazil. The Phase I clinical trial in Americaninhas, Brazil is focused on the collection of and on the interpretation of data on the efficacy and safety of the hookworm vaccine in a small group of human participants. I worked in collaboration with Dr. David Diemert, the Principal Investigator of the vaccine clinical trial to assist in the collection of this patient data. More specifically, I shadowed the two physicians who did the physical exams of trial participants looking for adverse effects of the vaccine.

I was also able to shadow several different physicians in various healthcare settings throughout rural Minas Gerais, Brazil. By working with various physicians in different settings and by getting to know the patients through their stories, I was able to truly see the social determinants of health that affect patients in rural Brazil such as the lack of access to clean water, lack of economic stability, and lack of education. I was also afforded an introduction to tropical medicine, seeing many diseases that are uncommon in the US such as schistosomiasis, scorpion bites, giardiasis, and amoebiasis.

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An Assessment of Cultural Perceptions and Recognition of Ebola Virus Disease, and its Correlation with Traditional Burial Practice in Rural Guinea

BACKGROUND

In the midst of the unprecedented Ebola outbreak in West Africa during 2014-2016, the humanitarian response to control the disease was hampered in part because there was a limited understanding of local traditional rituals or indigenous medicine (ethnomedicine) on the part of the responders. The Ebola outbreak claimed 11,310 lives, more than all other outbreaks combined. West African burial funeral ceremonies and surrounding rituals may have hindered interventions that included the forceful removal of the sick or dead from the community.

OBJECTIVE

Our objective was to understand transmission associated with traditional burial practices in rural Guinea. Through the lens of cultural and medical anthropology, this study aims to examine how knowledge of transmission might influence views on traditional burial practices, and how ethnomedical beliefs might block (or mediate) the effect of this knowledge.

METHOD

A survey of 385 household members was administered in 2015 throughout Guinea to capture knowledge and behaviors related to Ebola. Discrete and marginal change in probability models were used to examine disease transmission knowledge on the outcome of whether respondents practice traditional burial rituals. The independent variables were knowledge about person-to-person (PTP) transmission and personal protective equipment (PPE), and the dependent binary variable was the use of traditional burial practice. Within the context of burial behavior, this study controlled for three confounders: 1. demographics (age, sex, years lived in community, ethnicity, occupation, education), 2. knowledge of Ebola etiology & symptoms, and 3. access to medical care. STATA14/MP was used.

RESULTS

Once controlling for three potential confounders (demographics, knowledge of Ebola etiology & symptoms, and access to medical care), there was no significant association between the outcome, practicing traditional burial ritual, and knowledge about PTP (person-to-person infection: 12.2 percentage points, p 0.1).

CONCLUSION

The result implies that knowledge about PTP & PPE will not necessarily lead respondents to stop traditional burial rituals. To prevent another Ebola outbreak in the future, it is essential to design a social and behavioral intervention that is specially tailored to the culture of the traditional burial ritual.

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Outreach Services to Treat Women Living with Obstetric Fistula: A Systematic Review

BACKGROUND

Obstetric fistula is a condition experienced by women who, because of prolonged labor, become incontinent, forming one or more holes in between the rectum and the vagina or the vagina and the bladder (Heller, A., 2017). The hole causes uncontrollable stool and urine to leak from the woman. For most women with obstetric fistula, the duration of the labor leading to fistula varied between 5 hours and 9 days, averaging 3.0 days long (Heller, A., 2017). Women who suffer from this condition do not have access to quality medical care.

OBJECTIVE

This review will be to a) analyze effective outreach services to treat women with obstetric fistula; and b) identify gaps, challenges and impact of outreach activities. This critical analysis is to explore approaches to increase demand of obstetric fistula and the process for matching those who need obstetric fistula surgery with a health facility and surgeon who is equipped to repair the condition.

METHODS

A literature review was conducted using the following databases; PubMed, Medline, Scopus, AJPH and other relevant sources without a specific date range to include any research ever published. Only original empirical research published in English was included.

RESULTS AND DISCUSSION

Sixteen articles matched the research topic of outreach to obstetric fistula patients. The outreach design needs to be driven by the country context to be effective. One article discussed a hospital-based outreach program design, another article discussed screening women for obstetric fistula who participated in a large clinical trial. Two articles discussed using task shifting to screen women in their communities before transporting them to a health facility. Other articles examined medical records to pinpoint endemic areas to concentrate on specific regions while other articles discussed community mobilization as the key intervention to outreach to obstetric fistula patients.

CONCLUSION

Effective outreach programs consist of efficient coordination and collaboration with national, subnational and civic society entities. The outreach intervention focuses on increasing awareness about obstetric fistula and the available treatment. Efficient outreach programmes can reduce the length of time before women are repaired because of effective coordination. Strengthening the health system is essential to have effective sensitization and community mobilization programs. The results of each of these studies reveals that locating women with obstetric fistula is challenging but through strategic intervention the number of women who have been repaired is steadily increasing.

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Etiology and Management of Hospitalized and Outpatient Diarrhea among Children Less Than 5 Years of Age in Lambaréné, Gabon

OBJECTIVES

Diarrhea remains a significant cause of global under-5 mortality, particularly in Sub-Saharan Africa (SSA). To reduce morbidity and mortality, the World Health Organization (WHO) recommends oral rehydration salts (ORS), zinc supplementation, and continued feeding or breastfeeding for all children with diarrhea to prevent dehydration and malnutrition; antibiotics only for bloody diarrhea (i.e. probable shigellosis), suspected cholera, or severe non-intestinal infections (e.g. pneumonia or sepsis); and avoidance of antidiarrheals and antiemetics owing to lack of benefit and potential for harm in young children. Gabon is an upper-middle income country in SSA for which there is a lack of recent, high quality data on the etiology and management of childhood diarrhea. This prospective study aimed to describe the etiology and management of hospitalized and outpatient cases of diarrhea in Gabonese children under five years of age.

METHODS

Children ≤ 59 months presenting to the Albert Schweitzer or George Rawiri Regional hospitals (February-July 2017) in Lambaréné, Gabon were included if they had ≥ 3 liquid stools per day within the past 3 days. Data was obtained via medical records and standardized questionnaires with caregivers. Diarrheagenic *Escherichia coli*, *Salmonella enterica*, and *Shigella spp.* were detected using conventional culture techniques. Rotavirus, adenovirus, and *Cryptosporidium spp.* antigens were detected with commercial rapid immunoassays. Multiplex PCR was used for *Cryptosporidium spp.*, *Giardia intestinalis*, and *Cyclospora cayetanensis* detection.

RESULTS

Forty-five children were included, 34 of whom were hospitalized. Mean age was 12.2 months; 58% were female. 49% were infected with one or more sought-for pathogens, most commonly with *Giardia intestinalis* (28.9%) or *Cryptosporidium spp.* (24.4%). 33% and 36% of hospitalized and outpatient children, respectively, received ORS. Zinc was given to one (3%) hospitalized patient and zero outpatients. Antidiarrheals were frequently given to hospitalized (48%) and outpatient (73%) children. Antibiotics were prescribed in 85% and 36% of hospitalized and outpatient cases, respectively, while only 8 children (18%) presented with bloody stools. 79% of children presented with severe acute malnutrition; 21% had never been breastfed.

CONCLUSIONS

Ongoing education of healthcare workers and communities regarding WHO-recommended management of childhood diarrhea is needed. The overuse of antibiotics observed in this study is consistent with previous reports and is concerning given high levels of antimicrobial resistance in SSA. Strategies to increase provider awareness of indicated uses of antimicrobials in the setting of childhood diarrhea may help limit the spread of resistance.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

How Collective Norms and Media Use Affect Attitudes About Violence Against Women and Contraception Use in Sub-Saharan Africa

BACKGROUND

Contraceptive use and attitudes about violence against women, though enacted at the individual level, are also driven by factors at the interpersonal and social levels. The role of mass media in promoting social norms surrounding these attitudes and behaviors has not received much scholarly attention but can be helpful to illuminate areas for intervention.

HYPOTHESIS

We proposed and tested the hypothesis that collective norms (defined as a groups aggregate behavior or attitudes) would be associated with individual level attitudes (tolerance towards violence against women) and behaviors (contraception use). This relationship was further hypothesized to vary by media use, such that the relationship between collective norms and individual attitudes and behaviors would be strong when media use was low, and vice versa.

METHOD/DESIGN

Data come from the 2016 Ethiopian and Tanzanian Demographic and Health Surveys (N = 6,907 and N = 4,084 in the two countries, respectively). Multi-level regressions were run within nested models to predict individual level contraception use and tolerance for violence from collective norms for contraception use and tolerance for violence, media use, and their interaction, controlling for age, wealth, education and urban versus rural. Marginal probabilities were estimated to examine the interaction effects more closely and hierarchical multi level models were run to examine the between community variation.

RESULTS

Hypotheses, tested in the context of modern contraceptive use and tolerance for violence against women, were supported in three out of the four interactions, (OR = .99, $p < .001$) (OR = .99, $p < .001$) ($\beta = -.05$, $p = .05$).

CONCLUSION

These results support the idea that mass media can serve as external agents of change to attenuate the impact of unhealthy collective norms on individual attitudes and behaviors. Implications for public health campaigns are discussed.

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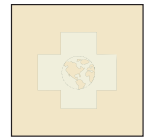
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Pre-Hospital Emergency Medical Systems: A Comparison between the Franco-German and the Anglo-Saxon Models

MOTIVATION

In collaboration with L'Hopital Tenon in Paris, France, I spent my summer riding ambulances alongside the physicians of the SAMU. My goal was to compare the Franco-German system of emergency medicine to that of the United States, in hopes of uncovering which part of each system is running more efficiently and why. In France, emergency medical services (EMS) are often led and coordinated by physicians, who are able to perform the appropriate medical interventions that other pre-hospital providers (EMTs and paramedics) are not licensed to perform. This is in contrast to the EMS system in the United States, where physicians do not lead the teams. Some research claims that the Franco-German method is superior because although it costs more money in the pre-hospital setting, it is leading to better outcomes. These researchers often criticize the American medical system for cutting costs at the expense of quality. On the contrary, studies point out the concern for the prolonged wait time on scene of the emergency in France, suggesting that this is the reason for reduced survival outcomes of certain parameters such as trauma and stroke.

METHODS

I spent a lot of time talking with the doctors and students and interviewing them about their take on their emergency medical system. I had the rare opportunity to watch the doctors work on the scenes of emergencies, and then ride alongside them to the hospital where I could watch the care be continued. My observations of the two systems were analyzed in light of the literature comparing outcomes and efficiencies between the two systems.

RESULTS

Only 65% of calls to the emergency center in France are actually dispatched due to triage by the physician who is receiving the call, in comparison to nearly 100% of the calls dispatched in the United States.

CONCLUSIONS

While a physician-led ambulance service results in more efficient triage in the field, such a system is unlikely to be adopted in the United States due to the cost burden of hiring physicians to staff ambulances and call centers. In order to reduce the emergency room burden in the United States, we should look at ways to improve pre-hospital triage by empowering paramedics and citizen call takers to make medically sound and more efficient decisions prior to and during dispatch.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Piloting an Enhanced VHT Research Trial in Rural Uganda

Omni Med is a non-governmental organization that has provided innovative and sustainable programs in the local communities of several countries including Belize, Kenya, Guyana, and Uganda. One of Omni Med Uganda's most impactful programs is the Village Health Team (VHT) training program, empowering these VHTs to operate as a cohort of health providers who in turn assist the local community to take charge of their own health in a sustainable manner. Currently, Omni Med hosts week-long training seminars for VHTs that cover a curriculum developed through partnership with the Uganda Ministry of Health and represents many areas of interest within global health. In addition to the VHT training program, Omni Med helps build clean water sources in rural villages and, in conjunction with another organization, properly ventilated cookstoves made from local resources.

The Enhanced VHT pilot will be the first formal research study on the incidence and prevalence of certain key preventable illnesses pre- and post-intervention within a village in the Mukono district of Uganda. For this pilot study, a data collection tool was created utilizing feedback from experienced VHTs and local community leaders. As a result, the data collection tool targeted several key areas of quantitative and qualitative measurements including the following: basic household demographic information, access to medical care and treatment, proper hygiene practices, safe water practices, cookstove usage, mosquito net usage, and rates of diarrheal illnesses, pneumonia, and malaria. Specifically, this investigation focused on the impact of VHT community involvement on three key outcome measures: 1) clean water sources and safe water usage on reducing the rates of diarrheal illnesses, 2) cookstove construction and usage on reducing the rates of pneumonia, and 3) mosquito net distribution and usage on reducing the rates of malaria. The pilot project has recently received approval from the International Review Board and preliminary results are being collected. Already, several VHTs have been trained in the village and are actively participating in both data collection and community education.

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Determining the Level of Awareness of Diabetic Retinopathy among the Adult Population in Chennai, India

Preventable blindness is a global health issue. The major causes of blindness are cataract, glaucoma, corneal scarring including trachoma, age-related macular degeneration, and diabetic retinopathy. Diabetic retinopathy is the leading global cause of visual impairment and blindness. Longer diabetes duration and poorer glycemic and blood pressure control are strongly associated with diabetic retinopathy. India is called the “diabetes capital of the world.” According to the International Diabetes Federation, there are about 41 million people with diabetes and this number is expected to rise to about 70 million by 2025 unless preventive steps are taken. Studies have shown that for every 5-year increase in duration of diabetes, the risk for diabetic retinopathy increases by approximately 1.89-fold. In addition a 2% increase in HbA1c results in about 1.7-fold increase in risk for diabetic retinopathy.

The purpose of this descriptive/exploratory study is to determine the level of awareness of diabetic retinopathy among a population of over 18 year olds who visit the Pranav Eye Clinic (and its outreach clinics) in Chennai, Tamil Nadu (India). Pranav Eye Clinic has partnered with Unite for Sight, a United States-based global health non-profit organization, to reduce the prevalence of preventable blindness in India. The determination of awareness will be done through administering an anonymous survey to a sample (convenience sample). The aim of the study is not only to determine the general level of awareness but also based on gender, education level, and other demographics. Another aim is to determine level of awareness for people based on clinical factors such as hypertension, diabetes, and eye history. Data is gathered using an Excel spreadsheet during the study; univariate and bivariate analyses is conducted using SPSS.

Based on the results of the surveys, it is seen that there is a positive association between diabetes and hypertension and more women had these chronic conditions than men. Approximately 92% of participants did not know what diabetic retinopathy was, and out of the percentage of people who did not know about diabetic retinopathy, over 50% had diabetes. These results are important because targeted interventions must be implemented in rural areas within India to educate the population about diabetic retinopathy and provide screening opportunities.

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Social and Clinical Determinants of Frequent Utilization of Emergency Department

OBJECTIVE

Frequent utilizers of EDs (FUEDs) utilize Emergency Department (ED) services at least four times/year, comprise less than 10% of ED patients but account for a quarter of ED visits. FUEDs comprise a high-cost-high-need vulnerable group of patients with multiple chronic diseases and poor health outcomes. Through application of the WHO CSDH Framework, this research sought to characterize the care utilization of FUEDs and elicit the influence of specific social and clinical determinants upon total and preventable ED utilization.

Study Design: Analysis of claims data merged with interview data from the George Washington University Hospital (GWUH) Frequent User Study was used in a retrospective cohort study design. We applied negative binomial regression to estimate patient level effects upon (i) total ED visits (ii) preventable ED visits. Independent variables included indicators of social and clinical determinants.

POPULATION STUDIED

474 DC Medicaid beneficiaries, 18-64 years, who attended GWUH between October 2015–2016 and attended any ED 3 or more times in the past 1 year.

PRINCIPAL FINDINGS

In one year, FUEDs had an average of 16.2 total ED visits and 30% of ED visits were preventable. People with mental illness had more ambulatory care visits (mean 11, SD 9.3) compared to FUEDs without. 60% of FUEDs had a diagnosed mental illness but there was significant underutilization of psychiatric evaluation and management (mean 1.2, SD 4.4). Multivariate analyses revealed that increased physical illness severity, poor behavioral health status, inadequate food and shelter were associated with increased number of total and preventable ED visits. Increased levels of social support were associated with a decrease in total (IRR 0.94) and preventable (IRR 0.86) ED utilization. Physical illness severity and CC had a significant positive interaction effect upon ED utilization. FUEDs whose CC could not be assessed due to inadequate ambulatory care (<3 visits/year) had the greatest ED utilization.

CONCLUSION

Addressing inadequate access to food and shelter and providing social support could reduce the number of preventable ED visits and further leverage the benefits due to care continuity in FUEDs with multiple physical and behavioral health conditions.

POLICY IMPLICATIONS

This research is directly applicable to DC Medicaid Care Coordination initiatives whereby patients with multiple chronic illnesses can receive a care coordination benefit. Curbing ED use by FUEDs will require a two-pronged approach: adequate and coordinated ambulatory care for those most at risk as well as attention to specific social determinants they experience.

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Hospital Readmissions among Patients with Skin Disease: A Retrospective Cohort Study, 2014

BACKGROUND

Hospital readmissions represent a costly and potentially preventable form of hospitalization; however, readmissions following dermatology hospitalizations remain poorly characterized.

OBJECTIVE

To assess the frequency and demographics of readmissions for skin disease.

METHODS

We performed a retrospective cohort study of dermatology hospitalizations using the 2014 Nationwide Readmissions Database.

RESULTS

Readmissions following dermatologic hospitalizations cost the United States healthcare system approximately \$1.05 billion in 2014. The 30-day all-cause readmission rate was 12.63% for the 647,251 identified hospitalizations for skin disease. Readmission was most common following hospitalizations for cutaneous lymphomas (39.62%), connective tissue disorders (26.28%), and cutaneous congenital abnormalities (23.86%). Predictors of readmission included public insurance (Medicaid odds ratio (OR) 1.61, 95% confidence interval (CI) 1.53-1.70, Medicare OR 1.55, 95% CI 1.48-1.62), residence in low income communities (OR 1.14, 95% CI 1.09-1.20), an increasing number of chronic conditions (OR 4.46, 95% CI 4.20-4.80), and large hospitals (OR 1.10, 95% CI 1.05-1.16). Non-teaching hospitals (urban OR 0.90, 95% CI 0.87-0.94, rural OR 0.78, 95% CI 0.73-0.82) were protective for readmissions from skin disease.

LIMITATIONS

We were unable to assess if inpatient dermatology consultation, or linkage to an outpatient dermatologist, influenced the likelihood of readmission.

CONCLUSIONS

There are significant healthcare and demographic disparities in readmissions for skin disease.

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Analysis of Policy Barriers to Emergency Medical Service Involvement in Hospice Care

PURPOSE

The life expectancy in the United States is longer than ever before. However, as the Baby Boom generation ages and people die increasingly slow deaths from chronic conditions, there will be a growing need for partnerships and programs to ensure end of life patients get the care they need in the setting that they want. One partnership in particular that has a growing following is that between hospice agencies and the Emergency Medical Services. This paper will examine potential policies at the Federal, State, and systemic levels that hinder or prevent EMS agencies from participating in hospice services.

METHODS

A review of literature was conducted. Academic literature from after 1974—the date of the first American hospice agency—and grey literature from after 2007 were considered. SCOPUS, CINAHL, and the Himmelfarb Library database were queried with various combinations of MeSH terms. Those results were then screened by date and content for relevance. A variety of government agencies and relevant NGOs were also searched for applicable content.

RESULTS

Significant barriers to EMS involvement in hospice services exist at the Federal and State levels. At the Federal level, there is a major problem with reimbursement for both EMS and Hospice services with regards to this type of care. The Drug Enforcement Administration also has policy barriers written into the Controlled Substances Act, but there is legislation waiting for the President's signature that may reverse these barriers. Additional barriers exist on a state by state basis, but these were more difficult to determine, and searching for each independently proved challenging.

CONCLUSION

Significant barriers to EMS involvement in Hospice care exist at Federal and State levels. Because some states allow for EMS agencies to provide home health services without transport, and because the major barriers to the federal controlled substance issue is expected to resolve soon, there is an opportunity for further research into EMS / hospice collaboration efficacy given the correct policy conditions. There is also an opportunity to explore novel reimbursement structures and criteria to support these programs and benefit the patient population they serve.

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How the European Union Is Embracing Cross-Border Telemedicine and What the U.S. State Medical Boards Can Learn From It

Despite the fact that there have been many advances in the field of telemedicine, the United States (U.S.) state and federal laws have not kept pace with these technological advancements and may operate as a barrier to growth in the field of telemedicine. On the other hand, the European Union (EU) has developed a robust legal framework for the practice of telemedicine. The aim of this research project is to evaluate what elements of the EU legal experience could be used to support efforts to better align telemedicine law with the practice of telemedicine in the U.S.

Based on the 2015 EU Guidelines, by 2020, a French physician may be able to see a German patient online and have instant access to the patient's medical record, automatically translated into the French language. The EU has prioritized the creation of a legal framework that fully supports cross-border telemedicine. As early as 2000, the EU broadened medical licensure requirements for telemedicine so that physicians licensed in one nation could provide telemedicine services to patients who reside in other EU nations without needing to obtain medical licenses from these nations. Furthermore, linguistic experts from several nations of the EU have been working together to develop ways of automatically translating and instantly delivering patient records to physicians as appropriate.

The state medical boards of the U.S, however, have struggled with efforts designed to achieve similar legislative changes. In most states, physicians are required to be licensed in both the state where they practice and the state where the patient resides. For example, a Texas physician is required to obtain a Georgia medical license in advance of providing telemedicine care to a patient in Georgia to ensure that their services are legal and reimbursable by insurance. While some states now provide a telemedicine license or expedite multistate licensing, these measures are insufficient to support the widespread practice of interstate telemedicine. With current regulations, obtaining medical licenses in all 50 states for telemedicine practice is impractical and prohibitively expensive for healthcare providers and organizations.

U.S. medical licensure requirements for telemedicine practice are comparable to EU regulations before 2000. Furthermore, U.S. telemedicine reimbursement regulations arbitrarily differ across state borders, and electronic medical record systems from various companies do not communicate properly with each other. At this time, physicians in the U.S. cannot retrieve patient records for unscheduled patient encounters in real-time unless the patient was previously treated using the same medical health records system, causing inconvenience to patients, treatment delays and duplicative medical testing.

Similar to the European approach, we recommend that the state medical boards allow physicians licensed in one state to provide telemedicine services to patients in other states. Furthermore, we recommend collaboration among the state medical boards, industry leaders, and state legislatures to come up with uniform telemedicine reimbursement regulations and to design a uniform electronic medical record inter-operability standard to allow the U.S. telemedicine industry to keep abreast of the global developments in telemedicine.

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The Changing Composition and Capacity of Medicare Providers

OBJECTIVE

Over the past decade, U.S. medical school enrollment has increased nearly 30 percent, and the growth in mid-level new graduates was even faster. Many of these new graduates are currently serving the large and growing Medicare population. Yet, little evidence so far has documented providers who are serving Medicare population. In the anticipation of physician supply shortages, it is important to understand who are taking care of Medicare population recently and whether there are changes in the overall capacity and patient risk profiles of Medicare providers.

METHODS

Data were from 2012-2015 Medicare Physician and Other Supplier Aggregate Tables at the Centers for Medicare & Medicaid Services website, which contain information on utilization, payment, and procedures provided to more than 10 Medicare Part B beneficiaries by U.S. physicians and nurses. We identified primary care physicians (i.e., family practice, internal medicine, general practitioners, and geriatric medicine), specialists, and mid-level providers (e.g., nurse practitioners, physician assistants, etc.) based on self-reported provider type in the data. We conducted trend analysis to examine the changes in the proportion of physicians and mid-level providers over time, and also compared utilization, payment amount, and patient risk profiles of physicians and nurses between 2012 and 2015, respectively.

FINDINGS

Over the study period, the number of providers with more than 10 Medicare patients increased from 709,982 in 2012 to 782,836 in 2015. The proportion of both primary care physicians and specialists declined consistently, while in contrast, the proportion of mid-level providers increased correspondingly, from 20% in 2012 to 24% in 2015. Compared to 2012, Physicians in 2015 served fewer Medicare patients, but provided more services to beneficiaries, and had no changes in payment received than in 2015. In contrast, mid-level providers served more patients, provided more services per patient, and received higher payments in 2015 than in 2012. Both physicians and mid-level providers served more patients diagnosed with depression, asthma, chronic kidney disease, and stroke in 2015 than in 2012.

CONCLUSION

Medicare provider composition has been changing in recent years, where mid-level providers are playing an increasing role in serving Medicare beneficiaries. State legislatures and policymakers may consider expanding scope-of-practice for mid-level providers and also weigh the importance of innovating new payment policy to better reimburse mid-level providers. Future research is needed to compare the capacity of new and existing providers and the relationship between year of practicing and capacity building to serve more Medicare patients.

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Narrative Perspectives on Clinician Advocacy

Many medical institutions and professional organizations include advocacy as part of their mission statement. The AMA states that, “physicians should advocate for the social, economic, educational and political changes that ameliorate suffering and contribute to human well-being.” However, the overall concept of advocacy remains broad and poorly defined. How should advocacy be taught in a medical institution, and how should these values be implemented? While physicians are obligated to advocate on behalf of an individual patient, public advocacy requires a broader examination of health at the community and population levels. As with any profession, medicine attracts a wide range of people with various interests and personality types. The same model of advocacy is not suitable for everyone. This study features a series of interviews with physicians of different specialties and backgrounds who incorporate advocacy into their practice. The goal of these interviews was to understand the formative experiences that led physicians towards specific policy interests. Each physician developed a way to advocate for issues consistent with their worldview, culture, values and professional expertise.

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Coverage for Obesity Prevention & Treatment Services: Analysis of Medicaid & State Employee Health Insurance Programs

BACKGROUND

Despite the high prevalence of obesity among U.S. adults, coverage for evidence-based obesity treatment modalities is inconsistent across states. The primary objective of this study was to examine changes in coverage for adult obesity prevention and treatment services within Medicaid programs and state employee health plans between 2009 and 2017.

METHODS

Changes in coverage were assessed by comparing data from plan year (PY) 2016/2017 to baseline data collected during PY 2009/2010. Data were obtained through an extensive review of administrative documents, health plan websites, provider manuals, subscriber handbooks, fee schedules, and drug formularies from Medicaid and state employee health insurance programs in all fifty states and the District of Columbia. Source materials were reviewed for indications of coverage and payment policies specific to evidence-based treatment modalities for adults (≥ 21 years of age) with obesity, including behavioral/nutritional counseling, pharmacotherapy, and bariatric surgery.

RESULTS

Like 2009, state programs were most likely to cover bariatric surgery and least likely to cover pharmacotherapy for members with obesity. Evidence of coverage for adult obesity treatment modalities increased in both Medicaid and state employee programs between 2009 and 2017, with more changes observed among state employee programs. The proportion of state employee programs indicating coverage increased by 37% for behavioral/nutritional counseling, 20% for pharmacotherapy, and 16% for bariatric surgery. The proportion of Medicaid programs indicating coverage increased by 18% for behavioral/nutritional counseling, 4% for pharmacotherapy, and 8% for bariatric surgery.

CONCLUSIONS

Our findings suggest that some states have bolstered coverage for evidence-based obesity treatment modalities in recent years. However, many states continued to deny reimbursement for non-surgical obesity treatment options that are supported by clinical consensus recommendations. Unclear guidance on what constitutes appropriate and reimbursable care for obesity-related services within Medicaid and state employee health programs likely prevents providers from referring highly-motivated beneficiaries with obesity to effective care. Where reimbursement for evidence-based obesity treatments has expanded, educating providers and beneficiaries on the availability and proper utilization of these services may improve obesity-related health outcomes.

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The Impact of Changing Scope of Practice Laws on Nurse Practitioner Billing Patterns

Over the last decades, scope-of-practice laws for nurse practitioners (NPs) have changed rapidly, allowing for increased practice and prescribing autonomy. Despite this trend toward enhanced autonomy, scope-of-practice laws vary widely by state. At the federal level, Medicare implemented legislation in 1998 that began reimbursing NPs at a rate of 85% of a physician's fee regardless of site of practice or geographic location, a change from previous versions that restricted NP reimbursement to rural areas and sites specific to long-term or follow-up care. Since then, the number of NPs who have been billing on their own, has been increasing over time. The current study examined whether a change in scope-of-practice law toward more autonomous practice changed the rate at which NPs billed independently for their services.

This project used a 5% sample of Medicare claims data from 1999 to 2014 to track the number of NPs who were billing Medicare for their services. Unique National Provider Identifier numbers were totaled and plotted over time by state to evaluate the change in trends. State changes to NP laws were catalogued through use of West Law, a legal research service that archives state legislative and regulatory changes. After identifying all relevant changes to scope-of-practice laws for NPs by state, NP billing trends were evaluated at times before and after these had gone into effect.

Changes in scope-of-practice laws for NPs did not change the trends in the number or rate of these providers billing for their services. In a given state, a change toward more autonomy in practice did not affect the rate of the increase. The same trend was also seen in states that had the most dramatic changes in their laws. In 2005 in Wyoming and 2010 in Maryland, each state passed legislation removing the requirement for NPs to have a collaborative agreement with a physician, effectively allowing for independent practice. Yet, the figures show the trends in NPs billing independently was consistent with rates seen before these legislative changes.

Understanding the effect of changing scope-of-practice laws on NP practice patterns will be essential to informing current and future regulation of these providers. While this trend has been increasing steadily over time, the rate at which NPs billed Medicare independently did not dramatically change with increased practice and prescribing autonomy in state legislation, which may be a key piece to alleviating some of the strain on the primary care workforce.

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Feasibility and Usability of Tele-Interview for Medical Residency Interview

Every year in the United States, medical students and residency programs dedicate millions of dollars to the residency matching process. On-site interviews for training positions involve tremendous financial investment, and time spent detracts from educational pursuits and clinical responsibilities. Students are usually required to fund their own travel and accommodations, adding additional financial burdens to an already costly medical education. Similarly, residency programs allocate considerable funds to interview-day meals, tours, staffing, and social events. With the rapid onslaught of innovations and advancements in the field of telecommunication, technology has become ubiquitous in the practice of medicine. Internet applications have aided our ability to deliver appropriate, evidence-based care at speeds previously unimagined. Wearable medical tech allows physicians to monitor patients from afar, and telemedicine has emerged as an economical means by which to provide care to all corners of the world. It is against this backdrop that we consider the integration of technology into the residency application process. This article aims to assess the implementation of technology in the form of web-based interviewing as a viable means by which to reduce the costs and productivity losses associated with traditional in-person interview days.

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Barriers to Implementing Advance Care Planning in the Healthcare Setting

OBJECTIVES

Current barriers to implementing Advanced Care Planning (ACP) will be examined as applied to the healthcare system.

METHODS

A literature review was performed looking at the current practices of ACP (e.g. filling out advanced directives (AD), Medical Orders for Life Sustaining Treatment (MOLST)/Physician Orders for Life Sustaining Treatment (POLST), etc.), physician comfort level with having end-of-life discussion (EOL), successful/unsuccessful interventions to increase ACP/EOL discussions among health care providers (HCP), and the current political environment with respect to physicians' ability to implement ACP/EOL discussions. Cochrane, Pubmed, and Google Scholar were searched for papers written in English after 2000 in the United States. In order to be eligible, the studies were required to discuss educational interventions, patient/physician barriers, and/or political barriers surrounding ACP/EOL discussions.

RESULTS

Seventeen articles were identified to meet the inclusion criteria and are included in this review. Barriers identified by both the physician and the patient were: lack of time, lack of awareness, lack of comfort, and lack of a systematic approach. Educational interventions for health care providers somewhat improved comfort levels. The introduction of the Medicare Reimbursement had a substantial impact on increasing the amount of ACP/EOL conversations reported.

CONCLUSIONS

Although there is some evidence that educational interventions aimed at health care providers improves the providers' knowledge, self-efficacy, and communication with regards to ACP, health-system and political barriers remain to impact ACP implementation. Medicare reimbursement not only allows physicians to be paid for their time facilitating these discussions, but legitimizes its need. It is recommended that a systematic approach to ACP, throughout the course of the patient's life, will improve implementation rates and physician/patient comfort levels with ACP/EOL discussions.

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An Analysis of the Impact of Medicaid Expansion on Changes in Opioid Prescriptions for Adult Enrollees

BACKGROUND

Between 2012 and 2016, the opioid overdose mortality rate in the U.S. almost doubled from 7.4 to 13.3 per 100,000 population, leading to calls for a national opioid crisis. This crisis has generated interest in Medicaid's dual role as a health insurance system that provides reimbursement for both prescription opioid *analgesics* like Oxycodone used to treat chronic pain, which could inadvertently fuel addiction, and prescription opioids used as *treatment medication* to help people survive and recover from drug abuse, such as Naloxone.

METHODS

In this study, we conduct a multi-variate analysis of Medicaid prescription drug utilization data for the years 2012 through 2016 to examine overall and per-enrollee changes in the number of prescriptions for opioid analgesics and opioid treatment medications and examine the impact expansion, opioid mortality, unemployment, and the availability of drug abuse treatment facilities that accept Medicaid have on the number of prescriptions.

RESULTS

Overall, we find that Medicaid expansion did not have a significant impact on the use of opioid analgesics or treatment medications per adult Medicaid enrollee. Based on our analyses, these changes in the use of opioid analgesics and treatment medications are driven largely by changes in opioid mortality rates, and somewhat by changes in unemployment rates. However, by significantly increasing Medicaid enrollment levels, the expansion did increase the total volume of both opioid analgesics and opioid treatment medications being covered by Medicaid.

Upon conducting a simple analysis to evaluate gross changes in opioid prescriptions between states that expanded and did not expand Medicaid, we find that the average opioid analgesic prescriptions per adult enrollee have gone down by almost a fourth in both expansion (24.1% decrease) and non-expansion states (28.4% decrease) from 2012 to 2016, signaling a nation-wide effort to curb the opioid crisis. We also find that the average opioid treatment medication prescriptions per adult enrollee have increased sharply in expansion states (55.9% increase) as compared to non-expansion states (9.9% increase).

CONCLUSIONS

Our findings suggest that, contrary to arguments that suggest that expanding Medicaid worsened the opioid crisis, the expansion has had no significant impact on prescription opioid use. In fact, the expansion has greatly increased the scope of treatment for drug abuse by providing states that were already hard-hit by the crisis with the funding they needed to expand treatment to cover a greater number of low-income and at-risk adults.

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Federal Strategies for Combating the Opioid Epidemic

Over the past two decades, opioid misuse and abuse has become a national public health crisis. Today it is one of the largest epidemics in history with 132 Americans dying every day due to fatal overdoses. The office of the Assistant Secretary for Planning and Evaluation (ASPE) in the Department of Health & Human Services has conducted research to better characterize the epidemic with the goal of creating strategic policy interventions. Data from the Substance Abuse and Mental Health Service Agency Uniform Reporting System was analyzed to identify trends in opioid misuse, prescribing rates, and overdose deaths. It was found that over 13 million Americans misuse opioids. Moreover, opioid prescriptions accounted for 94 percent of all opioid use and 70% of opioid related deaths. It was also found that the number of opioid prescriptions directly correlated with overdose deaths. This research has led ASPE to develop several federal policy recommendations aimed at decreasing opioid use and promoting access to addiction treatment. These recommendations include: expanding prescription drug monitoring programs, increasing access to medication assisted treatment, requiring law enforcement to carry overdose reversal medication, and reevaluating current prescription opioids for Risk Evaluation and Mitigation Strategies. This study and resulting policy interventions aim to curtail the growing opioid epidemic by leveraging the federal government. The comprehensive policies put forth have the potential to significantly decrease opioid misuse and prevent thousands of overdose deaths.

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2016 Survey of State-Level Health Resources for Men and Boys: Identification of an Inadvertent and Remediable Service and Health Disparity

This survey evaluated resources available to men and boys at the state level including state public health departments (SPHDs), state agencies, and governor's offices. Most of the resources and programs are found in the SPHDs and administer state initiated and federally funded health programs to provide services and protection to a broad range of populations. However, many men's health advocates believe that SPHDs have failed to create equivalent services for men and boys, inadvertently creating a health disparity. Men's Health Network conducts a survey of state resources, including those found in SPHDs, every two years to identify resources available for men and women, determine the extent of any disparity, and establish a relationship with SPHD officials. Data were obtained from all 50 states and Washington, D.C. An analysis of the 2016 survey data indicates that there are few resources allocated and a lack of readily available information on health and preventive care created specifically for men and boys. The data observed that most health information intended for men and boys was scarce among states or oftentimes included on websites that primarily focused on women's health. A potential result of this is a loss of engagement with appropriate healthcare providers due to a lack of information. This study continues to validate the health disparity between health outcomes for women and men and continues to highlight the need for better resource allocation, outreach, and health programs specifically tailored to men and boys in order to improve overall community well-being.

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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Community Health Centers' Response to Family Planning Needs in the Era of Health Reform

BACKGROUND

Community health centers represent the nation's largest delivery system for low-income individuals and families, including six million women of reproductive age. However, the changing landscape of health policy over the last several years has made health centers' capacity to respond to women's health needs unclear. This study aims to explore the challenges, barriers, opportunities, and successful models of family planning service delivery in health center settings in the context of rapidly shifting state and federal policy.

METHODS

Using a comparative case study approach, we conducted in-depth site visits at four community health centers from distinct geographic regions in different policy climates. We conducted semi-structured interviews with clinical, administrative, and executive staff members. Two investigators conducted thematic content analysis of interview transcripts until consensus on key themes emerged.

RESULTS

Within-case and cross-case themes encompass: perceptions of and responses to community-based reproductive health needs; models of family planning care; and the impact of federal and state policies on health center operations. Staff at all health centers described patient preferences as influencing the scope of family planning services and supplies available at their health centers. Although all health centers provided some level of family planning care, staffing patterns differed; some sites created a family planning team or employed dedicated reproductive healthcare staff, while others incorporated family planning into the same processes as their general primary care practice. Some health center staff considered family planning a portal of entry into primary care, while others perceived primary care as an entry point for family planning. All health centers described challenges related to uncertainty and instability in state and federal policy, including the Affordable Care Act, and a need for flexibility in response to continuing policy changes. Finally, leadership staff who are invested in family planning and see its value serve as a facilitator for high performance and as a key component of a health center's ability to navigate the current policy climate.

IMPLICATIONS

Community health centers provide essential health services for women of reproductive age. This study identifies commonalities and differences in health centers' approaches to family planning in a time of policy uncertainty. It also identifies barriers to and facilitators of providing family planning care that is responsive to community needs. As federal and state policies continue to shift, the findings from this study provide emerging models of care and best practices that can be implemented in health centers around the country.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Current and Future State of Alternative Payment Models (APMs) in Emergency Medicine

With the recent push for the U.S. healthcare system to improve the quality and cost-efficiency of care, the bipartisan Medicare Access and CHIP Reauthorization Act (MACRA) of 2015 was signed into law. MACRA shifted U.S. healthcare payment structures from a traditional volume-driven fee for service (FFS) model to value-based alternative payment models (APMs). However, the utilization, impact, and future of APMs in the emergency department (ED) is still ambiguous. This study aims to provide an overview of the current and future state of APMs in emergency medicine, through qualitative interviews with key opinion leaders such as healthcare administrators and leaders of emergency physician groups.

Interviews were semi-structured, following a basic outline and modified according to the participants' specific expertise and direction of discussion. All transcripts were reviewed by three investigators to identify general themes and generate a codebook using grounded theory for qualitative analysis. Preliminary analysis revealed several unifying themes. A common sentiment among participants was that current quality measurements focused heavily on process rather than outcome measures. Other common themes included the ED being overlooked by other stakeholders in the APM space, inadequate financial incentives to modify physician behavior, and hesitation among some emergency physicians to transition away from traditional fee for service models. In regards to future outlook, opinions were mixed. Some participants viewed the transition to APMs as a loss of compensation and autonomy of practice, while others viewed value-based payments as an opportunity to transform and enhance the role of emergency medicine. By revealing the barriers and opportunities of APMs in ED, we hope to provide direction for future studies on how to address common issues and facilitate a successful transition for emergency medicine into value-based care.

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Intravenous Immunoglobulin in Combination with Intravenous Methylprednisolone in the Treatment of Calcinosis Associated with Juvenile Dermatomyositis (JDM)

BACKGROUND

Calcinosis is one of the hallmark complications of juvenile dermatomyositis (JDM), and it is associated with long-term damage, functional disability, and poor quality of life. There is no known effective treatment of calcinosis and current treatment protocols have been limited to anecdotal retrospective studies. Few published case reports showed improvement of calcinosis in JDM patients treated with Intravenous Immunoglobulin (IVIg). We assessed the response of IVIg in combination with IV methylprednisolone in eleven JDM patients with calcinosis.

METHODS

Retrospective medical record review of over 200 JDM patients seen from 2008-2017 at The George Washington Myositis Clinic was performed. 53 of JDM patients developed calcinosis, 15 had at least one follow-up visit and 11 were identified that received IVIg treatment for calcinosis. The number of anatomic areas with calcinosis (head, upper extremities, lower extremities, chest, back, abdomen and buttocks), and the number of joints with improved range of motion (ROM) at final visit were used to assess treatment response. Additionally, the areas with calcinosis were assessed for presence of inflammation.

RESULTS

The median [IQR] age at baseline was 14 [12-16] years. The median [IQR] duration of IVIg treatment from baseline to final visit in calcinosis was 16 [9-60] months, with a dose ranging between 1g/kg- 2g/kg per month. At the time of the IVIg infusion, patients also received IV Methylprednisolone ranging from 100 mg to 1,000 mg. Treatment also included methotrexate (10 patients), oral prednisone (7 patients), rituximab (2 patients), infliximab (1 patient). The median [IQR] number of anatomic areas with calcinosis was 6.0 [1.0-7.0] pre- and 8.0 [2.0-8.0] post-treatment. The median [IQR] number of areas with inflammation was 2.0 [1.0-6.0] pre- and 1.0 [0.0-3.0] post-treatment.

The number of restricted joints decreased in 7 out of 10 patients. 9 out of 10 patients with restricted joints movement at baseline demonstrated an improved ROM at the final evaluation visit ($p=0.0011$).

CONCLUSION

IVIg in combination with IV methylprednisolone may improve the level of functional disability and quality of life in JDM patients with calcinosis. Larger, controlled studies are needed to determine the effectiveness of immunosuppressive and immunomodulatory therapies for treatment of calcinosis associated with JDM.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES
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Improving Access to Pediatric Sub-Specialty Care Using DTC Telemedicine by Addressing Barriers

BACKGROUND

Lack of access to pediatric subspecialty care is a barrier to pediatric health. On average patients wait 44.9 days for an in-person visit. Telemedicine is emerging as a new modality to provide pediatric care. However, most public and private insurers still do not pay for direct-to-consumer telemedicine services. In 2016, we established a sub-specialty direct-to-consumer (DTC) telemedicine program for underserved pediatric patients in a pediatric health system, providing subspecialty virtual visits, free of charge. In order to have a successful DTC telemedicine program our hospital system established a relationship with a DTC telehealth vendor. The underserved children this telemedicine program served are uninsured children and Medicaid children in DC, MD, VA.

OBJECTIVE

The goal of this study was to describe the impact of a DTC telemedicine program, track metrics for consultations with patients and assess provider's perceptions of the program.

METHODS USED

This was a mixed methods study utilizing the telemedicine platform, web based surveys, and focus groups. Descriptive statistics were used to summarize visit metrics, and survey responses. Patient and provider satisfaction surveys were updated and reviewed for thematic content.

SUMMARY OF RESULTS

Between April 2016 and September 2017, our program completed 226 DTC telemedicine subspecialty follow-up appointments. The average wait time for virtual visits across all specialties was 1.87 minutes, compared to the average wait time of 78.2 minutes across specialties for an in-person follow-up during the same time period. On average DTC telemedicine saved 4,542 miles travelled over 96 consults (58 miles/consult saved). Preliminary survey data from parents are currently being analyzed from patients and families utilizing our DTC telemedicine service. We are quantifying their opinions by asking them about their impression of their Telemedicine consult pre- and post-visit.

CONCLUSIONS

Our preliminary data has demonstrated a positive patient perception of DTC telemedicine. DTC telemedicine programs provide an opportunity for payers, hospitals and patients to address the needs of underserved pediatric patients for subspecialty care.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Soft Tissue Mobilization in the Management of Individuals with Patellar Tendinopathy: A Critically Appraised Topic

INTRODUCTION

Patellar tendinopathy is a common overuse condition affecting athletes that can lead to significant functional disability, including cessation of sports. Tendinopathy is a chronic degenerative disease associated with abnormal tendon structure, often resulting in localized tenderness and load-dependent symptoms. Current evidence supports using staged progressions of exercise to reduce pain and improve function for this population. While soft tissue mobilization (STM) is commonly used for tendon dysfunction, its effects on patellar tendinopathy are not well described.

METHODS

Five different electronic databases (PubMed, Scopus, CINAHL, SportDiscus, and the Cochrane Library) were searched using relevant keywords and appropriate MeSH terms to evaluate interventional trials of STM in management of patellar tendinopathy. Inclusion criteria was patients with patellar tendinopathy, randomized controlled trials (RCT) or cohort study designs, at least one STM technique, outcome measures of pain and/or function, full-text in English language, and human subjects. Studies were excluded if they did not meet the inclusion criteria, used instrument-assisted techniques, or were published greater than 20 years prior. After filtering results based on inclusion and exclusion criteria, three studies were included: two RCTs and one prospective cohort trial. Each trial was screened for quality using the PEDro or Critical Appraisal Skills Programme (CASP) scales.

RESULTS

Of the three included trials, two utilized transverse friction massage (TFM) to the patellar tendon, while the third used fascial manipulation directed towards the thigh. Of the two trials using TFM, one demonstrated a statistically significant additive effect on pain and function when combined with exercise. The second trial using TFM did not demonstrate a statistical improvement in outcomes when used as a stand-alone intervention. The trial utilizing fascial manipulation demonstrated a statistically significant effect in decreasing pain. Each trial was scored to be of high quality.

CONCLUSION

This study examined the current utilization and benefit of STM in the management of patellar tendinopathy. Based on our review, we conclude that there is limited and conflicting evidence for using STM to improve symptomatic and functional outcomes in patellar tendinopathy. There may be a benefit to improving outcomes when STM is added to an exercise program, however its usage as an independent intervention does not appear to be beneficial. Fascial manipulation may be useful for reducing pain in individuals with patellar tendinopathy. Notable study limitations included small sample sizes and short follow-up periods. Further research is indicated related to the utilization of STM for patellar tendinopathy.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Elusive Diagnosis of SMART Syndrome Demystified

A 32-year-old woman presented to the Emergency Department (ED) with severe headaches, acute neurologic changes and altered mental status. Her past medical history was significant for medulloblastoma treated with radiation and chemotherapy 24 years prior to this admission. Admitting diagnoses included recurrent tumor and stroke. Brain MRI showed areas of restricted diffusion, sulcal effacement and gyral +/- leptomeningeal enhancement in the left temporal lobe, and in short did not further narrow the differential diagnoses. The patient was treated symptomatically. The patient and her MRI findings subsequently returned to baseline. A couple of years later, she presented to the ED with similar clinical history and near identical MRI findings. The constellation of the recurring MRI findings led to the diagnosis of SMART syndrome (stroke-like migraine attacks after radiation therapy).

The clinical presentation of patients with SMART syndrome can be diverse and difficult to hone, requiring MRI imaging for further characterization. The MRI imaging can also be confusing to those unfamiliar to this entity. Restricted diffusion, which is one of the MRI findings in these cases, is typically associated with irreversible cell death either caused by compromised blood supply or less likely infectious agent. On the other hand, gyriform pattern of enhancement, which is another MRI finding in these cases, is typically not seen in the setting of acute cell death. Instead it is typically associated with the subacute phase of cytotoxic edema. As such, the concomitant presence of these two findings can appear as a challenge to fundamental rules of MRI interpretation.

In this presentation, the etiology of the MRI findings, their pathophysiology and how they reflect the SMART syndrome in a patient with previous cranial radiation treatment will be reviewed. This understanding will expedite diagnosis and treatment planning and decrease morbidity and mortality.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Hypertriglyceridemia among Transgender Patients on Hormone Therapy

The field of transgender medicine is growing but research is needed in many areas such as the long term effects of hormone therapy. This study sought to determine 1) hypertriglyceridemia prevalence in patients both before and during hormone therapy; 2) whether or not hypertriglyceridemia is related to dose and/or formulation of estrogen or testosterone; 3) whether hypertriglyceridemia was related to other factors such as medications, BMI, blood pressure, and race/ethnicity. This retrospective study collected data from patients at the MFA endocrinology clinic and from Whitman Walker Clinic. Specifically, it included approximately 500 subjects, both trans men and trans women, on various types of estrogen or testosterone therapy. The data has been collected but has not been analyzed. Although no conclusions can be drawn at this time, the results from this study will hopefully inform clinicians and patients regarding potential adverse effects of hormone therapy.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Brexipiprazole Induced Neutropenic Fever Complicated by Truncal Plaques with Central Erosions

INTRODUCTION

Neutropenic fever in patients without known hematologic malignancies and not receiving chemotherapy is challenging. Clinicians are faced by the need to detect the underlying cause of neutropenia as well as treating the infections that may be present. We are presenting a case of neutropenia that is caused by brexpiprazole, an atypical antipsychotic, complicated with an unusual skin infection.

CASE PRESENTATION

A 62-year-old man with history of psoriasis, esophageal spasm, and bipolar disorder presented with subacute odynophagia and rash on his abdomen and arms that developed over three weeks. He was chronically treated with lamotrigine, buspirone, and diltiazem. He was started on brexpiprazole one week before the onset of his symptoms by his psychiatrist for mood stabilization. His vital signs were stable except for a temperature of 39.4 degrees Celsius. Physical examination showed oropharyngeal erythema, anterior non-tender cervical lymphadenopathy, and multiple well-demarcated oval plaques with central erosions and purulent crusts most prominent on the abdomen and flank. Complete blood count revealed a white blood cell count of $0.18 \times 10^3/\text{mL}$ without any abnormalities in the other cell lines. Other laboratory values including lactate dehydrogenase were unremarkable. Microbiological investigations including blood cultures and viral serology for hepatitis B, hepatitis C, HIV, EBV and CMV were unrevealing. Chest X-Ray was suggestive of bilateral lower lobe pneumonia. Brexpiprazole was suspended due to temporal correspondence with his symptoms and rare reports of its association with agranulocytosis. Vancomycin, azithromycin and fluconazole were added over the following 3 days due to persistent fever and odynophagia. Esophagogastroduodenoscopy identified multiple small esophageal ulcers with negative staining and cultures. Skin lesion punch biopsy showed cutaneous ulceration with abundant colonies of bacteria on the surface. The corresponding wound culture grew methicillin susceptible *Staphylococcus aureus*. His neutropenia resolved after 5 daily doses of filgrastim and he was discharged home to complete a fourteen-day course of augmentin and a seven-day course of azithromycin.

DISCUSSION

Erythematous plaques with central erosions in the context of neutropenia are typically concerning for a deep fungal infection or ecthyma gangrenosum secondary to pseudomonal infection. Neither of these pathogens was isolated in our patient. This case demonstrates an unusual presentation of *Staphylococcus aureus* skin infection. Furthermore, our case raises the importance of keeping a high clinical suspicion for rare side effects of newly introduced medications. Brexpiprazole was the culprit in this case despite the classic association with neutropenia of certain medications in this patient's medication list (i.e., lamotrigine).

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Anti-MDA5 and Anti-MJ (NXP2) Autoantibody Associated Phenotypes of Juvenile Dermatomyositis (JDM)

OBJECTIVE

To examine frequency and characteristics of anti-MDA5 and anti-MJ (NXP2) autoantibody (Ab) associated juvenile dermatomyositis (JDM).

METHODS

We studied demographic, clinical, laboratory, treatment and outcome features of 35 pts with anti-MDA5 Ab and 116 pts with anti-MJ (NXP2) Ab associated JDM and JCTM/DM meeting Bohan and Peter criteria. Differences were evaluated by Fisher's exact and Mann-Whitney tests. Kaplan-Meier and Log-rank tests were used for time-to-event treatment analysis. Myositis Abs were tested by standard immunoprecipitation (IP) and IP-immunoblot.

RESULTS

Anti-MDA5 Abs were identified in 35 (7.7%) and anti-MJ (NXP2) Abs were identified in 116 (25.5%) pts from a cohort of 453 JDM and JCTM/DM pts. Anti-MDA5 Ab+ were older at diagnosis (8.7 [6.0-13.2] vs 6.3 [4.5-9.9], $p=0.0104$) compared to anti-MJ (NXP2) Ab+. There were no differences in gender distribution, delay to diagnosis, and onset severity between the two groups. Anti-MDA5 Ab+ had lower serum CK (median, IQR 184 [84.5-257.0] vs. 1669 [438-5280] U/L, $p<0.0001$) and aldolase (median, IQR 8.1 [6.9-12.1] vs. 12 [9.2-21.8] U/L, $p=0.0002$) levels. MDA5 Ab+ had more frequent fever (62.9% vs. 40.5%, $p=0.032$), weight loss (80.0% vs. 31.3%, $p<0.0001$), adenopathy (42.9% vs. 20.2%, $p=0.013$), arthralgia (88.2% vs. 65.5%, $p=0.0102$), arthritis (88.6% vs. 47.0%, $p<0.0001$), dyspnea on exertion (45.7% vs. 25.0%, $p=0.0336$), ILD (25.7% vs. 1.8%, $p<0.0001$) but less frequent falling episodes (17.1% vs. 48.7%, $p=0.0008$) and myalgia (45.7 vs. 73.7%, $p=0.0036$) compared to anti-MJ (NXP2) Ab+. The median skeletal (0.5 [0.5-1.0] vs. 0.5 [0-1.0], $p=0.005$), constitutional (0.5 [0.5-0.75] vs. 0.25 [0.25-0.5], $p<0.0001$) and overall total clinical system (0.28 [0.22-0.35] vs. 0.22 [0.16-0.32], $p=0.0028$) scores at diagnosis were higher and muscle system score was lower (0.28 [0.14-0.43] vs. 0.43 [0.29-0.57], $p=0.0163$) in MDA5 Ab+ compared to anti-MJ (NXP2) Ab+. MDA5 Ab+ had shorter steroid treatment duration (median, IQR 17.0 [8.1-36.0] vs. 27.0 [16.4-48.0] months, $p=0.432$) compared to anti-MJ (NXP2) Ab+. At most recent evaluation, anti-MDA5 Ab+ had more frequent active disease (68.6 vs. 47.8%, $p=0.035$), were more frequent ACR functional class II (25.7 vs. 10.3%, $p=0.028$) and had more frequent periungual capillary changes (39.4 vs. 20.0%, $p=0.036$) compared to anti-MJ (NXP2) Ab+. There was no difference in disease course and mortality between the two groups.

CONCLUSION

Anti-MDA5 Abs are seen in a distinct subset of JDM with frequent arthritis, arthralgia, weight loss, fever, adenopathy, and ILD, but less frequent falling episodes, myalgia and lower serum CK and aldolase compared to anti-MJ (NXP2) Ab associated JDM.

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Transcriptome Patterns in Hidradenitis Suppurativa

INTRODUCTION

Hidradenitis suppurativa (HS) is an inflammatory disease of the apocrine sweat glands affecting approximately 1-4% of the population. Patients with HS develop inflammatory nodules and abscesses. Until now, the molecular drivers of HS have been poorly understood. The purpose of the current study was to analyze transcriptome patterns in HS skin specimens to identify transcripts and upstream regulators that are differentially expressed in HS compared to normal skin.

METHODOLOGY

HS subjects (n=10) were enrolled in the Wound Etiology and Healing Study (WE-HEAL Study, IRB 041408). Control skin specimens (n=11) were collected from abdominoplasty procedures (IRB 101419). Total RNA was extracted with the aid of the RNeasy Fibrous Tissue Kit (Qiagen, Germany). 1µg of RNA was amplified, biotin-labeled, purified and hybridized to Illumina HumanHT-12 v4 Expression BeadChips (Illumina Inc., San Diego, CA). The BeadChips were scanned using a HiScanSQ system (Illumina Inc., San Diego, CA) and fluorescence was quantitatively detected for downstream analysis. mRNA expression profiles were analyzed using the limma package.

Differentially expressed genes were detected using Significance Analysis of Microarrays (SAM) at a false discovery rate of <math><0.05</math> and an absolute

RESULTS

In the HS to normal control comparison 436 genes were identified that were overexpressed and 363 genes that were under-expressed in HS patients ($\text{FDR} < 0.05$, $|\text{abs}(\log_2\text{FC}) \geq 1.00$, $p\text{-value} \geq 2$ or < -2). The top 5 pathways included interferon signaling, leukocyte extravasation signaling, Th1 pathway, Th2 pathway, and nuclear factor of activated T cell pathway. Upstream regulator analysis identified interferon alpha, interferon gamma, lipopolysaccharide, tumor necrosis factor and oncostatin-M as the top five upstream regulators.

CONCLUSION

The data presented show that HS is associated with dysregulation of multiple inflammatory pathways. Further study is needed to identify candidate molecular drivers of HS and potential therapeutic targets for this debilitating disease.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Clinically Amyopathic Juvenile Dermatomyositis (CAJDM)

OBJECTIVE

We examined features of clinically amyopathic juvenile dermatomyositis (CAJDM), in which patients have characteristic rashes with little to no evidence of muscle involvement, to determine if this is a distinct phenotype from JDM.

METHODS

Demographic, clinical, laboratory, treatment and outcome features of 12 (9 hypomyopathic, 3 amyopathic) patients meeting modified Sontheimer's criteria for CAJDM and from 60 myositis autoantibody (Ab) matched JDM patients meeting Bohan and Peter criteria were examined. Differences were evaluated by Fisher's exact and Mann-Whitney tests, random forests, and logistic regression analysis. Kaplan-Meier and Log-rank tests were used for time-to-event treatment analysis. Myositis Abs were tested by standard immunoprecipitation (IP) and IP-immunoblot.

RESULTS

Nine (75%) CAJDM patients had anti-p155/140 (TIF-1), one (8.3%) anti-MDA5 Abs and two (16.7%) were myositis Ab negative. CAJDM patients were younger at diagnosis (4.1 [2.2-6.1] vs. 7.3 [4.4-11.9], $p=0.005$) and frequently had mild disease at onset (75.0 vs. 11.7%, $p<0.0001$). CAJDM patients had less frequent myalgia (8.3 vs. 61.7%, $p=0.0009$), arthritis (0.0 vs. 48.3%, $p=0.0011$), contractures (8.3 vs. 61.7%, $p=0.0009$), calcinosis (0.0% vs. 33.3%, $p=0.029$), dysphagia (0.0 vs. 31.7%, $p=0.0284$), abdominal pain (0.0 vs. 36.7%, $p=0.0134$), and fatigue (33.3 vs. 81.7%, $p=0.0016$). The muscle (0.0 [0-0] vs. 0.29 [0.17-0.48], $p=0.0001$), skeletal (0.0 [0-0] vs. 0.5 [0-1.0], $p=0.0029$), and overall clinical (0.063 [0.034-0.12] vs. 0.21 [0.13-0.28], $p<0.0001$) scores were lower in CAJDM. Serum muscle enzymes were less frequently increased in CAJDM, and peak CK values were lower (176 [104-292] vs. 479 [186-2239] U/L, $p=0.0068$). CAJDM received fewer medications compared to JDM patients. Only 50% of CAJDM patients received oral prednisone, but the maximum dose and treatment duration did not differ from JDM. Random forest analysis showed the most important predictors of CAJDM compared to JDM were lower skeletal score (MDA100.0), less frequent myalgia (MDA 61.6), lower overall clinical system score (MDA 29.6), absence of arthritis (MDA 24.7), and mild illness severity at onset (MDA 22.9). The final logistic regression model revealed a lower skeletal score (OR 27.9, 95% CI [3.4-647.0], $p=0.009$) and less frequent myalgias (OR 0.042, 95% CI [0.002-0.264], $p=0.005$) as the most important factors in distinguishing CAJDM from JDM. At a median follow-up of 2.9 years, CAJDM patients had no documented functional disability, and none developed weakness, calcinosis, interstitial lung disease, or lipodystrophy.

CONCLUSION

CAJDM may be distinguished from JDM, in that they often have p155/140 (TIF-1) autoantibodies, have fewer systemic manifestations, and receive less therapy.

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SCHOOL OF NURSING

Examining Moral Distress in Registered Nurses

BACKGROUND

Moral distress is an emotionally stressful experience that many registered nurses will experience. Moral distress occurs when one knows the ethically correct action to take but feels powerless or is unable to take that action. Research has identified various sources and common clinical scenarios that often induce distress among registered nurses. This paper will examine the phenomenon of moral distress and explore the concept of moral residue.

METHODS

A cross sectional design using survey methodology with the 21 question MDS-R over a 4 week period to assess intensity and frequency of moral distress among registered nurses in a large suburban hospital in Northern Virginia.

OBJECTIVES

Assess the level and frequency of moral distress, examine the clinical scenarios that occur most frequently and with the most intensity. Compare critical care nurses to non-critical care nurses' total moral distress scores and determine if the survey data supports the theory of moral residue.

RESULTS

The study sample of 97 nurses included 44 in critical care, 21 non-critical care, and 32 who preferred not to answer. The mean composite score of all nurses was 103 out of a possible 336, indicating an overall low level of moral distress. Nurses in the medical/surgical intensive care unit has the highest mean score of 159. Nurses with more years of experience did not demonstrate higher moral distress. These findings did not support those of other studies which indicated nurses with more years of experience demonstrate higher moral distress.

CONCLUSION

The theory of moral residue was not evident in these study findings.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Progression of Female Authorship in Emergency Medicine Journals

PURPOSE

The purpose of this article is to observe the authorship trends of females within the specialty of emergency medicine. This is a longitudinal analysis, looking at the gender, educational training, geographical origin, and number of authors throughout the publishing history of two major journals within the specialty.

METHODS

We focused on the number of authors on each publication, the number of references per paper, the degrees and genders of the first and senior authors, in addition to geographical origin of the corresponding author. The data were collected from two journals, the Journal of Emergency Medicine and Annals of Emergency Medicine. Specifically, we looked at the Journal of Emergency Medicine from the years 1986, 1991, 1996, 2001, 2006, 2011, and 2016. Additionally, we looked at the Annals of Emergency Medicine from the years 1976, 1981, 1986, 1991, 1996, 2001, 2006, 2011, and 2016. All original work was analyzed.

RESULTS

A total of 3,377 articles were reviewed. 1,238 were reviewed from The Journal of Emergency Medicine; 2,139 were reviewed from the Annals of Emergency Medicine. The mean number of authors, regardless of gender or degree, per article did not increase dramatically from 1976 to 2016, but the amount of articles published per issue did. Throughout the years, the authorship majority has consistently been male.

Although the amount of female authors now compared to in 1976 has grown considerably, the increase relative to that of male authors since 1976 has not been substantial.

CONCLUSION

There has been an increase in the number of total authors, as well as female authors per article in major emergency medicine journals between 1976 and 2016.

CLINICAL RELEVANCE

This article provides insight on the increase in female authors contributing to emergency medicine journals. The data highlights that more women are publishing in the specialty, but the numbers still pale in comparison to their male counterparts. As academia grows, it is important to be aware of the trends of who is publishing and how these trends have evolved since the inception of publications in this medical specialty. Ultimately, the number of female authors being published should reflect the amount of female emergency medicine physicians who are practicing.

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The Influence of Gender on 30-Day Complications After Revision Total Hip Arthroplasty

INTRODUCTION

Gender has been shown to affect clinical outcomes in several surgical sub-specialties. Analysis of the impact of gender on primary total joint arthroplasty has shown gender to be an independent risk factor for certain complications. To the authors knowledge, the relationship between gender and post-operative complications following revision total hip arthroplasty (THA) has not been studied previously. We hypothesized that gender differences would be a variable associated with post-operative complications following revision THA.

METHODS

The National Surgery Quality Improvement Database (NSQIP) was queried for revision THA procedures between 2005 and 2014. The NSQIP database follows patients during their in-hospital stay as well as 30 days post-operatively. Univariate and multivariate analyses were performed to determine whether gender was an independent risk factor for several post-operative complications.

RESULTS

Univariate analysis demonstrated that men were more likely to experience acute renal failure ($p=.007$) and cardiac arrest requiring resuscitation ($p=.004$). Univariate analysis revealed that women were more likely to experience blood transfusion ($p<.001$), urinary tract infection (UTI) ($p<.001$), non-home discharge ($p<.001$), and longer hospital length of stay when compared to men ($p=.01$). Multivariate analyses demonstrated similar results; women had a higher likelihood of developing a UTI (OR 2.19, $P<.001$), receiving a blood transfusion (OR 1.22, $p<.001$), and being discharged to rehab or skilled nursing facility (OR 1.56, $p<.001$). However, female gender was determined to be an independent protective factor for cardiac arrest requiring resuscitation (OR .219, $p=.005$).

CONCLUSION

Gender is an independent risk factor for 30-day complications following revision THA, which are similar to the gender related complications previously identified in the setting of primary THA. These findings present an opportunity to appropriately counsel patients undergoing revision THA regarding their specific risk profile for a post-operative complication. In addition, further analysis is needed to evaluate the reasons behind the gender differences and to define peri-operative protocols to reduce risk where possible.

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Attitudes and Practices of Shared Decision Making Regarding CT Scan Testing for Abdominal Pain in the Emergency Department

BACKGROUND

Computerized tomography (CT) imaging is commonly ordered in the emergency department (ED). However, the utility of shared decision making (SDM) has not been studied in this context. This study assessed the attitude of patients and providers towards SDM regarding the decision to perform a CT scan in ED patients with abdominal pain; evaluated how SDM is utilized when CT testing is likely to be considered; and determined the association between SDM and CT usage.

METHODS

As part of a prospective observational study, ED patients with abdominal pain in whom a CT scan was likely to be considered a diagnostic option were screened. Hemodynamically-stable adult patients who met the inclusion criteria were approached for participation. For each patient and provider, a baseline preference for SDM using the Control Preferences Scale was established. The patient-provider encounter was then observed and assessed for how providers discussed the option of ordering a CT scan. These encounters were scored using the OPTION⁵ tool. Descriptive statistical analyses examining the association between preference for SDM and its in discussions were conducted using the chi-square test or Fisher's exact test.

RESULTS

Twenty-nine encounters were observed in the ED. CT was considered in 70% of encounters; in 55% of encounters, a CT scan was ordered. 60% of patients and providers reported that they preferred to *share responsibility* with each other when deciding treatment plans. In direct observation, all providers made *no effort* or *minimal effort* to discuss options regarding the decision to perform a CT scan. There was no association between SDM practice and CT utilization.

CONCLUSIONS

High rates of provider and patient preference to perform SDM for diagnostic management plans were reported but minimal to no effort was observed regarding the use of CT scan for ED patients with abdominal pain.

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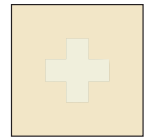
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Targeted Application of Unmanned Aerial Vehicles (Drones) in Telemedicine

Recent advances in technology have dramatically transformed the healthcare field. Unmanned Aerial Vehicles (UAVs) represent the next wave of advancements that can revolutionize the field. Originally developed to be used in the military, UAVs are making their way into the public sphere. Because they can be flown autonomously and reach almost any geographic location, UAVs have the unique advantage of broadening the reach of medicine. A literature review was conducted to investigate current research projects that focus on the use of drones in medicine. A compressive review was conducted via PubMed using search terms such as "unmanned aerial vehicles," "UAVs," and "medicine." Based on the articles searched, we grouped the application of UAVs into three distinct categories: Prehospital Emergency Care; Expediting Laboratory Diagnostic Testing; and Surveillance. Some of the medical applications of drones include the delivery of automated external defibrillators (AEDs), medical specimens, and hematological products. They have also been used to identify mosquito breeding grounds as well as drowning victims at beaches. These recent studies showcase the potential application of UAVs to increase the access of healthcare to individuals who may be restricted by cost or geography. However, before UAVs can be fully integrated in the medical field, several ethical, safety, and technical issues need to be addressed. These include the cost to maintain drones, current Federal Aviation Administration (FAA) guidelines, and Health Insurance Portability and Accountability Act (HIPAA) regulations. Despite the many challenges that remain, the application of drones appears to be promising and can help to increase the quality and accessibility of healthcare.

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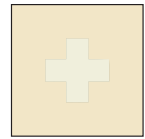
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Creating a Multidisciplinary and Patient Centered Referral Model at the Bridge to Care Clinic

Linking patients to referral resources is an integral part of all community clinics. In a Student Run Free Clinic, this service is even more essential and oftentimes more difficult. Volunteer turnover makes continuity difficult and referral sites are constantly in flux. Determining what resources, if any, patients are eligible for is a constant battle. At the Bridge to Care Clinic, we use the Patient Navigator Program to link patients to insurance. Historically, all patients who needed a referral were referred to the Patient Navigator Program regardless of the nature of the referral. A Patient Navigator would then work with the patient to connect them to a referral site. This process was often difficult to track and often unsuccessful at providing optimum care.

OBJECTIVE

This project aimed to delineate different types of referrals that were sent to the Patient Navigator Program, better educate volunteers on the referral context at the clinic, and provide other resources that would make our care more patient centered.

METHODS

We piloted using Masters in Public Health students as Patient Navigators and worked to better organize the resources we had in a flow chart. We also created categories of education resources that volunteers could distribute to patients when appropriate.

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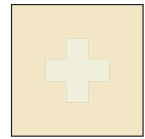
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Health-Related Social Problems Reported by Caregivers During Emergency Department Visits

BACKGROUND

Social determinants of health (SDH) such as childhood poverty, parental unemployment, and domestic violence are known contributors to pediatric morbidity, adverse childhood experiences, and poor adult health and achievement. Yet, these social issues are often addressed individually or not at all in healthcare environments.

Addressing SDH during an emergency department (ED) visit may provide an opportunity to intervene and improve the health of our most vulnerable children. To our knowledge, no prior studies have attempted to quantify and identify predictors of high numbers of SDH in the pediatric ED setting.

OBJECTIVE

To quantify SDH and behavioral risk factors that affect patients and families visiting a pediatric ED and to identify healthcare-related conditions (obesity, frequent non-urgent ED visits, and/or poor asthma control) that may be associated with high numbers of SDH.

DESIGN/METHODS

This is an ongoing cross-sectional study of caregivers of patients ages 0-12 years who present to a high-volume, urban, pediatric ED. Participants completed an electronic questionnaire designed to identify SDH within 13 domains. We performed multivariable logistic regression analyses to identify whether endorsing high SDH (≥ 3) was associated with obesity (BMI percentile ≥ 90), frequent non-urgent ED visits (≥ 3 ED visits in 12 months), or poor asthma control as measured by the PACCI-ED caregiver survey.

RESULTS

285 caregivers were approached, and 118 (41%) completed the electronic survey. Almost half of the caregivers reported SDH involving safety (40%) and/or parental or child mental health (39%). Nearly 1/3 identified housing risk factors. Issues around health care access (25%) and poverty (23%) affected approximately 1 in 4 families. A majority of caregivers (79%) screened positive for at least one SDH. Over one-third of participants (38%) screened positive for at least three (3) SDH. Endorsing high SDH was not associated with obesity (aOR 2.154, 95% CI: 0.590-7.871), frequent non-urgent ED visits (aOR 1.9, 95% CI 0.6-5.8), or poor asthma control (aOR 0.959, 95% CI 0.793-1.161).

CONCLUSION(S)

The majority of caregivers presenting for care to a pediatric ED endorsed at least 1 SDH, with one-third endorsing a large number of SDH. Future research will incorporate assessment of SDH in adolescents and their caregivers, further study predictors that will identify patients at high risk for SDH who may benefit from proactive social intervention, and assess the impact of social interventions on ED recidivism and other patient outcomes.

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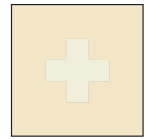
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Patient and Caregiver Attitudes Towards Comprehensive Behavioral Health Screening in the Emergency Department

PURPOSE

The American Academy of Pediatrics recommends routine screening for behavioral and mental health risk (BHS) in adolescents. Because adolescents who seek care in emergency departments (EDs) may have riskier behaviors than adolescents who access primary care, the ED may be a strategic setting for screening. The objective of this study was to assess patient and caregiver acceptance of a comprehensive behavioral health screen in the pediatric ED.

METHODS

A cross-sectional study of 14- to 21-year old patients and their caregivers who presented to an urban pediatric ED. Participants completed a computer-assisted questionnaire to assess acceptance of ED-based screening for the following domains of behavioral health: depression, suicidality, access to firearms, substance use, sexual activity, violence, human trafficking, and housing instability. We calculated screening acceptability for each domain and performed multivariable logistic regression to assess differences in acceptance between adolescents and caregivers.

RESULTS

The 516 study participants (347 adolescents and 169 caregivers) reported the following rates of screening acceptance: depression 70.0%; suicidality 78.1%; firearm access 50.4%; substance use 76.9%; sexual activity 73.8%; violence 71.9%; human trafficking 59.3%; housing insecurity 65.1%. After adjustment for race/ethnicity, gender, and insurance status, patients were less likely than caregivers to support screening for depression (66.9% vs 76.3%; aOR 0.6 [0.4, 1.0]), firearm access (45.0% vs. 61.5%; aOR 0.5 [0.3, 0.7]), substance use (73.5% vs 84.0%; aOR 0.5 [0.3, 0.8]), violence (69.2% vs 77.5%; aOR 0.6 [0.4, 1.0]) and human trafficking (55.3% vs 67.5%; aOR 0.6 [0.4, 0.9]). Almost all caregivers would allow their children to participate in confidential screening (91.6%), allow physicians to speak privately with their children following screening (82.6%), extend their ED stay to speak with social work (77.3%) and follow up with resources provided (89.8%).

CONCLUSIONS

Comprehensive behavioral health screening in the ED is acceptable to both adolescents and caregivers. Acceptability of screening varies across domain areas, but the majority of adolescents and caregivers are in favor of screening in all areas. Across most domains, caregivers have higher rates of screening acceptance than adolescent patients.

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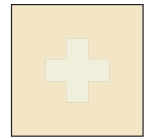
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Frequency of Prescription Filling Among Adolescents Prescribed Treatment for STIs in the Emergency Department

BACKGROUND

Adolescents are frequently diagnosed with sexually transmitted infections (STI) in the emergency department (ED). Untreated, STIs can lead to pelvic inflammatory disease (PID), infertility, and severe morbidity. Although many patients are presumptively treated in the ED with single dose antibiotics, many are prescribed outpatient treatment. However, it is unknown how often those prescriptions are filled after hospital discharge.

OBJECTIVE

To determine the frequency of filled prescriptions for adolescents prescribed antibiotics for outpatient management of STIs in an urban pediatric ED and identify factors associated with prescription filling.

METHODS

We performed a retrospective medical record review of all ED visits made by adolescents aged 13-19 years who were prescribed antibiotics for the treatment of *Chlamydia trachomatis* (CT) or *Neisseria gonorrhoeae* (GC) cervicitis/urethritis or PID in an urban pediatric ED in 2016. We extracted data on outpatient prescription filling, patient demographics, and visit characteristics. We calculated the proportion of outpatient prescriptions filled, and performed multivariable logistic regression to identify patient- and visit-level factors associated with prescription filling.

RESULTS

During the study period, 337 patients were diagnosed with an STI. Of these patients, 127 (37.7%) were prescribed outpatient antibiotics for CT/GC (n=42) or PID (n=85) treatment. The mean age was 17.1 (+/- SD 1.4) years, and the majority was female (89.8%), of non-Hispanic black race/ethnicity (78.7%), and publicly insured (85.0%). 18.1% of patients were admitted for inpatient management of PID. Of the 127 patients prescribed outpatient antibiotics, the overall fill rate was 46.5% (95% CI 37.7, 55.3) [CT/GC (43.3%; 95% CI 31.2, 55.4) and PID (50.5%; 95% CI 39.8, 61.4)]. After adjusting for age, race/ethnicity, and insurance status, prescription fill rates were significantly higher among admitted patients (aOR 3.3; 95% CI 1.2, 8.7) compared to patients discharged from the ED.

CONCLUSION

Overall, adolescents evaluated in an urban pediatric ED had low rates of filling outpatient prescriptions for treatment of STIs, placing them at risk for increased morbidity and complications from untreated STIs, as well as further transmission of infection. Hospital admission was associated with higher prescription filling rates. Future studies should focus on understanding barriers to prescription filling to inform interventions for improvement in treatment adherence.

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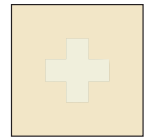
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Cost-Effectiveness of Alternative Anticoagulation Strategies for Postoperative Management of Total Knee Arthroplasty Patients

BACKGROUND

Anticoagulation is essential for deep vein thrombosis (DVT) and pulmonary embolism (PE) prevention following total knee arthroplasty (TKA). Some research has suggested that longer duration anticoagulation can substantially reduce the risks of DVT and PE; however, in the absence of definitive recommendations, physicians are left weighing the risks of DVT and PE against those of anticoagulation, including gastrointestinal (GI) and central nervous system (CNS) hemorrhage and increased likelihood of prosthetic joint infection (PJI). We conducted a cost-effectiveness analysis to evaluate the benefits and risks of 14- and 35-day therapy with the most commonly prescribed anticoagulants post-TKA.

METHODS

Using a probabilistic microsimulation Markov model, we assessed clinical and economic outcomes of 14-day and 35-day anticoagulation therapy following TKA with rivaroxaban, low molecular weight heparin (LMWH), fondaparinux, warfarin, and aspirin. Complications of TKA and anticoagulation included including DVT, PE, prosthetic joint infection (PJI), and bleeding. Bleeds at the operative site increased risk of PJI, while non-operative site bleeds increased mortality. Each anticoagulant carried a unique risk reduction in DVT and PE and risk increase in bleeding, compared to no anticoagulation. Daily costs, obtained from RedBook Online, ranged from \$1 for aspirin to \$43 for fondaparinux. Primary outcomes included quality-adjusted life years (QALYs), direct medical costs, and incremental cost-effectiveness ratios (ICERs) at one-year post-TKA. The preferred regimen was the regimen with highest QALYs maintaining an ICER below the willingness-to-pay threshold (\$100,000/QALY). We conducted probabilistic sensitivity analyses, varying complication incidence and anticoagulation efficacy, to evaluate the impact of parameter uncertainty on model results.

RESULTS

Aspirin resulted in the highest cumulative incidence of DVT and PE, while prolonged fondaparinux led to the largest reduction in DVT incidence (15% reduction compared to no prophylaxis). Despite differential bleeding rates (ranging from 3% to 6%), all strategies had similar incidence of PJI (1-2%). Prolonged rivaroxaban was the least costly strategy (\$3,300 one year post-TKA) and the preferred regimen in the base case. In sensitivity analyses, prolonged rivaroxaban and prolonged warfarin had similar likelihoods of being cost-effective.

CONCLUSIONS

For all anticoagulants, extending the duration of anticoagulation therapy in the post-operative period to 35 days increases QALYs compared to standard 14-day prophylaxis. Prolonged rivaroxaban and prolonged warfarin are most likely to be cost-effective in TKA patients; the costs of fondaparinux and LMWH precluded their being preferred strategies. As warfarin and rivaroxaban are comparable from a cost-effectiveness standpoint, patient preferences can help inform the appropriate post-TKA prophylaxis.

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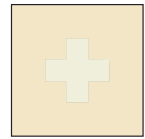
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Communication Among Multidisciplinary Team Members Treating Patients with Disorders of Consciousness Following Traumatic Brain Injury

The purpose of this research is to understand how clinicians who work with patients with disorders of consciousness (DoC) following traumatic brain injury (TBI) communicate about patients' behavior regarding changes in consciousness. Communication and collaboration among multidisciplinary teams is central for person-centered rehabilitation and clinical progress. A deficiency in person-centeredness may decrease the quality of care a patient receives (Epstein & Street, 2007). This process is more complicated in patients with DoC since these patients are unable to participate in the dialog (Papadimitriou & Cott, 2015). This qualitative analysis explores unique challenges clinicians face communicating with team members when treating patients with DoC following TBI in inpatient rehabilitation.

A grounded theory interview study explored how clinician's perceive they communicate patients' changes in consciousness with team members (Green & Thorogood, 2014). Three hospital systems recruited twenty-one clinicians who have experience working with DoC patients.

Clinicians participated in semi-structured interviews with two trained interviewers. Interviews were audio-recorded, transcribed verbatim, and NVivo 11 Plus software was used for open coding. The team developed a codebook using thematic analysis and constant comparative strategies to finalize the codebook (Glaser, 1965).

Three major themes emerged: 1) clinicians' difficulty interpreting patients' behaviors of change in consciousness, 2) a lack of confidence when selecting a treatment, and 3) an uncertainty of how to leverage caregivers' interpretation of patients' behaviors. For example, the data describes challenges clinical teams face in discharge planning. A social worker perceives the caregiver to agree on what it takes to bring their family member home while the occupational therapist did not share this perception. The social worker tried to convey to the team that the caregiver was equipped to take the patient home, "I was turning blue in the face communicating to the team that I did strongly feel that his [caregiver] had a reasonable expectation and an understanding of the severity of his deficit". This exemplifies how each discipline has a different vantage point surrounding a complex task such as discharge planning.

Communication challenges for clinicians treating patients with DoC were grounded within the three themes, which conveyed uncertainty with interpreting patients' behaviors and linking it to clinical progress, a lack of research to support interventions, and being cautious when talking to family. Uncovering how clinicians make sense of patient's behaviors and how they communicate these behaviors can aide in creating a foundation for improving the exchange of information and person-centered rehabilitation.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Influence of Sex as an Intrinsic Biological Variable in a Primary Cell Model of HIV Latency

BACKGROUND

Several cohort studies have shown that there are sex differences in the pathogenesis of HIV-1. Recently, it has been shown that females are more likely to develop a lower reservoir size than male during long-term ART. The immunologic and virologic mechanisms underlying these clinically relevant observations are not currently understood. We wanted to address whether sex was an intrinsic difference in CD4 T cells that could explain some of the clinical observations.

METHODS

We have used a primary cell model of HIV-1 latency that recapitulates the generation of latently infected cultured TCM and uses a replication competent virus and ART. Using this primary cell model, we have characterized whether sex influences the intrinsic ability of HIV to replicate and to establish latency in cultured TCM cells. Furthermore, we have characterized the ability of different Latency-Reversing Agents (LRAs) to reactivate latent HIV.

RESULTS

We have found that cultured TCM from both sexes can replicate HIV at similar ratio and generate equal levels of latent infection. Analysis of the ability of several LRAs to reactivate latent HIV suggest that sex is not an intrinsic biological variable to the activity of these specific LRAs.

CONCLUSIONS

Our results show that sex is not an intrinsic biological variable in CD4 T cells in terms of the ability of HIV to replicate, to establish latency or to reactivate from latency with several LRAs. Other extrinsic factors may be accountable for the sex differences observed clinically.

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HIV/AIDS



INSTITUTE FOR BIOMEDICAL SCIENCES

Role of Mitochondrial Antiviral Signaling Protein in Reactivation of Latent HIV-1 in CD4⁺ T Cells

The mitochondrial antiviral signaling protein (MAVS) is involved in response to viral infection, and mediates signaling that culminates in type I interferon production and activation of the transcription factor nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). HIV-1 has NF-κB binding sites in its long terminal repeat, allowing it to use NF-κB for viral transcription. We hypothesize that stimulation of MAVS in CD4⁺ T cells can reactivate latent HIV-1, and investigated the potential of targeting MAVS as a latency reversing strategy.

To assess MAVS stimulation as a potential strategy for reactivation, we have used a primary CD4⁺ T cell model which recapitulates latency in vitro, as well as resting CD4⁺ T cells from aviremic participants. We also employed a CRISPR/Cas9 strategy to study the role MAVS plays in viral reactivation using the latent HIV-1 model JLAT 10.6. We have shown that chemical activation of MAVS, triggered by reactive oxygen species is sufficient to reactivate latent HIV-1. Interestingly, we have found that several widely studied latency-reversing agents (LRAs) mediate their effect partly through the activation of MAVS. Our results show that targeting MAVS in latently infected HIV-1 cells can lead to viral reactivation. Thus, MAVS is a potential therapeutic target for reversing HIV-1 latency.

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Antibody Responses to HIV Protein and Commensal Bacteria After Treatment with Probiotics in a Rhesus Macaque Vaccination Model

To date there is no highly effective HIV vaccine, and therefore improving vaccine efficacy is of high importance. HIV preferentially replicates within mucosal tissue, and therefore, boosting mucosal immunity may be one strategy to increase vaccine efficacy. Here we studied the effects of microbiome manipulation on antibody responses to vaccination and infection in a rhesus macaque model, and analyzed responses to commensal strains of bacteria.

Male rhesus macaques were divided into treatment groups receiving either daily oral probiotic treatment alone, in conjunction with a DNA (SIV p55 and HIV gp160) plus protein (HIV gp140 trimer) subtype C vaccine, or vaccine alone. Following 26 weeks of treatment, macaques were challenged intra-rectally six weeks later with multiple low doses of subtype C SHIV (SHIV_{C.CH505.375H_dCT}). Plasma was collected longitudinally throughout treatment course and SHIV infection. Plasma antibody responses were analyzed by indirect ELISA to determine levels of IgG against HIV proteins and 5 bacteria strains.

In the first cohort of macaques (n=3 per group), background cross-reactive antibodies to HIV gp41 but not gp120 protein were detectable before vaccination. Microbiome manipulation through probiotic treatment moderately dampened the anti-gp41 and gp120 antibody response to HIV vaccine and early SHIV infection compared to the vaccine alone group. Antibody responses to gram positive bacteria *L. plantarum*, *L. rhamnosus*, and *B. cereus* as well as gram negative *A. junii* remain stable post-vaccination and infection in the presence or absence of probiotic treatment; however, antibody responses to gram negative *E. coli* increased in all macaques post-SHIV infection.

Our preliminary findings suggest that probiotic treatment may moderately affect the antibody response to HIV vaccination or infection, but does not affect the anti-bacterial response in rhesus macaques. This study is currently ongoing and more animals will be studied to increase the sample size. Whether these changes significantly impact immune responses to HIV must be further explored in future studies.

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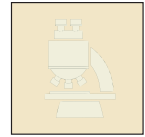
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Acquired Hemophagocytic Lymphohistiocytosis: Identifying the Trigger in a Rare Hyperinflammatory Disorder

Hemophagocytic lymphohistiocytosis (HLH) is a rare disease entity characterized by abnormal activation of the immune system, resulting in unchecked proinflammatory cytokine release and pathologic amplification. Untreated HLH has high mortality rates. HLH may be classified as a primary (genetic) or secondary (acquired) disorder. A variety of pathological states may act as a trigger for acquired HLH, including infections, malignancies, and autoimmune diseases.

A 47-year old African-American female kidney transplant recipient with systemic lupus erythematosus (SLE) and end-stage renal disease (ESRD), was admitted to our center with fever, chills and nasal congestion, diarrhea and anorexia. The patient had a living kidney donor transplant in 2001 and a deceased donor kidney transplant in 2016. Her immunosuppressive treatment on admission consisted of oral prednisone, mycophenolate mofetil and tacrolimus.

Clinical and laboratory findings were suggestive of sepsis. Empiric broad-spectrum intravenous antibiotics were started and immunosuppressive therapy reduced accordingly. Viral work up was negative for BK virus, hepatitis B virus, hepatitis C virus, Epstein-Barr virus and human immunodeficiency virus however cytomegalovirus testing was positive. Bacterial infection was excluded on serial blood cultures. Antiviral therapy with valganciclovir was initiated but she remained febrile. In the context of therapy-refractory fever and pancytopenia with disproportionately elevated levels of ferritin, lactate dehydrogenase, triglycerides and soluble interleukin-2 receptor (sIL-2r/sCD25) a suspected diagnosis of HLH was established.

CT chest/abdomen/pelvis identified a new cluster of small nodules in the peripheral right upper lobe, small right pleural effusion and multiple old mediastinal lymph nodes, but no hepatosplenomegaly. CT Neck revealed a prevertebral effusion with endplate erosions at C4-C5 level. This was followed up with an MRI Neck that showed end-plate edema without significant edema in the disc space.

Histoplasma capsulatum species was isolated from bone marrow culture. There was no evidence for viral, bacterial, parasitic infection, malignancy or active SLE.

After initiation of liposomal amphotericin therapy fevers resolved and treatment was transitioned to oral itraconazole. Laboratory parameters including ferritin, LDH, triglycerides and all cell lines improved. Given patients clinical response to antifungal therapy, the development of HLH was attributed to disseminated histoplasmosis. The patient was discharged 43 days after the initial admission.

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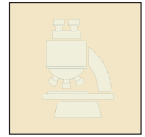
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Comparative Analysis of Serum Samples from Immunized versus Naïve Mice in Malaria Using Untargeted Metabolomics

Malaria is a life-threatening parasitic infection caused by Plasmodium species. The causal organism of malaria was discovered over 100 years ago and over the last several decades, molecular biology has enabled major advances starting with traditional gene cloning, cell biology and pathogenesis studies. This was followed by the sequencing, annotation and investigation of complete genomes from several species, including human and mice. These advancing technologies have aided the development of rapid diagnostic tests, development of drugs, monitoring of drug resistance and advanced research towards developing malaria vaccines. However, there are still remaining gaps in our understanding of the relationship between Plasmodium and its host, and relatively few host-parasite interactions are currently known for malaria. Systems biology, comprising transcriptomics, proteomics, and metabolomics among other “omics” is a very promising field of study that could give us the answer to those questions. Metabolomics is the study of chemicals in biosystems, and is a very powerful tool that can investigate metabolism in-depth as well as its byproducts and associated networks. The goal of this project is to identify putative metabolites and associated pathways that are differentially expressed in the serum of mice immunized with radiation attenuated sporozoites that confers sterile immunity versus that of naïve mice. This was achieved by (1) preparation of serum samples collected from immunized and naïve mice after challenge with sporozoites for LC/MS-MS, (2) untargeted metabolomic analysis using XCMS and MetaboAnalyst, (3) metabolite identification using Compound Discoverer, and (4) pathway analysis using Mummichog. After data analysis, 219 metabolites and 40 pathways were found to be differentially expressed between naïve and immunized mice. Research is still ongoing, now directed towards validating our results with targeted metabolomics using metabolites that are both differentially expressed and part of pathways that are known to be involved in cellular or humoral immunity.

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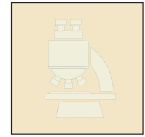
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The Role of DFMO in *Helicobacter Pylori* Infection: Modulation of ROS Response

BACKGROUND

Gastric cancer remains the third foremost cause of cancer deaths worldwide. The leading cause of gastric cancer, *Helicobacter pylori* is a thought drive carcinogenesis by inducing chronic inflammation. One pathway implicated in the host immune response involves polyamines, which have been shown by our laboratory to contribute to gastric carcinogenesis. Difluoromethylornithine (DFMO), an inhibitor of ornithine decarboxylase (ODC), the rate-limiting enzyme for polyamine synthesis reduce gastric inflammation and progression to cancer in gerbils infected with *H. pylori*. Paradoxically, cell-specific deletion of the *Odc* gene in macrophages increased inflammation in murine experiments, indicating the likely involvement of alternative mechanisms by which DFMO could be mediating cancer progression, including direct effects on the bacteria. We hypothesize that DFMO modulates the interaction between *H. pylori* and gastric cancer by affecting the bacteria exposed to oxidative stress generated in an inflammatory environment.

METHODS

Strains for *H. pylori* were derived from the parental 7.13 and were either grown on plates passaged 19 times with or without DFMO exposure, or harvested from gerbil stomach tissue after 12 weeks with or without exposure to DFMO in drinking water. Murine macrophages and *H. pylori* strains were co-cultured, and mRNA was harvested from cells 6 h post-infection. RT-PCR was used to analyze expression of proteins indicative of M1 response (NOS2, TNF- α , IL-1 β). For the second focus, we cultured *H. pylori* 7.13 in liquid media over 24 h with 50 mM DFMO, 50 mM ornithine, or no additional reagent. At each 2 h time-point, we noted the OD_{600nm} and isolated RNA from the bacteria. To assess oxidative response, we used RT-PCR to compare mRNA expression of genes involved in *H. pylori* defense, such as *sodB* and *tpx*. We performed RT-PCR for *katA* and *tlpB* in the parental, *in vitro* passaged, and gerbil output strains. Lastly, we grew the parental strain and 4 gerbil output strains in Brucella broth, or broth treated with 500 μ M or 1 mM H₂O₂, and plotted growth curves.

RESULTS

In co-culture experiments, M1 gene expression levels did not differ between macrophages infected with DFMO-treated or control strains. In our analysis of *H. pylori* gene expression, we found induction of *sodB* and *tpx* at the 2 and 4 h time-points in the samples collected from the DFMO-treated compared to ornithine-treated media or untreated controls. Furthermore, expression of *katA* and *tlpB* were lower in DFMO output versus control output strains. Bacterial growth curves demonstrated attenuated growth in H₂O₂-treated DFMO-exposed *H. pylori* strains compared to untreated DFMO-exposed controls. Additionally, unexposed control gerbil output strains showed no difference in growth in acutely H₂O₂-treated strains compared to untreated controls.

CONCLUSIONS

Our results from this study suggest that chronic exposure of *H. pylori* to DFMO impedes bacterial response to environmental stress by affecting expression of oxidative defense genes. These data also imply that treatment with DFMO may be contributing to environmental oxidative stress, which leads to an immediate response by the bacteria to prevent ROS-induced DNA damage. Further study may establish the specific role of DMFO in the modulation of *H. pylori* growth through induction of oxidative stress. The implications are that DFMO has benefits in its effects on *H. pylori* that add to its chemopreventive potential.

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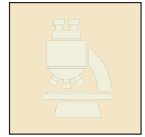
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

An Orphan Disease—Idiopathic Retroperitoneal Fibrosis

Idiopathic Retroperitoneal Fibrosis (IRF) is a rare disorder in which there is a fibrous and inflammatory reaction that occurs in the retroperitoneal space. Patients can present with a wide variety of symptoms depending on the specific location where inflammation occurs and due to this, diagnosis and treatment can often be delayed. Additionally, IRF has yet to be claimed by an Internal Medicine subspecialty which can further complicate the management of these patients. Understanding the presentation and management of patients with IRF is therefore useful.

A 69-year-old man with a history of hyperlipidemia, hypertension, heart failure with reduced ejection fraction, and mild cognitive impairment presented to an outside hospital (OSH) with bilateral flank, abdominal, and testicular pain and was found to be in acute renal failure with creatinine of 3.5 (baseline 1.0). CT abdomen and pelvis were performed which showed a large retroperitoneal fibrotic mass encroaching on both ureters, distal abdominal aorta, and common iliac arteries. Urology was consulted for decompression to improve the acute renal failure secondary to obstruction. J stent was placed successfully in the left kidney however due to the fibrotic nature of the mass and its proximity to the right ureter, J stent placement was unsuccessful on the right side. Subsequently, Interventional Radiology (IR) proceeded with percutaneous nephrostomy on the right side. The patient was ultimately transferred to our facility for higher level of care and further diagnostic workup with tissue biopsy to differentiate between IRF and malignancy. Due to the location of the fibrosis near vasculature, there was concern for the risk of vessel penetration during biopsy. Further imaging was performed including a PET scan which did not show any hypermetabolic areas which was favorable for the diagnosis of IRF. Multiple specialties including Nephrology, Urology, General Surgery, Interventional Radiology, and Hematology participated in the conversation regarding the role of tissue biopsy in confirming the diagnosis. However, it was ultimately decided not to pursue a high-risk procedure and instead proceed with treatment of presumable IRF. Treatment with steroids—80mg daily for 3 months—was initiated almost one month after the patient's initial presentation at the OSH. Hematology decided to follow the patient as an outpatient.

Presentation of IRF can vary between patients and because it is adopted by different specialists based on presenting symptoms, management can vary. This is a case of a patient with presumable IRF with delay in treatment due to pending diagnostic workup. Given the lack of management guidelines for IRF, a shared decision-making process was pursued between the patient, primary team, and multiple subspecialists.

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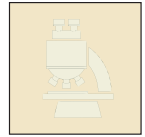
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Tricuspid Pseudomonas Endocarditis with Rare Sequelae of Left-Sided Endocarditis: Subarachnoid Hemorrhage

CASE

A 60 year-old female with recent intravenous drug use (IVDU), presented with a week of cough, shortness of breath, orthopnea, and lower extremity edema. On physical examination the patient was afebrile, tachycardic, and tachypneic. She had lower extremity edema and bibasilar crackles but a normal cardiac examination without murmur. Labs were significant for leukocytosis to 18,000, acute kidney injury (AKI) with creatinine of 2.9, and an elevated BNP to 11,000. CT chest revealed innumerable septic pulmonary emboli. Subsequent transthoracic echocardiograms (TTE) revealed multiple vegetations on the tricuspid valve (largest >1cm), mild tricuspid regurgitation, mild thickening of aortic valve with moderate aortic regurgitation, and no patent foramen ovale. Due to altered mental status, CT head and MRI was performed and revealed a subarachnoid hemorrhage (SAH). MRA was negative for aneurysm but showed reduced flow in the V4 segment of the left vertebral artery. Treatment for infective endocarditis (IE) was started with vancomycin and piperacillin/tazobactam. Blood cultures returned positive for *P. aeruginosa* with antibiotics adjusted to meropenem and ceftazidime. Cultures cleared after gentamicin was added after renal function improved.

DISCUSSION

Pseudomonas Aeruginosa is a rare cause of IE seen most often with concomitant IVDU. Prior case studies have reported left-sided pseudomonas endocarditis. This, however, is the first reported case of tricuspid involvement. TTE showed possible left sided involvement, which has a higher mortality rate than right sided endocarditis though a transesophageal echocardiogram was unable to be performed for confirmation. IE may have multiple neurological sequelae, but SAH is certainly a rarer complication and commonly results from mycotic aneurysm rupture or left sided cardiac vegetations. A review of the literature does not reveal any case reports of tricuspid valve pseudomonal endocarditis associated with SAH, further raising the suspicion of undiagnosed left-sided involvement. Typical treatment for pseudomonas endocarditis includes an aminoglycoside and a secondary pseudomonal agent in combination with surgery. While our patient met multiple criteria for early surgical intervention such as signs and symptoms of heart failure, difficult-to-treat pathogen, and persistent infection, this was unable to be performed due to her SAH. Despite this our patient improved steadily with medical therapy alone. This case highlights SAH as a rare neurological complication of IE with a first report of its association with pseudomonal endocarditis secondary to IVDU, which generally predisposes to right-sided involvement though our patient likely also had left-sided involvement that may have precipitated her neurological sequelae.

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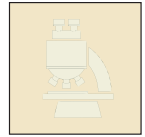
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CD4 T Cell Exhaustion in Toxoplasmosis

T cell exhaustion/dysfunctionality plays a major role in persistent, chronic infections and cancer progression. It is characterized by up-regulation of inhibitory receptors on T cells, which subsequently leads to loss of their effector function. Programmed cell death protein-1 (PD-1) has been identified as a key inhibitory receptor involved in T cell exhaustion, which down-regulates the immune system by suppressing their inflammatory activity. In mouse models of cancer, it has been shown that exhausted CD8+ T cells, with up-regulated expression of multiple inhibitor receptors including PD-1, are correlated with variable levels of T cell dysfunction (loss of proliferative capacity and cytokine production). Toxoplasmosis is a chronic infection caused by an intracellular parasite, *Toxoplasma gondii*. CD8+ T cells control the infection through cytotoxic killing of infected cells, and CD4+ T cells help to maintain the effector and memory function of CD8+ T cells. Because of constant exposure to the antigen, CD4+ T cells become exhausted, which then leads to CD8+ T cell exhaustion and loss of control of the infection. Using the murine model of Toxoplasma encephalitis, we investigated CD4+ T cell exhaustion by evaluating the expression of the levels of inhibitory receptors: PD-1, 2B4, Tim-3, LAG-3 and CTLA-4 in mice carrying chronic infection. We used flow cytometry to demonstrate that higher PD-1 expression by CD4+ T cells was concomitant with increased expression of different multiple inhibitory receptors as compared to cells expressing lower levels of PD-1. Interestingly, our data show attrition in *T. gondii*-specific CD4+ cells, while an increase in total CD4+ T cell population was observed. Our data suggests that as chronic infection progresses, increased expression of PD-1 in CD4 T cells from chronically infected mice may result in multiple inhibitory expression that is correlated with increased severity of CD4 dysfunction.

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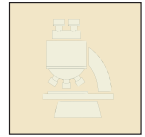
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Tracheal Aspirate Cultures in Intubated Neonates: A Descriptive Epidemiological Cohort Study

BACKGROUND

Considerable variability in antibiotic prescribing practices in neonatal intensive care units (NICUs) and increasing knowledge about the adverse consequences of antibiotic exposure in neonates highlights the need for a better understanding of antibiotic prescribing practices. Antibiotic prescribing practices related to positive tracheal aspirate culture results, which could represent either colonization or invasive infection, is unknown.

METHODS

We conducted a retrospective cohort study of intubated neonates admitted to Children's National Health System (CNHS) who had one or more tracheal aspirate cultures sent May to December 2016. Data collected through chart review included changes in vital signs, secretion characteristics, ventilator settings, oxygen requirement, white blood cell count, C-reactive protein (CRP), and chest x-ray results in the 48 hours preceding tracheal aspirate culture order. Outcome measures collected include duration of antibiotic therapy, hospital and NICU length of stay, ventilator days, discharge on respiratory support, recurrence of respiratory infection, bronchopulmonary dysplasia, colonization with multidrug-resistant organism (MDRO), and mortality. Clinical factors present in those with an identified pathogen were compared with those without, using chi squared for dichotomous and t-test for continuous variables.

RESULTS

We identified 51 intubated neonates who met inclusion criteria; 43 (84%) were preterm with median gestation 28 weeks (IQR 25-31). Median birth weight was 1140 g (IQR 744-2360) and 47% were female. A pathogen was identified in 37% of isolates. *S. aureus* (7) was the most frequently isolated pathogen, followed by *K. pneumoniae* (5) and *Enterobacter spp* (4). Hemodynamic instability and abnormal laboratory values were the common clinical factors in the 48 hours preceding cultures. Antibiotics were prescribed for 45 (88%) neonates with a median of 14 days (IQR 6-16). The most frequently prescribed antibiotics were vancomycin (67%) and gentamicin (63%). Those with respiratory culture positive for a pathogen had a higher odds of having had change in respiratory secretion characteristics (OR 14.3; 95% CI 1.3-130.9) and increase in oxygen requirement (OR 4.1; 95% CI 1.0-16.6).

CONCLUSIONS

Although most neonates are treated with antibiotics, fewer than half of respiratory cultures identified a pathogen. Those with an identified pathogen were more likely to have changes in respiratory secretion characteristics and increased oxygen requirement.

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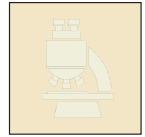
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Study of Changes in the Transcriptome of Mouse Bladder Following Bladder Wall Injection of *Schistosoma Haematobium* Eggs

BACKGROUND

Infection with *Schistosoma haematobium* leads to urogenital schistosomiasis (UGS), which afflicts over 100 million people. UGS can cause hematuria, calcification of the bladder, and increased risk of secondary infections by bacteria or viruses, and it is also linked to bladder cancer. Previous studies have used a mouse model that involves injection of *S. haematobium* eggs into the bladder wall to examine the effect of parasite eggs on host bladder biology, and they have identified changes in genome-wide methylation, as well as changes in the transcript level of some genes by microarray analysis. Here, we perform RNA-Seq on egg injected bladders to expand the detection of changes in gene transcript level to the scale of the whole transcriptome.

METHODS

We followed a combined infection/injection animal model in which female BALB/c mice were infected with *S. haematobium* cercariae and then, after 5 weeks, administered either parasite eggs or hamster liver extract by bladder wall injection. Another group of control mice did not receive surgery. RNA-Seq was performed on the RNA isolated from the bladders 4 days after bladder wall injection.

RESULTS/CONCLUSIONS

RNA-Seq analysis of egg-injected bladders and controls will reveal host gene pathways activated by the presence of *S. haematobium* eggs. Of particular interest are urothelial cell-related genes, including cancer pathways, differentially expressed genes associated with infiltrating and resident leukocytes, and fibrosis-related gene pathways. RNA-Seq analysis of schistosome-specific genes highlight the challenges of performing the parasite side of dual RNA-Seq in the setting of low amounts of parasite RNA relative to host RNA.

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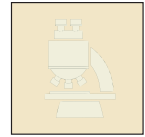
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Anti-IL-13R α 2 Promotes Recovery from Murine Inflammatory Bowel Disease by Enhancing the Pro-Regenerative and Anti-Inflammatory Activity of IL-13

IL13RA2 transcript number is elevated in the colons of inflammatory bowel disease (IBD) patients, and its levels are highest in the colons of IBD patients who do not respond to the standard therapy, anti-TNF α . IL-13R α 2 is a non-signaling decoy receptor that binds the cytokine IL-13 with high affinity and sequesters its broad anti-inflammatory and pro-wound repair functions. In this study, we investigated the role of IL-13R α 2 and evaluated the impacts of its blockade on IBD. We conducted genome-wide association studies on an IL-13 gain-of-function variant (R130Q) that has reduced affinity for IL-13R α 2 to establish if IL-13 has a protective role in IBD. We found that human subjects carrying R130Q had a lower odds ratio for Crohn's disease. To interrogate the role of IL-13R α 2 in IBD, we used the dextran sodium sulfate (DSS) model of mouse colitis with a 7-day recovery period. We show that administration of DSS increased the expression of IL-13R α 2 protein in serum and colon tissue. DSS-induced colitis was less severe in *Il13ra2*^{-/-} mice as longer colon lengths were measured and less inflammation in the distal colon was scored compared to wild type controls. Next, we investigated the mechanism mediating the reduced inflammation in the colons of *Il13ra2*^{-/-} mice following 7 days of recovery. We identify decreased expression of pro-inflammatory genes but increased expression of TH₂ genes in the colon tissue of *Il13ra2*^{-/-} mice compared to wild type controls. Consistent with our gene expression data, we observe an increase in type 2 immune cells and mucus production in the colons of *Il13ra2*^{-/-} mice compared to wild type controls after 7 days of recovery. Therapeutic targeting of IL-13R α 2 with a novel anti-IL-13R α 2 antibody in wild type mice only during recovery significantly improved colon health compared to mice administered IgG1 isotype control antibody. Lastly, we demonstrate that the resolution from DSS colitis is IL-13-mediated with IL-13-neutralizing antibodies administered during recovery. Collectively, ablating or neutralizing IL-13R α 2 to increase IL-13 bioavailability in DSS-induced murine IBD decreases pro-inflammatory responses and promotes resolution of IBD. As IL-13R α 2 is markedly upregulated in IBD patients that have failed anti-TNF α therapy, therapeutics that neutralize IL-13R α 2 could be particularly beneficial in this patient group.

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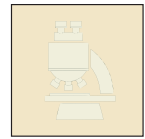
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IMMUNOLOGY/INFECTIOUS DISEASES



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Gemella Sanguinis as a Rare Cause of Infective Endocarditis

INTRODUCTION

Pathogens responsible for endocarditis among IV drug abusers with prosthetic heart valves are not always the most common organisms. Other rare species should always be considered when faced with such a patient.

LEARNING OBJECTIVES

Recognize the clinical importance of considering alternative organisms as it may help expedite the diagnosis of infectious endocarditis in such patients.

CASE

This patient is a 67 years old male with a complicated past medical history including coronary artery disease (CAD), endocarditis (s/p aortic valve replacement with a 25mm Edwards tissue valve) and primary patent foramen ovale repair that was done 04/25/16, hemomediastinum after epicardial pacer wire removal, chronic kidney disease, hepatitis C, severe pulmonary hypertension and poly-substance abuse who came in to the ED complaining of right shoulder pain. The pain initially started the morning of admission when he was trying to tie his shoes. His symptoms were concerning for acute coronary syndrome. On arrival his troponin was elevated to 0.137 without EKG changes and he was admitted for treatment of NSTEMI. His vital signs were stable. His urinary toxicology screen was positive for methadone and opiates.

Given his history of endocarditis, blood cultures were sent. He was afebrile on admission, but became febrile the night of admission. He was also tachycardic and had a WBC of 20 with 9% bands. His blood cultures were positive for gram positive cocci (GPC) and he was started on empiric Vancomycin for treatment of presumed *S. aureus* bacteremia. A TTE was obtained which showed no evidence of vegetation, but given his IV drug use history, personal history of endocarditis, prosthetic valve, and GPC bacteremia a TEE was obtained which showed a 1.8cm aortic valve vegetation.

It was not until 4 days into his admission that the blood culture speciation was completed showing *Gemella sanguinis*. Infectious disease was consulted and his antibiotics were transitioned to rifampin 300mg TID and penicillin 3 million units q4h. His antibiotics were changed again to ceftriaxone 2g BID after final speciation. The patient remained hemodynamically stable and his WBC returned to normal after three days of antibiotics. He was discharged on a 6 week course of ceftriaxone.

DISCUSSION

1- *Gemella sanguinis* Catalase negative, facultative anaerobe, gram positive cocci, that is usually part of the oral, upper respiratory track, intestinal track flora, is a rare yet possible cause of acute bacterial endocarditis in patients with prosthetic heart valves with the aortic valve being the most common site of infection (1), up to our knowledge there are only 5 cases reported yet.

In most cases it has been related to abnormal dentation (1), but in our patient we believe that the cause of his Endocarditis is related intra venous drug abuse given that he had normal dentation, and active drug use.

2- Bacteremia in such patients necessitates the need for a TEE even if initial blood cultures appear consistent with more common pathogens.

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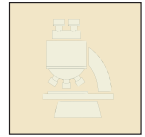
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CHILDREN'S NATIONAL MEDICAL CENTER

Exposure to Early Life Cycle Stages of *Schistosoma* Haematobium Infection Influences Subsequent Immune Responses to Eggs

Urogenital schistosomiasis causes bladder dysfunction, hematuria, fibrosis, and urothelial changes that could lead to carcinogenesis. Exposure to schistosome infested waters, a major concern particularly for school-aged children, can lead to loss of productive life years due to heavy morbidity. Heavy morbidity contributes to the vicious cycle whereby schistosomiasis is the cause as well as the effect of poverty. Despite the global impact of urogenital schistosomiasis, relatively little is known about the mechanisms that lead to its pathophysiology. This is primarily due to the lack of an experimentally tractable animal model - rodent models of urogenital schistosomiasis result in little to no involvement of the urogenital system, thus failing to recapitulate the human disease. Hence, we sought to develop a mouse model of urogenital schistosomiasis that bypasses critical weaknesses of current models, specifically, to study the effect of prior cercarial-, schistosomular-, and worm-triggered immune responses on the subsequent egg-induced granulomatous reaction. 4 groups of BALB/c mice underwent the following treatments: 1) bladder wall injection with vehicle alone; 2) bladder wall injection with 3000 *S. haematobium* eggs; 3) percutaneous infection with 150 *S. haematobium* cercariae via tail immersion and bladder wall injection with vehicle; and 4) both percutaneous infection and egg bladder wall injection. Briefly, mice were infected at week 0. At week 5, mice underwent bladder wall injections. Mice were sacrificed at week 8 to collect bladder specimen for cytokine analysis. Sera were collected one day prior to sacrifice for cytokine analysis. A distinct immune response was observed from mice receiving bladder wall injection with viable eggs following percutaneous infection compared to mice that received egg bladder wall injection without cercarial exposure. We were able to reproduce fundamental immunological aspects of human urogenital schistosomiasis, such as a collective type 2 inflammatory response in the bladder and sera of egg-injected, cercaria-exposed animals compared to vehicle injected, cercaria unexposed animals. Furthermore, we observed Th0 and Th1 responses in egg-injected, cercaria-exposed animals, possibly attributed to exposure to cercariae, schistosomula, and/or adult worms, thus highlighting an important advantage to the combined model for understanding systemic immune responses to *S. haematobium*. Development of the proposed model herein can lead to better tools for progress on therapeutics or vaccines for this neglected global health problem.

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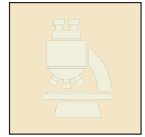
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Characterization of the Memory Antibody Response to Zika in a Flavivirus-Endemic Region of Colombia

With an increasing number of Zika vaccines moving through clinical trials, there is a need to better understand the antibody response caused by Zika infection in flavivirus endemic areas. In this study, we sought to determine the longevity and characteristics of the memory antibody response to Zika infection in 40 Colombian individuals infected during the 2016 epidemic. Luciferase-based neutralization assays using a recombinant viral particle (RVP) system were performed to determine individual's neutralizing antibody titers against dengue serotypes 1 and 2 and Zika. Based on the results of the Zika RVP assay, individuals were classified as positive (ID₅₀>500; n=20) or negative (ID₅₀<500; n=20) for previous Zika infection. Within the Zika+ group, neutralization was further tested for sensitivity to a mutation in the lateral ridge (LR) of the Zika domain III E protein (K394A). Zika+ individuals had significantly higher neutralizing titers against dengue-1 and dengue-2 than Zika- individuals. There was no significant difference observed in the overall ability of the Zika+ group to neutralize the K394A mutant as compared to wildtype, but rare individuals demonstrated a reduction in neutralization of the mutant virus. Overall, we observed that the effects of Zika infection on an individual's antibody response are long-lasting. Elevated titers of dengue neutralizing antibodies appear to persist at least 8 months post infection. This observation suggests that Zika infection triggers a boost in neutralizing antibody responses across dengue serotypes in flavi-immune individuals. Despite the isolation of potent neutralizing antibodies against the LR in both humans and mice challenged with Zika, we did not detect significant titers of Zika neutralizing antibodies targeting the LR. While these antibodies might be present, they do not appear to be the immunodominant response in the majority of persons infected with Zika in Colombia.

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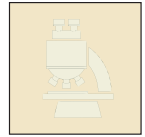
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Defining the B-Cell Response to a Stabilized Pre-Fusion Respiratory Syncytial Virus F Subunit Protein Vaccine

Respiratory syncytial virus (RSV) causes substantial morbidity in children and the elderly, and the only licensed product is a passively administered monoclonal antibody palivizumab. Therefore, a safe and effective RSV vaccine is needed. An effective vaccine will require the induction of neutralizing antibodies, which can be elicited to several antigenic sites present on the pre-fusion (pre-F) and post-fusion (post-F) conformations of the RSV fusion (RSV F) protein. Recently described antigenic sites \emptyset , V and other surfaces unique to the pre-F conformation are targets for neutralizing antibodies that are more potent than palivizumab, invigorating efforts to create a pre-F vaccine. A stabilized form of the pre-F protein achieved through cysteine substitutions and cavity filling mutations (DS-Cav1) is currently in a phase I clinical trial, where participants receive two immunizations with DS-Cav1 either with or without alum adjuvant in one of three doses (50, 150, or 500 micrograms). We have created tetrameric probes consisting of either the stabilized pre-F or post-F protein bound to a fluorescently labeled streptavidin. These probes bind to the B-cell receptor on the surface of B cells specific for the F protein, and can be used to measure responses elicited by DS-Cav1 vaccination. We have validated the conformation and specificity of the pre-F and post-F probes using antibody binding assays and by staining B cells from antigen-experienced mice. The validated probes, in conjunction with a panel of B cell phenotypic markers, will allow us to interrogate B cell responses longitudinally for antibody repertoire and epitope-specific B cell phenotypes, and compare the responses between participants in the six arms of the clinical trial.

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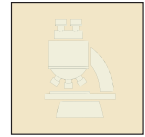
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Characterization of Bcl-6/Bcl-xL B Cell Immortalization in Rhesus Macaques for Antibody Discovery

The ability to isolate and characterize neutralizing antibodies from vaccinated animals is invaluable to the analysis of vaccine trials, and methodologies that streamline this process are therefore of great interest. Rhesus macaques are the primary pre-human model for HIV and other vaccine studies. We have optimized a method of human B cell immortalization for use in rhesus macaque B cells in which Bcl-6 and Bcl-xL are overexpressed through a retroviral vector. Here, we characterize this system and describe its efficacy in multiple B cell populations.

Standard methods for antibody discovery are often undesirable in terms of cost, time, or behavior of cultured B cells. In contrast, we show that through immortalization as described here, we generate primary B cell lines that proliferate long term, express high levels of surface B cell receptor, and secrete immunoglobulin into the culture supernatant. This allows for production of clonal cell lines, identification of cells based on antigen affinity (probe sort), and serum functional assays such as HIV neutralization to isolate desired antibodies. Narrowing B cells based on antibody function eliminates the cost of sequencing and cloning thousands of cells, and freezable clonal lines allow for repeat testing.

We successfully immortalized naïve IgD, IgM memory, and IgG memory B cells. We see transduction efficiency from 21-55% and detect high levels of both cell surface and secreted immunoglobulin. We transduced IgG+ B cells from PBMC, spleen, and lymph node samples which grew from single cell clones and secreted IgG in culture up to 20 µg/mL. We find lower transduction efficiency, doubling times, and single cell efficiency in PBMC memory B cells and highest in germinal center B cells.

The ability to rapidly and cost-effectively generate clonal lines of primary B cells will allow for more thorough analysis of vaccine trials which will inform future vaccine design. Overall, Bcl-6/Bcl-xL B cell immortalization is a valuable tool for vaccine-elicited antibody isolation in rhesus macaques.

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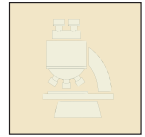
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Preliminary Analysis of the Impact of Pharmacokinetics and Pharmacodynamics on Improvement in Pulmonary Function in Children with Cystic Fibrosis

Cystic Fibrosis (CF) is an autosomal recessive pulmonary disease that causes recurrent and chronic infections. Broad spectrum antibiotics are commonly used to treat acute lung infections, also known as acute pulmonary exacerbations. Dosing of the antibiotics is an important area of concern because sub-therapeutic doses may promote bacterial resistance instead of pathogen killing. Pharmacokinetic modeling can be used to predict pharmacodynamics indices to optimize bacterial killing and guide antibiotic therapy. We sought to determine whether sub-therapeutic antibiotic exposure impacted recovery of pulmonary function for treatment of acute pulmonary exacerbations. This is a prospective study of 25 patients with CF who are 18 years of age or younger admitted for treatment of IV antibiotics. Clinical data collected for the first 15 study patients included patient demographics, symptoms at the onset of the exacerbation, respiratory culture results, and results of pulmonary function tests (PFTs). Plasma drug concentrations of IV β -lactam antibiotics were obtained during the treatment course to model the subjects' antimicrobial exposure. At exacerbation onset, 53% of patients had a decrease of at least 10% in their FEF25-75, while 47% had at least a 10% decrease in their FEV1. Of the 13 patients who had PFTs performed, there was a significant improvement following antibiotic treatment (FVC 92.9% vs 100%, $p < 0.05$ and FEF25-75 69.7% vs 92.9%, $p < 0.05$). We also evaluated for differences between those who had therapeutic ($n=4$) and sub-therapeutic ($n=9$) beta-lactam antibiotic courses. FVC %predicted was significantly higher in the therapeutic group at the onset of exacerbation than the sub-therapeutic group (106% vs 87%, $p=0.03$). When comparing the improvement at the end of antibiotic treatment from onset of exacerbation, there was no significant difference between groups. Further analysis of the full cohort will be important to identify whether antibiotic pharmacokinetics and pharmacodynamics are important determinants in improvement of pulmonary function.

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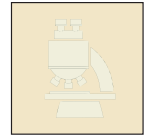
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Target Validation of Differentially Expressed miRNA in Ectopic Germinal Centers of Myasthenia Gravis Thymus

Myasthenia gravis (MG) is an autoimmune neuromuscular disorder resulting in weakness of voluntary muscles. The autoantibodies are directed against proteins present at the post-synaptic surface of neuromuscular junction (NMJ). A characteristic pathology of patients with early onset MG (EOMG) is thymic hyperplasia with ectopic germinal centers (GC). However, mechanisms that trigger and maintain thymic hyperplasia are poorly characterized. Previous study assessed the central mechanisms involved in the formation of GCs in the thymus through analysis of the microRNA (miRNA) and mRNA expression. Briefly, thymus samples from EOMG patients were grouped based on appearance of GC. MiRNA and mRNA were evaluated using GeneChip® miRNA 4.0 Array and GeneChip® Human Transcriptome Array 2.0, respectively. Partek Genomic Suite 6.6 and Transcript Analysis Console 2.0 programs were used for further analysis. Thirty-four mature miRNAs and forty-six annotated mRNA transcripts were differentially expressed between the two groups (>1.5 fold change, ANOVA $p < 0.05$). Reciprocal pairing analysis of miRNA and mRNA identified 11 pairs of miRNA and target mRNA. Target Scan identified Regulator of G protein Signalling 13 (*RGS13*), known to be involved in GC regulation, as potential target for miR139-5p and miR 452-5p. Interferon Regulatory Factor 8 (*IRF8*) expressed in GC positive samples was identified as another target for miR-452-5p. Both *RGS13* and *IRF8* are upregulated in GC positive samples.

In this study, we validated the reciprocal pairing of miRNA (miR139-5p and miR452-5p) and the target mRNAs (*RGS13* and *IRF8*). Dual luciferase assay was used to validate target binding. Putative miRNA binding region from 3' untranslated region (UTR) of these genes were cloned into pmirGlo vector downstream of firefly luciferase gene. The constructs were co-transfected with respective miRNA mimics and negative controls in 293T cell lines. Luciferase assay was performed 48 hours post transfection. Firefly luciferase activity was normalized to the Renilla luciferase activity as internal control. There was significant decrease in firefly luciferase activity on transfection of miRNA mimic as compared to negative control. Our results shown that target genes *RGS13* and *IRF8* are regulated by the miRNA.

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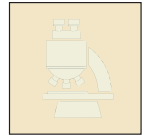
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Role of SUMOylation in Human Th1 and Th2 Responses

In order to study this phenomenon, naïve human CD4 T cells will be isolated from PBMCs of health donors and activated with IL-12 or IL-4 in order to induce a TH1 or a TH2 response respectively (objective #1). This activation will be done in the presence of 3-Hydroxy-1,2,3-benzotriazin-4(3H)-one (HODHBT), a benzotriazole which was previously been characterized by the Bosque lab to have the highest activity blocking the SUMOylation of STAT5. Levels of phosphorylation of STAT4 and STAT6 will be measured by flow cytometry and western blot using phosphospecific antibodies (objective #2). TH1 and TH2 responses will be measured by intracellular cytokine staining (TH1: staining for IFN-gamma, TH2: staining for IL-4) after stimulation with PMA and Ionomycin (objective #3). Further characterization of the cytokine expression profiles of these cells will be done by a TH Cytokine Panel from Biolegend® and subsequent flow cytometry (Objective #4). The panel which includes IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17A, IL-17F, IL-21, IL-22, IFN- γ and TNF- α , will enable us to distinguish between the production of a TH1, TH2, TH9, TH17, TH22 and TFH response. A detailed analysis of the data collected from this study will contribute to a greater understanding of the role of SUMOylation in the control TH1 and TH2 responses with respect to STAT4 and STAT6 activation (Objective #5).

The results of my research have yet to be fully elucidated, however, preliminary analysis seems to be inconclusive.

This study may require further work in order to understand the role of HODHBT in STAT4 and STAT6 Sumoylation, however, as previously stated, the results of my research have yet to be fully elucidated.

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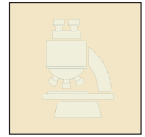
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Alpha-Fetoprotein Inhibition of Lymphocyte Proliferation *In Vitro* Cell Culture Related to Myasthenia Gravis

BACKGROUND

Autoimmune myasthenia gravis (MG) is a disorder of the neuromuscular junction caused in the majority of patients by autoantibodies directed against the postsynaptic nicotinic acetylcholine receptor (AChR). The prevalence of myasthenia gravis in the United States is estimated at 14 to 20 per 100,000 population and women are more often affected than men. Cholinesterase inhibitors, corticosteroids and immunosuppressant are commonly used classes of drugs to treat MG patients but these drugs do not prevent disease progression and are associated with serious side effects. Alpha-fetoprotein (AFP), a serum protein produced by the yolk sac and the fetal liver, is present in high amounts during pregnancy. The clinical remission of myasthenia gravis during the second half of pregnancy may be attributed to the immunosuppressive effect of AFP.

METHOD

The peripheral blood lymphocytes (PBLs) were obtained from MG patients and healthy controls (HCs) by using density gradient media (Ficoll). PBLs were cultured 5 days after the proliferation dye combination, and then the effect of PHA, hAChR and AFP on the proliferation of lymphocytes were investigated by using flow cytometry.

RESULTS

Both PHA and hAChR treatment can promote lymphocytes' proliferation. The human AChR selectively induced MG patient's lymphocytes proliferation, but not affect the cell growth of the healthy control. AFP treatment can significantly inhibit lymphocytes proliferation in a dose dependent manner without any effect on the healthy control.

CONCLUSION

AFP inhibits the peripheral lymphocyte proliferation of MG patients by *in vitro* cell culture. However, AFP did not affect proliferation of PBLs in healthy control samples. The immunosuppressive effect of AFP demonstrated AFP might be a potential therapeutic reagent for autoimmune myasthenia gravis patients.

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The Role of B Cells in Modulating Microglial Activation in EAE

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) characterized by demyelination, blood-brain barrier dysfunction, and focal areas of inflammation. During disease, there is an influx of peripheral immune cells such as B cells that is accompanied by an activation and proliferation of microglial cells in the CNS, exacerbating the neuroinflammation. B cell depletion therapy efficiently reduces MS relapses, suggesting that B cells play a central role in MS. The precise role of B cells in modulating disease including propagating microglia induced inflammation and neurodegeneration remains unclear. In the current study, we induce experimental autoimmune encephalomyelitis (EAE), an animal model for MS, to investigate microglial activation and B cell infiltration in the mouse spinal cord. Subcutaneous injection of myelin oligodendrocyte glycoprotein induces EAE, and we have examined microglial activation and B cell infiltration using Iba1 and CD19 immunostaining in this model. In addition, we have analyzed pro-inflammatory cytokine levels produced by microglial cells in response to activated B cells *in vitro*. Induction of EAE leads to inflammation in the spinal cord, quantified by increased Iba1+ cells. Activated B cells modulate the inflammatory response of microglial cells through secretion of pro- and anti-inflammatory cytokines, suggesting that B cells can influence the pathological pathways. Together, these results indicate a potential disease-relevant interaction between infiltrating B cells and resident microglia in the CNS, which may influence the propagation of MS-related inflammation.

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Dynamic Functional Changes in White Matter During Development

The optic nerve is a pure white matter tract and in the adult, virtually all axons are myelinated. In the mouse optic nerve, myelination begins around postnatal day 7 and continues until about 5 weeks of age. In this study, axonal conduction in the mouse optic nerve (aged 4-12 weeks) was measured using the Stys suction electrode method. Nerves were dissected behind the retina and at the optic chiasm prior to being inserted into stimulating and recording suction electrodes in an oxygenated artificial cerebrospinal fluid bath for extracellular recordings. Electrical stimulation stimulated axons to fire action potentials that were recorded as compound action potentials (CAP). The resultant CAP waveform can be used to provide a relative measure of the total number of responsive neurons and to distinguish axonal populations by speed of conduction. The total number of responsive axons steadily increased through development until 12 weeks of age, while the distribution of axon firing rates varied. In 4 week old mice, there were two distinct populations of responsive axons which may reflect unmyelinated and myelinated populations. In 5 and 6 week old mice, the distribution expanded to a wider range of conduction velocities, with the majority of axons conducting at intermediate speeds. This entire distribution shifted to become faster in 8 week old mice, with an increase in intermediate-speed axons. In 12 week old mice, the distribution shifted to predominantly favor faster speeds. This data suggests that the functional properties of the nerve are dynamic, favoring faster axon conduction during development. Given that morphological studies suggest myelination is largely complete by 5 weeks, the subsequent refinement of axonal conduction rates may reflect more effective myelination, changes in nodes of Ranvier or axonal maturation. Current studies are designed to distinguish between these possibilities.

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A Forebrain-Hypothalamic Circuit Mediates Hepatic Steatosis

Non-alcoholic fatty liver disease (NAFLD), characterized by an accumulation of hepatic triglycerides (i.e. steatosis), is a growing health epidemic. We recently demonstrated a role for the brain in NAFLD. In particular, disruptions in the subfornical organ (SFO) - a small circumventricular forebrain nucleus - appear to play a key role in the development of hepatic steatosis. However, the neural network(s) through which the SFO contributes to NAFLD remains unknown. The paraventricular nucleus of the hypothalamus (PVN) is a central regulator of peripheral autonomic and endocrine function, and the SFO has dense excitatory projections to the PVN. Taken together, we hypothesized that activation of excitatory SFO PVN-projecting neurons would result in NAFLD development. We first confirmed that SFO PVN projecting neurons are excitatory by using retrograde viral labeling from the PVN (CAV2-GFP) combined with SFO immunohistochemistry for the excitatory neuronal marker calcium-calmodulin-dependent kinase II (CAMKII). Nearly 100% of the retrograde tracer co-localized with CAMKII in the SFO (not shown, n=3). Subsequently, we employed an intersectional viral strategy in which a retrograde transported canine adenovirus was targeted to the PVN to allow for expression of Cre-recombinase in SFO PVN-projecting neurons (CAV2-Cre-GFP), combined with SFO-targeted delivery of a Cre-inducible designer receptors engineered against designer drugs (DREADDs) excitatory construct (AAV2-DIO-hM3Gq-mCherry). With this approach, the pharmacological ligand clozapine-N-oxide (CNO; 3 mg/kg i.p.) was administered once daily over 6 days to activate SFO PVN-projecting neurons (n=4). Oil Red O staining of the liver demonstrated that, relative to control animals, 6-day activation of SFO PVN-projecting neurons resulted in a clear development of hepatic steatosis (2.69 0.02 vs. 2.92 0.02 au x 10⁷, saline vs. CNO, p<0.05). Real time qPCR analysis further indicated that activation of SFO neurons that project to the PVN resulted in a marked upregulation of liver markers of de novo lipogenesis and gluconeogenesis (e.g. *DGAT1*: 3.6 0.3 fold saline, p<0.05; *G6Pase*: 2.6 1.0 fold saline, p=0.12). Importantly, these changes occurred independent of differences in body weight (25 1 vs. 25+1 g, saline vs. CNO, p<0.05) and food intake. Collectively, these findings indicate that short-term activation of excitatory SFO PVN-projecting neurons results in a NAFLD phenotype characterized by elevated liver triglycerides and disruptions in liver metabolic markers. Furthermore, these findings suggest that manipulating this forebrain-hypothalamic network in the context of obesity may be a novel approach to target NAFLD.

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Exploring 22q11.2 Deletion Syndrome in Murine Laryngeal Motor Neurons: An Electrophysiological Approach

Pediatric dysphagia, difficulty in swallowing and feeding, is one of the most common problems associated with various developmental disorders, and is especially prevalent in patients with 22q11.2 Deletion Syndrome (22q11DS). The act of swallowing is largely regulated through vagal innervation to the larynx from laryngeal motor neuron cell bodies located within the medullar portion of the brainstem. One laryngeal structure in particular, the epiglottis, is especially important as it works to seal off the trachea during active swallowing, preventing aspiration into the lungs. Using a large deletion (LD) mouse model for 22q11DS, the objective of this work aims to establish and characterize changes in the electrophysiological properties of laryngeal motor neurons that occur in LD animals. The spontaneous firing, evoked firing, voltage-gated currents, as well as both excitatory and inhibitory synaptic neurotransmission to laryngeal motor neurons recorded from the LD animals was quantified and compared to those from wild-type (WT) littermates. Preliminary data suggests that laryngeal neurons from LD animals possess a higher spontaneous action potential (AP) firing frequency than those from WT animals. Additionally, while excitatory postsynaptic currents (EPSCs) appear to occur at the same frequency in both LD and WT laryngeal motor neurons, the spontaneous excitatory events are reduced in amplitude in the LD neurons compared to those from the WT animals. Our overall goal is to determine the different electrophysiological properties of laryngeal neurons from LD animals compared to WT littermates. This work aims to provide the foundation needed to later identify therapeutic targets and hopefully develop novel treatments to restore laryngeal activity, as well as future possible treatment strategies for pediatric dysphagia associated with 22q11DS.

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The Relationship of Language and Explicit Memory in Pediatric Epilepsy

OBJECTIVE

Memory and language are often at risk in pediatric epilepsy but findings are mixed. We investigated the relationship between explicit memory and language in children with epilepsy and controls using data-driven statistical methods applying model-based clustering to explore if different cognitive profiles emerge.

PARTICIPANTS AND METHODS

276 children ages 6.1 to 17.5 were evaluated as part of ongoing studies. 149 patients with focal epilepsy (EPI) and 127 typically developing children (TD) completed language (EOWPVT, WASI VIQ) and memory (CVLT-C) measures. Six normative z-scores were used (4 from CVLT-C) for: (1) Pearson r correlations and (2) the model-based clustering procedure. For the latter, we applied Gaussian finite mixture model-based clustering on the 6 scores through R package mclust using Bayes Information Criterion to determine if scores clustered into distinct profiles and how EPI and TD fell in each profile. Epilepsy variables were compared to ascertain if they related to group membership.

RESULTS

Language scores were positively correlated with all memory scores (r 's > 0.26, p 's \leq 0.001). The optimal cluster number was 2 across TD and EPI; language and memory separated into high ($n=206$, $M z=0.44$, $EPI=46\%$, $TD=54\%$) and low performance groups ($n=70$, $M z=-1.04$, $EPI=77\%$, $TD=23\%$). The groups did not differ on age. Within EPI only, 2 was also the optimal number of clusters. Even though the majority of the low group was EPI, it represented only 1/3 of all patients. Epilepsy variables were no different across groups.

CONCLUSIONS

Language and memory are associated and when included in model-based clustering two distinct groups were revealed. The method found heterogeneity within EPI that may explain prior mixed results. Parsing groups in a data driven manner may reveal subgroups that may have biomarkers for their cognitive profiles thus indicating a protective factor or a risk. Further studies will test for biomarkers (e.g. findings from structural or functional imaging) that predict these cognitive profiles.

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Environmental Enrichment Promotes Generation of New Oligodendrocytes and Attenuates Hypoxia-Induced Perinatal White Matter Injury

Hypoxic damage to the developing brain sustained as a consequence of preterm birth is associated with permanent neurodevelopmental disabilities. This oxygenation failure predisposes preterm infants to white matter (WM) injury and is associated with many anatomical changes, the most distinctive of which is damage to the periventricular WM. This diffuse WM injury results in the loss of glial cells and causes a significant disruption in myelination, which leads to cognitive and behavioral impairments throughout childhood. However, the mechanisms underlying glia susceptibility and altered WM development as well as the potential for functional recovery from hypoxic injury are not fully understood. Here, we focus on utilization of an enriched environment to attenuate the effects of perinatal hypoxia (HX) on WM development.

Environmental enrichment (EE) is a noninvasive combination of social and physical enhancement of surroundings that provides mammals with more complex social interactions, exposure to novel stimuli, and an opportunity for voluntary physical activity. Previous studies demonstrated that the environment affects both neural plasticity and functional recovery after brain injury. Furthermore, social, family, and environmental factors contribute to improved cognitive outcome of premature children. Therefore, the environment plays a crucial role in promoting functional recovery in the CNS, and may play a role in the repair of developing WM after HX injury.

Data obtained using an established rodent model demonstrate that EE ameliorates the effects of perinatal HX and enhances oligodendrocyte regeneration after injury. Further, EE improved performance on a WM-specific behavioral task. Interestingly, EE did not have a WM effect on mice maintained under normal physiological conditions, but did induce hippocampal neurogenesis in a set of normoxic control experiments. *This project will test the hypothesis that the resultant oligodendrogenesis and behavioral improvement seen following HX and subsequent EE will lead to enhanced myelination.* Control experiments will be performed to determine the relative individual contributions of locomotor activity and increased socialization, as well as an investigation of alternate time-sensitive paradigms of EE to determine whether critical periods of exposure and recovery exist. Further, using genetic manipulation, we will determine if WM-dependent behavioral improvements seen with EE require de novo myelination.

While considerable progress has been made in identifying and modulating the mechanisms involved in premature brain injury, additional research is needed. The proposed study will not only shed light on the cellular and molecular mechanisms of WM injury, but will also aid in the development of new therapeutic approaches for enhancing recovery after early postnatal hypoxic injury during critical periods of neurodevelopment.

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Hypertensive Actions of Long Chain Fatty Acids are Paralleled by Toll-Like Receptor 4 Upregulation and Nuclear Factor- κ B (NF κ B) Activation in the Subfornical Organ

Obesity-induced hypertension is characterized by a low-grade inflammatory state along with elevations in circulating long-chain fatty acids (LCFA). Toll-like receptor 4 (TLR4) is a transmembrane receptor that is activated by LCFA, resulting in downstream inflammatory processes. The central nervous system (CNS) is critical for the control of blood pressure, with the circumventricular subfornical (SFO) organ playing a critical role. The contribution of CNS TLR4 in blood pressure regulation, particularly within the SFO, remains unclear. We hypothesized that an SFO LCFA-TLR4-inflammatory pathway is associated with elevations in blood pressure. Adult male C57B1/6 mice were instrumented with radiotelemeters for the measurement of blood pressure and implanted with an intracerebroventricular (ICV) cannula. Following recovery, a LCFA (oleic acid, 30 nmol), or vehicle control, was administered once a day over 2 days. Whereas mean arterial blood pressure was unchanged in control animals, 2-day ICV infusion of LCFA resulted in a pro-hypertensive response (day 2: 95 ± 2 vs. 110 ± 2 mmHg, vehicle vs. LCFA, $p < 0.05$, $n = 4$). Real-time quantitative PCR analysis revealed SFO TLR4 mRNA upregulation following central LCFA administration when compared to vehicle (1.1 ± 0.3 vs. 2.3 ± 0.4 fold vehicle, vehicle vs. LCFA, $p = 0.05$, $n = 4$). Based on this, we further evaluated TLR4 protein expression in the SFO using immunohistochemical analyses. TLR4-expressing cells were found predominately within the medial to caudal regions of the SFO. Co-immunolabeling indicated that SFO TLR4-expressing cells were exclusively microglia (Iba1 co-localization: $75 \pm 4\%$ TLR4 cells, $n = 3$), whereas no co-expression was found on astrocytes or neurons. Given that TLR4 activation results in the activation of the inflammatory transcription factor NF κ B, we subsequently assessed LCFA-TLR4 mediated activation of NF κ B in the SFO using an in vivo bioluminescence imaging technique. Male C57B1/6 mice ($n = 2$) underwent SFO-targeted injection of an adenovirus encoding firefly luciferase downstream of the NF κ B consensus sequence to allow for in vivo imaging of SFO NF κ B activity. Two-day ICV LCFA administration resulted in SFO NF- κ B activation that was evident within 24 hrs (1.3 ± 0.2 fold baseline) and maintained at 48 hrs (1.3 ± 0.4 fold baseline). These findings indicate that LCFAs act within the CNS to increase arterial blood pressure. Moreover, the hypertensive actions of LCFA are paralleled by SFO TLR4 upregulation and NF κ B activation, suggesting that a LCFA-TLR4-NF κ B network in this nucleus may contribute to hypertension development, such as during obesity.

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Determining the Role of Pre-Synaptic NMDA Receptors in Retinofugal Topographic Map Formation

Efficient processing of sensory information is a critical function of the nervous system. Deficits in sensory processing and integration are commonly seen in neurodevelopmental disorders such as autism and fragile X syndrome. In the visual system, neurons are organized topographically, such that neighboring neurons monitor adjacent regions of space; retinal ganglion cells (RGCs) project topographically to the superior colliculus (SC) and dorsal lateral geniculate nucleus (dLGN). The establishment of topography in both the SC and the dLGN is dependent on spontaneous correlated activity. However, the mechanisms by which activity mediates topographic map formation remain uncertain. Previous studies suggest that N-methyl-D-aspartate receptors (NMDARs) play a critical role in the establishment of topography by RGCs; however, it is unclear if they are required pre- or post-synaptically. To determine the role of pre-synaptic NMDARs in retinofugal topographic map formation, we used a conditional genetic strategy to specifically ablate NMDAR function in RGCs. We focally labeled RGCs and visualized the termination zone (TZ) of their projections in the SC and dLGN. Our data suggests that there was no change in TZ size in adult mice. To determine if eye specific segregation was disrupted in these animals, retinogeniculate projections were visualized with cholera toxin beta. Both adult and mouse pups showed no significant difference in eye-specific lamination at various ages. Together, these data suggest that retinogeniculate and retinocollicular topographic map formation do not require pre-synaptic NMDAR activity.

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Outcomes of Patients with Unicoronal Craniosynostosis Treated by Endoscopic Strip Craniectomy

BACKGROUND

Unicoronal craniosynostosis (UCS) results in craniofacial deformities including recessed forehead, orbital dystopia, and angulation of the nose and face. This condition traditionally has been treated with bifronto-orbital advancement, but facial and nasal angulation can remain as a significant issue. Endoscopic strip craniectomy (ESC) and helmet therapy is being used more frequently to treat craniosynostosis. This study evaluated the change in fronto-facial asymmetry in infants with UCS who were treated with ESC.

METHODS

This IRB-approved, retrospective study included 16 patients who underwent ESC and postoperative helmet therapy. Cranial anthropometric data was collected preoperatively and during follow-up visits after surgery. Pre-operative and follow-up photographs of patients were analyzed using ImageJ software. Craniometric analysis was conducted for forehead asymmetry (defined by difference of midline occipital to left frontal and midline occipital to right frontal measurements), nasal angulation, and facial angulation.

RESULTS

The mean follow-up was 30 months. In the ESC patients, mean nasal tip angulation improved from 12.4 degrees preoperatively to 4.3 degrees at follow-up ($p < 0.01$). Mean facial midline angulation improved from 4.8 degrees preoperatively to 1.5 degrees at follow-up ($p < 0.01$). Forehead asymmetry improved by 60 percent in the first 11 months after ESC, and by an additional 4 percent at 30 months post-surgery ($p < 0.05$). The greatest improvement in anthropometric measurements, particularly the recessed forehead, was noted at approximately 11 months after surgery.

CONCLUSIONS

Our study provides evidence of statistically significant improvement of forehead asymmetry, nasal angulation, and facial angulation in patients who underwent ESC followed by helmet therapy.

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Prevalence of MCI and Dementia in Parkinson's Disease

BACKGROUND

Although Parkinson's disease (PD) was traditionally defined by its motor symptoms, cognitive impairment has increasingly been considered as part of the disease process. Although one third of patients will have mild cognitive dysfunction at initial presentation, studies have postulated that over 80% of patients will continue to develop dementia. We aimed to assess the prevalence of both MCI and dementia in participants who were deemed to have PD on autopsy.

METHODS

One of the goals of the Johns Hopkins Morris K. Udall Parkinson's Disease Research Center autopsy study is to examine the relationship between the clinical symptoms of PD and the disease process in autopsy brain tissue. We analyzed cognitive testing, depression and anxiety scales, caregiver burden scales, and the most recent medical records prior to death to assess whether each participant had normal cognition, MCI, or dementia based on the Movement Disorder Society (MDS) Task Force guidelines for diagnostic criteria for PD-MCI and PDD.

RESULTS

There were 174 participants with an average of 77.1 years old at the time of autopsy, 31.6% of whom were women. Participants completed an average of 15.99 years of education and suffered from PD for an average of 15.86 years. Depression was present in 41 participants (23.56%). Dementia was diagnosed in 129 participants (74.13%), whereas 18 participants had normal cognition (10.34%). MCI accounted for 14 participants (8.04%). Another 4 participants were postulated to have MCI based on the records we analyzed, however due to missing data they did not meet the strict criteria. In total, 13 (7.04%) of the participants had insufficient data to use the MDS diagnostic criteria to determine their cognitive status.

DISCUSSION

The majority of participants developed PDD at some point in their disease course. However, there were a subset of patients with similar disease duration who had MCI that did not progress to PDD. Further investigation should be done to explore the cognitive domains affected by MCI and dementia to determine whether MCI is a separate disease entity or part of the spectrum of neurocognitive disorder.

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Toward a Physiological Model of Consciousness: A Proposed Website and Study Design to Integrate Connectome-Based Data Repositories, EEG/Sleep Waveforms, and Network-Based Models of Consciousness

Several major efforts are underway to construct neurological connectomes that will model typical (and atypical) brain anatomy (i.e., neural circuitry) at various stages of human development. How consciousness emerges from the working brain is still under considerable debate. Stanislas Dehaene et. al. devised a method to observe (using EEGs) the difference in brain activity when a stimulus is perceived versus when it is not. As a result, they have identified at least four signatures of consciousness that aid in our ultimate goal to construct a physiological model of consciousness.

As consciousness may have a different meaning to different people, it is important to state an operational definition for it. Here, we operationally define consciousness as “the brain state of being awake; a state of awareness ranging from alert to drowsy, but not including the various stages of sleep, minimal consciousness, coma, or brain death.” While there are many network-based models of consciousness (e.g., The information workspace model, the default mode network, the anticorrelated network, etc.), these functionally based models tend to ignore anatomical and other physiological constrictions (such as the inhibitory or excitatory nature of specific neurotransmitter cell types).

With our operational definition in mind, there are two purposes to this poster: 1) Create a data exchange format in order to automatically extract or exchange connectome data; and 2) Design an EEG-based study to determine the location of the neural circuitry involved in conscious activity.

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Interpreting Clinical Exome Sequencing Results in Unexplained Neurodevelopmental Disorders

Autism spectrum disorder (ASD) and intellectual disability (ID) are disorders that affect brain development often leading to impairments in daily life skills and posing a burden on families and the healthcare system. Recent efforts to better understand these conditions have centered around exploring the genetic component of these diseases. Clinical exome analysis, which is the process of examining the portion of a genome coding for proteins, is now standard clinical practice when it comes to investigating cases of unexplained ID and/or ASD. This project focuses on two cases who present with a spectrum of neurodevelopmental delay, including, ID, ASD, attention-deficit/hyperactivity disorder (ADHD) and seizures. Through exome analysis, it was discovered that affected individuals had mutations in the CC2D1A gene. CC2D1A is a signaling scaffold that was found mutated in individuals with ASD, ID, and seizure disorders and could be a good candidate to explain the presentation of these individuals.

To determine if CC2D1A mutations are responsible for the pathology in these cases, we retrospectively analyzed the medical records of a cohort of patients with other CC2D1A mutations. Comparison of these groups of patients showed that their clinical presentations were similar. The mutations in our two cases alter the sequence of the CC2D1A protein, but not its expression, and their effect on protein function is uncertain. To determine whether these mutations could be damaging, we are using pathogenicity prediction software and are performing functional studies on the CC2D1A protein in human cell lines. We hope that through the studying of these mutations we can determine that they are causative and be able to give an explanation to the process that is occurring at the molecular level, leading to the clinical presentation.

In conducting this retrospective analysis, we have established a foundation for future work with the goal of identifying a link between mutations in the CC2D1A gene and the clinical presentation observed in those patients with a spectrum of ASD and ID. Future work will examine the in-vivo manifestations of these mutations in the brain to better understand how they affect neural function.

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Behavioral Impact of the Disinhibition of the Dopaminergic Neurons in the VTA via Inhibition of VTA GABAergic Neurons Using the Subchronical Variable Stress Paradigm

Depression is the leading cause of disability worldwide, with over 300 million people affected by the disorder (World Health Organization, 2018). Women are twice as likely to be diagnosed with depression as men, yet most animal research into the disorder and its symptoms is performed in only males. This creates a gap between preclinical experiments and their potential clinical use. Females display different neurobiological, behavioral and transcriptional responses when dealing with stress that leads to depressive phenotypes (Dalla et al., *Physiology and Behavior*, 2008; Hodes et al., *Journal of Neuroscience*, 2015; La Plant et al., *Biol Psychiatry*, 2009). Subchronic variable stress (SCVS) is a stress paradigm that induces depression and anxiety like symptoms in female mice, and leaves male mice behaviorally unaffected.

The ventral tegmental area (VTA) is a crucial hub in the mesolimbic reward pathway, sending dopaminergic projections to regions like the nucleus accumbens (NAc) and prefrontal cortex. Due to its role in reward seeking behavior and motivation, dysregulation of the VTA circuitry has been implicated in mood disorders. The function of dopaminergic neurons within the VTA is controlled by the GABAergic networks both locally, in the VTA, and by inputs from outside the VTA. In the VTA, GABAergic neurons are activated by stress and inhibit the dopaminergic VTA neurons that are involved in reward seeking and motivation. In addition, several studies using animal models of depression have found that there is altered activity of the dopaminergic neurons of the VTA (Nestler, E., Carlezon, W A., *Biol Psychiatry*, 2006). The role of VTA GABAergic neurons in stress-induced depressive behavior has not been studied. In this project, we used SCVS to study the effect of chemogenetic inhibition of local GABAergic neurons in the VTA on the behavioral responses to stress. AAVs encoding Cre-dependent inhibitory designer receptors exclusively activated by designer drugs (DREADDs) were injected into the VTA of VGAT-cre mice, allowing VTA GABA neurons to be selectively inhibited by the otherwise-inert ligand CNO. The impact of this manipulation was tested through a variety of behavioral tests that assayed for anxiety and depressive-like phenotypes. We hypothesized that disinhibition of the dopaminergic neurons in the VTA via inhibition of VTA GABAergic neurons will alleviate the behavioral effects of SCVS in female mice.

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Reduced Corneal Innervation in the CD25KO Model of Sjögren Syndrome

PURPOSE

Decreased corneal innervation is a frequent finding in patients with Sjögren Syndrome (SS). The purpose of this study was to investigate the density of intraepithelial corneal nerves (ICNs) and corneal sensitivity using the well-characterized IL-2 receptor alpha chain (CD25KO) model of SS.

METHODS

Corneal barrier function was examined by uptake of a fluorescent dye and graded by two masked observers in CD25KO and wild-type (WT) mice. Whole-mount corneas were used to quantify ICN density and thickness using BIII tubulin staining. Mechanical corneal sensitivity was measured using a modified Cochet-Bonnet esthesiometer. Quantitative PCR was performed on RNA isolated from the corneal epithelium to quantify expression of beclin 1, LC3, Lamp-1, Lamp-2, CXCL-1, BDNF, NTN1, DCC, Unc5b1, Efna4, Efna5, Rgma, and p21 in corneal epithelial mRNA.

RESULTS

CD25KO mice had significant greater corneal barrier disruption than WT mice. This was accompanied by a significant reduction in axon density and mechanical corneal sensitivity. Real-time PCR results indicated that CD25KO mice have increased expression of genes regulating phagocytosis and autophagy (beclin-1, LC3, LAMP-1, LAMP-2, CXCL1 and BDNF) while no change was observed in genes related to axonal targeting and extension (NTN1, DCC1, Unc5b1, Efna4, Efna5, Rgma and p21).

CONCLUSIONS

Decreased anatomic corneal innervation in the CD25KO model of SS is accompanied reduced corneal sensitivity and increased expression in the corneal epithelium of genes regulating phagocytosis and autophagy.

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Activation of Angiotensin Type 2 Receptor (AT₂R) Contributes to Fear Memory

BACKGROUND

Previous clinical studies identify the renin-angiotensin system (RAS) as a potential therapeutic target in post-traumatic stress disorder (PTSD), however the mechanism(s) are unknown. We propose that brain angiotensin receptors modulate inhibitory and excitatory fear circuits critical to the consolidation and extinction of fear memory in PTSD.

METHODS

Using a transgenic brain angiotensin type 2-receptor (AT₂R) eGFP-BAC reporter mouse combined with pharmacological and behavioral approaches, the aim of the study was to examine the role of the brain AT₂R in fear memory.

RESULTS

We first assessed AT₂R-eGFP⁺ immunoreactive cell types in the mouse brains, which were highly co-localized with the neuronal specific marker NeuN. There were no detectable levels of co-localization in astrocytes (GFAP as a marker) or microglia (Iba-1 as a marker). We then quantified the number of AT₂R-eGFP⁺ expressing neurons in the major subnuclei of the amygdala, an important structure in the consolidation and extinction of fear memory. AT₂R-eGFP⁺ neurons were predominately observed in the medial amygdala (MeA) (203.8 ± 39.4 cells/mm²) and the medial division of central amygdala (CeM) (221.2 ± 15.3 cells/mm²), while the basolateral amygdala (BLA) (11.7 ± 1.8 cells/mm²) contained very few AT₂R-eGFP⁺ neurons. Moreover, within the CeM, 96% of the AT₂R-eGFP⁺ neurons expressed the GABAergic marker GAD1, while approximately 40% GABAergic cells expressed interneuron markers calbindin and nNOS. To examine the behavioral role of AT₂R in fear memory, we used classic Pavlovian fear conditioning, pairing auditory cues with footshocks. Following the acquisition of fear, AT₂R mRNA expression was significantly elevated ($t(22) = 2.5$; $p < 0.05$) within the CeA but not following extinction learning. In separate studies, a bilateral intra-CeA injection of the AT₂R agonist C21 (0.06ug/ul) was administered prior to fear acquisition testing and freezing behavior was quantified. Compared to vehicle controls, mice receiving C21 into the CeA displayed enhanced extinction by a decreased percentage of freezing (61.7% ± 5.4 vehicle v.s. 42.1% ± 5.7 C21 group, $p < 0.05$, $n = 10-12$) during repeated conditioned stimuli (30 second auditory tones). These behavioral results were independent of general anxiety-like measures as C21 did not affect locomotor activity or center entries in the open field test.

CONCLUSIONS

Together, these data provide anatomical, functional and behavioral evidence for activation brain AT₂R in the consolidation and extinction of conditioned fear. Further studies are required to determine the neurobiological mechanism(s), which may involve changes in cerebral vascular blood flow and/or modulation of neuronal excitability and plasticity.

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Non-Invasive Blood Tests to Detect Significant Fibrosis In Morbid Obesity (MO)

Studies have found a correlation between non-invasive blood test indices and significant fibrosis (SF) on liver biopsy in patients with obesity and Nonalcoholic Fatty Liver Disease (NAFLD). Patients with MO (BMI ≥ 40 kg/m²) have a high prevalence of NAFLD and SF on liver biopsy, but the ability of non-invasive tests to predict SF has not been well studied in MO. This study is designed to find the prevalence of non-alcoholic steatohepatitis (NASH) and SF in patients with MO and the ability of non-invasive tests to predict SF.

METHODS

The study is a retrospective review of all patients with Morbid Obesity who underwent gastric bypass surgery with wedge liver biopsy during Y2015-2017 at GWU in whom clinical and lab data was available in the EMR within 6 months before surgery. Inclusion criteria were diagnosis of MO (BMI ≥ 40 kg/m² or > 35 kg/m² with Diabetes or Hypertension) and data for sex, age, BMI, Diabetes, platelets, AST, ALT and albumin; exclusion criteria were no other potential causes of liver pathology, including alcohol. Review of biopsy reports noted SF (moderate-bridging fibrosis/ cirrhosis) or non-significant fibrosis (NSF—none/mild) and evidence of NASH. Non-invasive indices and cut-offs to estimate SF on biopsy included NAFLD fibrosis, BARD, APRI and Fib4 scores (based on combinations of age, BMI, Diabetes, AST, ALT, platelets and albumin), using on-line calculators (GIHep.com).

RESULTS

Total 105 patients with MO met study criteria, 7 with SF and 11 with NASH. All patients with SF had NASH. Patients were age 45 ± 10 yrs, BMI 47.2 ± 9.1 kg/m² and 85.7% female. Diabetes was more prevalent in patients with SF vs NSF (85.7% vs 43.9%) and in those with NASH (63.6%). ALT was elevated (> 40 IU/L) in 25.7% of cases, 85.7% of cases with SF and 72.7% with NASH. Other Predictive values for non-invasive blood tests to detect SF on biopsy found:

ALT-	sensitivity 85.7%,	specificity 78 %,	PPV 22.2%,	NPV 98.7%;
APRI -	0 %,	100 %	0 %	93.2%;
Fib4 -	0 %,	91.6%	0 %	92.6%;
BARD -	86 %,	35.1%	8.7 %	97.1%;
NAFLD -	28.6%,	84.2%	11.8 %	94.1%.

CONCLUSIONS

In comparison to the more sophisticated non-invasive test indices used for detecting SF on liver biopsy in NAFLD, this study found that a simple ALT test had the best sensitivity and specificity for detection of SF on liver biopsy in patients with MO.

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Obesity and Postoperative Complications in Patients Undergoing Laparoscopic Hysterectomy

BACKGROUND

The prevalence of obesity in American women is 38.3%. Hysterectomy is the second most common surgery in reproductive age women; most of these procedures are performed laparoscopically. From 2011 to 2015, 3.2% of women age 15-44 years underwent hysterectomy; 89.6% of these procedures were performed for management of medical conditions including uterine fibroids, menstrual disorders, uterine prolapse, and endometriosis. The high rates of obesity and hysterectomy in women demand better understanding of the relationship between obesity and postoperative complications following laparoscopic hysterectomy.

METHODS

We conducted a retrospective cohort study using the American College of Surgeons National Quality Improvement Database (ACS-NSQIP) by identifying all patients who underwent laparoscopic total hysterectomy, laparoscopic assisted vaginal hysterectomy, or laparoscopic supracervical hysterectomy from 2007 to 2013 using Current Procedural Terminology (CPT) codes. These patients were stratified by BMI (<30, 30-39, >40); univariate and multivariate analyses were then performed to evaluate the incidence of postoperative complications in these groups.

RESULTS

Patients with BMI > 30 were more likely to experience postoperative complications including superficial surgical site wound infection, deep surgical site infection, failure to wean from the ventilator > 48 hours, unplanned reintubation, deep vein thrombosis, pulmonary embolism, urinary tract infection, renal insufficiency, renal failure, and extended hospital length of stay > 2 days. Multivariate analysis suggests that BMI > 30 is an independent risk factor for superficial surgical site infection, deep vein thrombosis, and pulmonary embolism.

CONCLUSION

Patients with obesity and morbid obesity were more likely to present with risk factors and comorbidities than nonobese patients. While complication rates following laparoscopic hysterectomy are low across BMI groups, patients with BMI > 30 were more likely to suffer from at least one postoperative complication. Data indicate that obesity may contribute to a significantly increased risk of deep vein thrombosis and pulmonary embolism in the postoperative period, suggesting the need for additional venous thromboembolism prophylaxis. Obesity should be considered when planning for and performing laparoscopic hysterectomy.

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An Alternative Measurement of Central Obesity: Abdominobesity Index (ABI)

Obesity has reached epidemic proportions in the developed world. Approximately 35.0% of men and 40.4% of women in the United States were considered obese in 2013-2014. Obesity, and more specifically central obesity, is associated with a myriad of health problems. Central obesity, also known as abdominal obesity, refers to an excess fat deposit around and within the abdominal cavity. Central obesity has been linked to hypercholesterolemia, high blood pressure, type 2 diabetes, coronary artery disease, and other health concerns.

We have established the concept of Abdominobesity Index (ABI), a new measurement to be used in quantifying a person's central obesity. We propose such a new measurement because obesity rates continue to rise in our country and various places around the world. To best solve a problem, one must understand it, in this case by measuring it as accurately as possible. Therefore, we propose this new measurement as a supplement to those that already exist for measuring obesity, such as Body Mass Index (BMI) and Waist to Hip Ratio (WHR). Our measurement is an important supplement because it specifically focuses on quantifying a person's degree of central obesity. ABI departs from previous measurements in that it specifically targets the abdominal fat by comparing abdominal circumference with chest circumference. We set forth the formula for our new ABI measurement along with a discussion of the preliminary data analysis that demonstrates the utility of ABI as a measurement distinct from BMI. In the future, we hope to conduct further studies that also track patient outcomes. In conjunction with other obesity measurements, we believe ABI will help advance further obesity research and improve risk stratification in obese patients.

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Effect of Demographic and Psychological Factors on 12-Month Outcomes in Adolescent Bariatric Surgery

BACKGROUND

Weight loss surgery is an increasingly utilized treatment for adolescents with severe obesity. This study aims to investigate the effect of demographic variables (age, gender and ethnicity) and pre-surgical mental health on the change in BMI (% excess BMI loss) after Laparoscopic Sleeve Gastrectomy (LSG) in adolescents with obesity.

METHODS

Retrospective chart review of a prospective LSG patient database (N=196, 75% female, 75% minority) was performed. Change in BMI at 3, 6 and 12 months after surgery was assessed. Mental health diagnoses evaluated using a structured interview (KSADS) were obtained at the pre-surgical evaluation. A non-linear Latent Variable Growth Model (LGM) was estimated, including demographic variables and presence/absence of diagnoses in the classes of anxiety, depression, attentional disorders, and eating disorders.

RESULTS

The presence of a diagnosis of anxiety, depression, or ADHD was not associated with change in BMI at any time point. The presence of a diagnosed eating disorder was associated with less excess BMI loss at 3 months, but not thereafter. Change in BMI at 3 months was significantly associated with change in BMI at 12 months ($r=0.892$, $P<0.001$). 6 month outcomes ($I=0.650$) had a larger effect on 12 month outcomes than those at 3 months ($I=0.516$). Age, gender, and ethnicity were not associated with 12 month change in BMI.

CONCLUSIONS

Our data indicate that there is no association of demographic variables or mental health diagnoses with 12 month change in BMI following LSG in adolescents. Thus neither age nor presence of a mental health diagnosis should be contraindications to LSG; but assessment and treatment of disordered eating should remain a key part of preparation for surgery. Also, the larger effect of the 6 month change in BMI on the 12 month outcome suggests there may be a window in which patients exhibiting suboptimal BMI change at 3 months can be identified and an intervention provided to optimize % excess BMI loss.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Insulin Receptor Signaling in the Subfornical Organ Protects Against the Development of Metabolic Syndrome

Metabolic syndrome encompasses a combination of conditions including obesity, diabetes, and hypertension. Brain insulin resistance has emerged as a contributor to the development of metabolic syndrome, although the neural regions involved remain unclear. While most investigations have focused on insulin action in the hypothalamus, recent evidence suggests that the insulin receptor (IR) gene is also expressed in the subfornical organ (SFO); a circumventricular organ well known for cardiovascular/fluid regulation and recently recognized as a metabolic nucleus. We therefore hypothesized that IR signaling in the SFO is involved in metabolic regulation. We first examined protein levels of SFO IR in male C57Bl/6 mice (n=3) using immunohistochemistry, and observed that IR expressing cells are rich in the SFO. Co-immunohistochemistry further revealed heterogeneous cellular expression of the SFO IR, with $11.9 \pm 2.2\%$ of IR-ir detected on astrocytes (GFAP), $57.2 \pm 2.6\%$ on endothelial cells (TIE2), and $18.3 \pm 0.8\%$ on neurons (NeuN). Interestingly, neuronal expression of IR in the SFO was restricted to glutamatergic cells, but absent in GABAergic cells. To test the functional role of SFO IR, we next utilized mice harboring a conditional allele of the IR gene (*IR^{fl/fl}*), and selectively knocked down the SFO IR via SFO-targeted delivery of an adeno-associated virus encoding Cre-recombinase (AAV-Cre-eGFP; n=4), or control vector (AAV-eGFP; n=3). Both groups remained on normal chow, and metabolic parameters were continuously monitored using indirect calorimetry for 12 weeks. Selective removal of SFO IR did not influence food and water intake, but resulted in a greater increase in body weight (e.g. 12 weeks: 27.9 ± 1.5 vs. 31.4 ± 1.4 g, AAV-eGFP vs. AAV-Cre-eGFP, ANOVA interaction $p=0.0005$). This was associated with a significantly lower energy expenditure (e.g. 12 week average: 12.5 ± 0.6 vs. 11.7 ± 0.2 kcal/hr/kg, AAV-eGFP vs. AAV-Cre-eGFP, ANOVA interaction $p=0.013$) and a slight reduction in ambulatory activity in AAV-Cre-eGFP mice relative to controls. Examination of regional adipose tissue also revealed a ~40% increase in overall adiposity following ablation of SFO IR (total adipose: 1.4 ± 0.4 vs. 2.2 ± 0.3 g, AAV-eGFP vs. AAV-Cre-eGFP, $p=0.1$). Whole body glucose clearance and insulin sensitivity were comparable between groups. These data demonstrate that ablation of SFO IRs under normal diet conditions results in a deleterious metabolic state. Moreover, these findings indicate a tonic metabolic regulatory role for SFO IR, and suggest that impairments in IR signaling in the SFO may contribute to a development of metabolic syndrome.

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Characteristics of Correctly Identified Pediatric Obesity and Overweight Status and Management in an Academic General Pediatric Clinic

OBJECTIVE

The goals of this study were to identify and characterize the rates of documentation and guideline-based management of overweight and obese children within an academic pediatric clinic.

POPULATION/METHODS

Overweight, obese, and severely obese children were identified from 7,422 well child visits in 2016 within a primary care clinic that cares for a primarily urban, minority (80% African American), and Medicaid (85%) population until the age of 12. During this 1-year study, there were 79 pediatric residents, 19 attending pediatricians, and 5 nurse practitioners who treated patients. Through a retrospective electronic medical record review, diagnosis and treatment including counseling, referral to a dietician, or referral to a pediatric weight management clinic, were analyzed by the patient's weight diagnosis, sex, age, and provider training level. Orders for laboratory testing as well as follow up visits were also reviewed. χ^2 analyses were performed to identify whether independent variables such as age of patient, sex, provider level of training, or weight diagnosis affected provider behavior in diagnosis and weight management. Logistic regression was utilized to calculate odds ratio estimates of likelihood of treatment by provider training level, age of patient, weight diagnosis, sex, laboratory testing and follow up.

RESULTS

As expected, older and heavier patients were more likely to be diagnosed and to receive weight management. Surprisingly, nurse practitioners and faculty demonstrated lower adherence to pediatric obesity guidelines. The percentages of correctly identified severely obese (90.2%), obese (77.0%), and overweight (42.0%) children were much higher than in previous retrospective chart reviews; however, less than 30% of children were referred for more intensive weight management to a dietician or pediatric obesity weight management program and less than 60% received counseling.

CONCLUSIONS

Despite progress in the rates of identification of weight status at primary care visits, significant improvement in adherence to intensive pediatric weight management guidelines is needed. Strategic modifications to electronic medical records that automatically offer BMI associated weight diagnoses with a link to treatment pathways and resources are needed to facilitate improved compliance with current pediatric obesity guidelines in the primary care setting.

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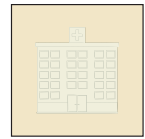
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PREVENTION AND COMMUNITY HEALTH



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Designing a Social Norms-Based Intervention to Reduce Anemia in India: A Formative Research Protocol

BACKGROUND

Economic and gender inequalities are important determinants of anemia in low and middle income countries. Gender dimensions of food security contribute to the undernutrition among women. More than half of women of reproductive age in India are anemic. Anemia causes increased risk of preterm delivery, higher maternal mortality and contributes to fatigue, which influences women's work productivity. The World Health Organization (WHO) recommends daily oral iron and folic acid (IFA) supplements during pregnancy and weekly supplements for women of reproductive age. Despite the efforts of government programs and global donors to reduce anemia in India, both initial uptake and compliance of IFA remain inadequate. Innovative, multi-level, theory-based methods are urgently needed to address the problem.

OBJECTIVE

This study will design and test the hypothesis that a social norms-based intervention in Odisha, India will promote changes in social norms, knowledge, attitudes, and behaviors of women of reproductive age and pregnant women.

METHODS AND ANALYSIS

Based on the Theory of Normative Social Behavior (TNSB), we will use a mixed-method approach that uses both qualitative and quantitative techniques. For our formative research, focus group discussions, in depth interviews, observations, and perceptual mapping techniques will be adopted. Our study sample will include reproductive age women (both pregnant and not pregnant), their husbands, their mothers/in-laws, women's self-help group leaders, local health officials, and health care providers. The formative research will examine the barriers, facilitators, attitudes and availability of IFA supplements. After analyzing the results, we will hold a convening in India with stakeholders, participants, interventionists, and researchers to collaboratively design the intervention. Following the intervention design, we will test various components of the intervention, gather user feedback and make edits as necessary. Additionally, to improve adoption and sustainability of the intervention, we will conduct ongoing policy dialogue with key stakeholders throughout the formative research.

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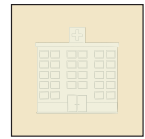
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PREVENTION AND COMMUNITY HEALTH



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Exploring the Association Between Spirituality and Condom Self-Efficacy Among Young Black Men Who Have Sex with Men (YBMSM)

BACKGROUND

While spirituality has been shown to serve a protective role in the lives of many in the Black community, it may serve a more nuanced role in the lives of young Black men who have sex with men (YBMSM). This study aimed to determine the relationship between spirituality and condom self-efficacy among a population ($n = 543$) of YBMSM from two cities in Texas.

METHODS

YBMSM were recruited via venue-based sampling and completed self-report measures of frequency of spiritual activities and strength of spiritual beliefs (predictors), condom-use self-efficacy (outcome), and internalized homophobia, belief that health is in God's hands, and resilience (mediators). We tested relationships among variables using multivariate ordinary least squares regression models, and assessed mediation using the bootstrap estimation approach with 5,000 samples.

RESULTS

The results showed that the frequency of spiritual activities was negatively associated with condom self-efficacy ($B = -0.042$, $SE B = 0.042$, $p = 0.315$), and these effects were mediated by internalized homophobia (95% BCa CI [-0.075, -0.010]) and the belief that health is in God's hands (95% BCa CI [-0.069, -0.016]). The strength of spiritual beliefs was significantly positively associated with higher condom self-efficacy ($B = 0.053$, $SE B = 0.031$, $p = 0.092$), and these effects were mediated by internalized homophobia (95% BCa CI [-0.059, -0.013]), the belief that health is in God's hands (95% BCa CI [-0.043, -0.008]), and resilience (95% BCa CI [0.012, 0.074]). Thus, men who participated more frequently in spiritual activities and men who held stronger spiritual beliefs had greater internalized homophobia and a greater belief that health was in God's hands, both of which were associated with less condom self-efficacy. However, men with stronger spiritual beliefs also had higher levels of resilience, which was associated with greater condom self-efficacy.

CONCLUSIONS

These results suggest that the relationship between spirituality and self-efficacy is multifaceted, and frequency and strength may represent different sub-constructs of spirituality. Ultimately, these results suggest that interventions to increase condom self-efficacy among YBMSM can include spiritual components to increase resilience, but these interventions must also address the internalized homophobia that these men may have developed as a result of their spiritual activities and beliefs. In addition, interventions should encourage the men to be in control of their own destiny to counter the negative effects of the belief that health is in God's hands.

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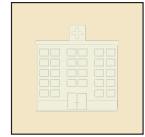
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Breast Lesions Detected via Molecular Breast Imaging: Physiological Parameters Affecting Interpretation

RATIONALE AND OBJECTIVES

To evaluate correlations between molecular breast imaging (MBI) descriptor characteristics and positive predictive value (PPV) in detecting breast cancer.

MATERIALS AND METHODS

A retrospective review was performed on 193 suspicious findings from 153 women (31-81 years) with positive MBI examinations. We assessed associations between: (i) lesion pattern (mass vs. non-mass) and PPV; (ii) lesion pattern and suspected likelihood of cancer (low vs. moderate vs. high); (iii) background parenchymal uptake (BPU) (homogeneous vs. heterogeneous) and PPV; (iv) breast density (dense vs. non-dense) and PPV; (v) BPU and density.

RESULTS

One hundred ten of 153 patients were diagnosed with malignancy or high-risk pathology (PPV1 = 71.9%), and 130/193 biopsies resulted in malignant or high-risk lesions (PPV3 = 67.4%). Biopsies of mass vs. non-mass findings had comparable PPV3 (71.7% vs 61.3%; $p = 0.0717$). Mass findings were correlated with higher suspicion for cancer than non-mass findings ($p < 0.001$). There was no significant difference in PPV3 when comparing biopsies from homogeneous vs. heterogeneous BPU (72.5% vs 60.7%; $p = 0.103$). No association was found between patients' BPU and diagnosed cancer or high-risk lesions ($p = 0.513$). Biopsies from non-dense breasts demonstrated higher PPV3 than biopsies from dense breasts (85.4% vs 60.6%; $p = 0.0025$); patients with non-dense breasts were more likely to be diagnosed with cancer or high-risk pathology (PPV1 = 87.8% vs 66.0%; $p = 0.00844$). Dense breasts had a greater association with heterogeneous BPU ($p = 0.0844$).

CONCLUSION

Neither variability in mass or non-mass positive MBI findings, nor variability in BPU on MBI were significant determinants for the probability of malignancy. Dense breasts were associated with lower predictability and heterogeneous BPU on MBI.

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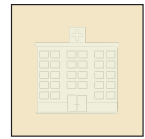
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PREVENTION AND COMMUNITY HEALTH



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Exploring How Universal Health Care in the Icelandic Community Impacts the Management of Pediatric Allergy

BACKGROUND

Iceland is a small Nordic country (population of 300,000) that has publicly funded healthcare, with the government paying for 80% of healthcare services and a small percentage of physicians working in private practice (fee-for-service). Experiential learning is a method in which an individual interacts with, observes, and reflects upon their environment in order to achieve new understanding, ideas and applications.

OBJECTIVE

The objective of this project was to understand how allergic disease in pediatric populations (a problem of increasing prevalence) is being handled by Icelandic physicians, community organizations and their healthcare system using experiential learning principles.

METHODS

Methods used to explore these research questions included key informant interviews, site visits, literature review, and shadowing pediatric providers over a period of two months.

RESULTS

Student gained an in-depth understanding of the factors in Iceland that affect medical care in the context of pediatric allergy. These factors include a culture of stewardship and equity in the healthcare setting, a newly emerging concept of public health pertaining to asthma prevention and food allergy awareness, a high education level of the general population affecting the utilization of healthcare resources, and the restrictions of cost and availability of services in a government funded healthcare system.

CONCLUSION

The benefits and drawbacks of the Icelandic healthcare system tended to be very specific to the country's ideology, geography, and resources. However, exploration on how the culture of a universal health care model might apply to the US healthcare system and medical education are of interest for future research.

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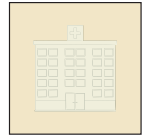
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PREVENTION AND COMMUNITY HEALTH



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Omni Med Enhanced VHT Pilot

Omni Med is a Non-Governmental Organization in Uganda. In partnership with the Ministry of Health, Omni Med uses the Village Health Team (VHT) model to target health promotion and disease prevention through its initiatives. Omni Med trains VHTs to operate as educators and leaders in their communities to spread awareness of healthy practices such as condom use, sanitation and hygiene. In addition to using the VHT model, Omni Med has incorporated several other projects to enhance the VHT program's impact in the community. These projects include building clean water sources, constructing clean burning cook stoves, and distributing mosquito nets which respectively aim to decrease the incidence of diarrheal diseases, pneumonia, and malaria.

The aim of this pilot study is to evaluate the impact of Omni Med's Enhanced VHT program. It is a qualitative and quantitative evaluation of community health indicators before and after the implication of Omni Med's Enhanced VHT model in a community where Omni Med has not previously operated. To evaluate the program, we developed a questionnaire in collaboration with Omni Med staff and VHT leaders to address three key indicators: 1) the incidence of diarrheal diseases; 2) the incidence malaria; 3) the incidence of pneumonia. The questionnaire will be administered by community health workers to collect the data. The project has received approval from an International Review Board

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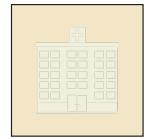
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Nationwide Epidemiological Approach to Firearm-Related Emergency Department Visits from 2005-2015

BACKGROUND

The majority of gun violence research focuses on local data and examines all violent assaults broadly. We analyzed the epidemiological risk factors associated primarily with firearm-related injuries that were managed within emergency departments (ED) nationwide.

METHODS

This study uses the CDC's National Hospital Ambulatory Medical Care Survey (NHAMCS) to complete a retrospective analysis of firearm injuries managed within US EDs from 2005-2015. All visits related to intentional injury were examined, and an analysis of gunshot injuries was completed, and compared to other assaults resulting in ED visits. Bivariate analyses and logistic regressions were performed to elucidate the relationship between these visits and patient demographics.

RESULTS

From 2005-2015 NHAMCS data, 318,114 patient visits were included which represented an estimated 1.25 billion ED visits. Of these, 644,711 were the result of a gunshot wound. In total, gunshot victims demonstrated increased odds (OR 3.4 95% CI 2.4-4.9 $p < 0.001$) of identifying as Black. These Black gunshot victims were overwhelmingly male (90.2% vs 75.7%) and had a younger average age (26.8 vs 32.8) than their White counterparts. Black patients aged 15 to 25 represented 26.7% of all US ED visits within their age-range, but represented 66.1% (95% CI 49.3-79.7 $p < 0.001$) of gunshot victims and 33.7% (95% CI 29.4-38.2 $p < 0.001$) of all assault victims. In this same age group, Black youth represented a disproportionately smaller proportion of ED visits for self-inflicted injury (15.9%, 95% CI 12.9-19.5). Young Black gunshot victims showed increased odds of being intubated in the ED (OR 20.1, 95% CI 8.0-54.0 $p < 0.001$), dying within or en-route to the ED (OR 13.7, 95% CI 3.5-53.6 $p < 0.001$), having an assault-related injury (OR 57.2, 95% CI 24.4-134.7), or receiving any imaging services (OR 6.4 95% CI 2.6-15.7 $p < 0.001$).

CONCLUSION

Black male youth between the ages 15 and 25 are particularly at risk for sustaining gun violence related injuries. This same subset of patients is more likely to utilize an increased number of resources within EDs for management of injuries.

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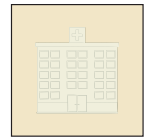
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PREVENTION AND COMMUNITY HEALTH



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Depression, Substance Abuse and Women's Health

BACKGROUND

Substance abuse during pregnancy is a serious and dangerous problem that can lead to adverse child health outcomes. Several studies have explored the effects of alcohol, tobacco and opioid use upon fetal development and consequences in early childhood. The linkages between mental health and substance abuse are unequivocal and have been well known for several years. However, there are very few studies which explore associations between mental health, substance abuse and health outcomes for women of reproductive age.

PURPOSE

The specific aim of this secondary data analysis is to examine maternal mental health, substance abuse and health outcomes for mothers. This study will also consider sociodemographic characteristics that may show disparities among substance abuse in pregnant women. This project aims to find relationships between maternal depression and substance abuse during and after pregnancy.

METHODS

This project will utilize SPSS software to conduct a secondary data analysis using cross-sectional data of the 2015 National SAMHSA dataset for National Surveys on Drug Use and Health (NSDUHs). This project will replicate data analysis of previous NSDUH analysis starting with the 2015 data and merge the data sets of previous years if more data is needed. This project will also consist of a literature review to find any correlations which support the findings in this topic area.

RESULTS

Multivariate analytic techniques will look at maternal depression and substance abuse before, during and after pregnancy; health outcomes and mental health status among women who reported prenatal substance abuse or substance abuse during pregnancy and the sociodemographic characteristics that may show disparities among substance abuse in pregnant women.

DISCUSSION

Results will be used to formulate policy and analysis surrounding women's health, substance abuse and mental health.

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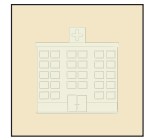
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PREVENTION AND COMMUNITY HEALTH



MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Examining Race, Weight, and Mental Health Among Young Adults

BACKGROUND

With the growing obesity epidemic, young adulthood is a high risk period for weight gain and obesity. In the U.S., approximately one-third of young adults are obese and at risk for weight gain. Recent studies suggest depressed young adults are at a higher risk for the development and persistence of obesity. Research suggests that demographic factors moderate the relationship between obesity and mental health. Weight stigmatization is also a common perception that is related to negative health outcomes for overweight and obese individuals including anxiety, depression, low self-esteem, and body dissatisfaction. A personal fear of being stigmatized can prevent young adults from seeking mental health services and is linked to decreased rates of self-reporting a mental health diagnosis, adherence to psychotropic medications, and therapy.

PURPOSE

The purpose of this study is to examine the relationship among self-disclosure of diagnosis and treatment for mental health. The primary research questions are: 1) how does weight status relate to the prevalence of mental health diagnoses; 2) what is the concurrence between self-report of mental health diagnoses and self-report of psychotropic medications. Two supplemental research questions include: how both of the above vary by sociodemographic characteristics (i.e. race/ethnicity, sex, age).

METHODS

We will conduct data analysis from the online screening questionnaire of the Healthy Body Healthy U study. Data referring to mental health history, psychotropic medication, as well as demographic information will be analyzed using SPSS software.

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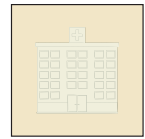
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The Impact of Campaign Related Conversation Regarding the truth® Anti-Smoking Campaign Among Youth and Young Adults

BACKGROUND

In 2014, the national truth® campaign launched a new phase of the campaign targeted at a broad audience of youth and young adults, to help end the tobacco epidemic. The purpose of this study was to examine the impact of campaign-related conversation about a national youth smoking prevention campaign and campaign exposure on anti-smoking attitudes.

METHODS

Analysis were conducted using data from the Truth Longitudinal Cohort, a probability-based, nationally representative cohort. The sample for this study was limited to those with data at baseline and five subsequent follow-up surveys.

RESULTS

Among nonsmokers (n=5,594) linear regression models indicate that having a campaign-related conversation are significantly associated with reporting higher levels of agreement of campaign-targeted anti-tobacco beliefs and attitudes. Results also suggest a that respondents with high campaign exposure compared to low campaign exposure are 5.6 times the odds of having conversation about the campaign.

CONCLUSIONS

Findings from linear and logistic regression models show that anti-smoking messages are conveyed through campaign exposure and campaign-related conversation. Theoretical and practical implications for campaign planning of public education mass media campaigns are a key component to changing tobacco use attitudes and behavior among youth and young adults.

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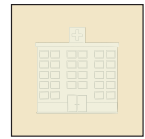
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PREVENTION AND COMMUNITY HEALTH



SCHOOL OF MEDICINE AND HEALTH SCIENCES

Cancer Screening Rates in the Bridge to Care Student-Run Free Clinic Population of Prince George's County Maryland

BACKGROUND

Breast, colon, and cervical cancer screening reduce morbidity and mortality. Cancer screening in underserved communities is lower than national averages leading to increased incidence and mortality in this population. GWSMHS's student-run free Healing Clinic site in Prince George's County, Maryland is thought to have a largely uninsured and Hispanic, population. It has the ability to perform pap smears on site. There are 5 known referral clinics for breast cancer screening, and 1 known referral clinic for colorectal cancer screening. Formal assessment of the clinic's demographics and cancer screening rates are crucial to decrease health disparities and improve the health of the Bridge to Care clinic population.

METHODS

A 10-item questionnaire was verbally administered in English or Spanish to each participant by a member of the research team in a private area of clinic. Telephone interpretation provided through Globo was utilized for some Spanish speakers and all other non native-English speakers. The questionnaire screened for previous mammography in the last 2 years, Pap smear in the last 3 and 5 years, fecal occult blood test in the last year, and colonoscopy in the last 5 and 10 years. Inclusion criteria were based on the 2016 breast, 2012 cervical, & 2008 colorectal USPSTF cancer screening guidelines. Participants were deemed eligible if current age met screening criteria or if age at last screening met criteria.

RESULTS

There were 39 total participants, of which 56% were male, 44% female; 67% were Hispanic, 31% African American, and 3% Asian. The population had an average age of 49.5, SD 14.1. 11, 20 and 14 patients were eligible for breast, cervical and colorectal cancer screening respectively. 5/11 eligible patients had been referred for mammogram, 3/11 from Bridge to Care, 2/11 from outside clinics. 60% of referred patients had a mammogram. 14/20 eligible patients had a pap smear, 10/20 from Bridge to Care, 4/20 from another clinic. 4/14 eligible patients had a colonoscopy, all referred from outside clinics.

CONCLUSIONS

Cervical cancer had the highest rate of screening. All screening rates were lower than PG County and National averages. Cervical cancer screening approached national averages, 70% versus 83%, likely given pap smears can be done in clinic. Further research into patient demographics and screening rates are needed for a statistically significant sample. We recommend investigating screening barriers such as distance from referral site, insurance, citizenship, and culture, which might contribute to lower rates of cancer screening at BTC.

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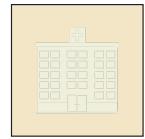
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PREVENTION AND COMMUNITY HEALTH



JOINT PA/MPH PROGRAM

Recommendations for Health Care Providers When Caring for Women Who Have Experienced Female Genital Mutilation/Cutting

In the United States, awareness of female genital mutilation/cutting (FGM/C) has increased in recent years due to current events and the increase in FGM/C research. FGM/C is practiced globally but international migration has led to an increase in FGM/C in the Americas, Europe, and Oceania. The CDC estimates that approximately 51,411 women and girls have undergone or are at risk of undergoing FGM/C in the D.C. metropolitan area. With the increase in survivors and girls at risk of FGM/C in the DC metropolitan area there is a need for well-trained health care providers. Many health care providers are not familiar or prepared to care for the physical, emotional, and social complications associated with FGM/C. This project sought to identify some of the best practices and recommendations for health care providers when caring for survivors of FGM/C.

METHODS

Health care providers (physicians, mental health professionals, counselors, physician assistants, nurse practitioners, nurse midwives) in the D.C metropolitan area with experience caring for survivors of FGM/C, were interviewed using a standardized questionnaire. The interviews were conducted to ascertain information about the health care providers experience working with survivors of FGM/C, challenges they experiences working with survivors, best practices when caring for survivors, recommendations for other health care providers, and gaps in health care provider knowledge and training.

RESULTS

A total of 25 interviews with health care providers were completed and reviewed for recommendations. The health care providers identified recommendations for formal training, medical care, communication, and resources to be included in a toolkit available to health care providers. The recommendations for training included training for practicing health care providers as well as health care students. The medical care recommendations were provided by health care providers practicing in a variety of specialties, therefore some of the recommendations are specific to certain specialties and others for general care. Recommendations for communication included both verbal and non-verbal recommendations. The toolkit recommendations included information about the practice FGM/C, printable materials, interactive materials, and referral lists.

DISCUSSION

The recommendations obtained from the interviews provided a substantial list of care techniques, tools, and best practices for all health care providers regardless of whether or not they have encountered survivors of FGM/C in their practice. These recommendations will be helpful in creating a toolkit for health care providers as well as advocating for more training opportunities on the subject of caring for women who have experienced FGM/C.

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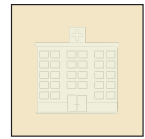
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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Tobacco Use Echo Chambers in Social Media: The Reinforcement of Inequalities in Smoking Norms

INTRODUCTION

Inequalities in smoking norms make it more likely for those in low socioeconomic or minority populations to use tobacco. These unequal social norms may be further reinforced in social media echo chambers, where smokers are likely exposed to more photos/videos of friends smoking. This study qualitatively explores how young adults—smokers and nonsmokers—are processing social media posts featuring combustible tobacco use.

METHODS

In-depth interviews were conducted with eight smokers and ten nonsmokers, ages 18 to 24, from the DC metro area. Interviews were audio-recorded, transcribed, and statements coded using NVivo and sorted to identify themes.

RESULTS

Most young adults interviewed saw posts featuring combustible tobacco use only occasionally but a few (primarily low income smokers) saw such posts frequently. Young adults were careful to curate an image that matched group norms in their network, and smokers and nonsmokers alike said smokers in their networks either “owned” their identity as a smoker and posted smoking pictures/videos often (a minority) or actively avoided such posts, not wanting smoking to be part of their image (the majority). While looking like a smoker was seen negatively - “attention-seeking” or “glorifying” a harmful behavior—posts where smoking was incidental and that were artistic or aesthetically pleasing, or featured social smoking (especially of cigars or hookah), were far more acceptable. Even those with strong anti-tobacco beliefs did not share these reactions on social media in order to protect their own image or the image of their smoking peers. Although young adults did not consciously think smoking posts had an impact on them, the influence of presumed influence (IPI) model suggests this presumed influence likely influences their attitudes/behaviors.

CONCLUSIONS

Social media echo chambers—where disadvantaged smokers see more smoking, most young adults see social smoking, and nobody speaks up against tobacco use—may reinforce inequalities in norms around prevalence and acceptability of smoking. Innovative social media interventions—including those focused on norms around the acceptability of smoking posts and the presumed influence posts have on peers, as well as network interventions that purposefully leverage network characteristics to influence behavior change—could be developed to mitigate or counter this influence.

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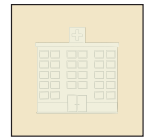
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Exploring the Relationship Among Role Models, Physical Activity and Dietary Behaviors Among Young Adults Enrolled in a Weight Management Trial

BACKGROUND

Role models can have a profound impact on an individual's development and lifelong behaviors. However, there are gaps in research when it comes to the impact of role models among young adults, particularly related to health behaviors. Previous research has primarily focused on youth, leaving a gap of knowledge surrounding the developmental life stage of young adulthood. Little research has been done examining health risk behaviors such as physical inactivity and unhealthy dietary practices. It is important for young adults to develop healthy habits in college, for many habits will follow young adults into their adult lifespan.

PURPOSE

To investigate the relationship between self-identified role models with physical activity and diet among young adults ages 18-35. This will be done by analyzing three research questions: (1) do reported role models differ based on weight status, gender, ethnicity/race, and school year? (2) do role models differ for diet and physical activity?; and (3) how do young adult role models relate to physical activity and eating habits?.

METHODS

Young adults aged 18-35 enrolled in a healthy body weight randomized controlled trial completed assessments prior to study enrollment. These included clinic measured height and weight, objective physical activity monitoring via accelerometer, online 24-hour food recalls, and questionnaires assessing physical activity behavior, as well as activity and healthy eating role models.

RESULTS

The analyses are ongoing as part of the first author's MPH Culminating Experience Project. Preliminary results will be available to present during research day.

CONCLUSION

It is anticipated that results will confirm the importance of role models for young adults, yet there will be important demographic and behavior-specific findings. Results and implications will be discussed, giving suggestions for future research areas and closing a gap in research in the young adult population.

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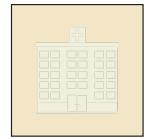
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The Role of Cultural Competency in the Development of mHealth Technology to Address Childhood Obesity Amongst Female African-American Adolescents

BACKGROUND

Research has indicated that African-American (AA) youth are consistently disproportionately affected by the childhood obesity epidemic, especially amongst AA females. The prevalence of childhood obesity in the United States has increased from 13.4% to 24.4% amongst AA adolescents, while the prevalence of obesity in all adolescents in this age bracket rose from 10.5% to 18.1%. By 2014, 42.5% of African-American (AA) girls were obese; the highest prevalence of any age group by gender, race or ethnicity. With statistics indicating 80% of obese adolescents will become obese adults, these AA females are on a trajectory towards worsening health outcome. There is a paucity of resources available to target obesity and mHealth technology has shown promises to create positive healthy behavior changes.

OBJECTIVE/PURPOSE

Create a culturally competent mHealth technology that will address obesity in AA female adolescents.

METHODS

Six focus groups were conducted amongst D.C. pediatric providers, AA female adolescents and their mothers. These groups discussed current strategies and barriers in addressing childhood obesity, specifically amongst AA female adolescents.

RESULTS

In collecting data to inform the development of the software, there were key cultural nuances identified that should be considered. First, tools currently used to manage obesity need to be seen as applicable to this patient population. Many providers voiced that their patients' parents were resistant to the BMI growth chart due to the inaccurate portrayal of their body type. Second, perceptions about health and weight are key influencers in health behaviors. Body image development occurs in a cultural context. Female AA adolescents noted their perceived ideal size was significantly larger in comparison to the standard norm for adolescent BMIs. Third, language and representation are very important in successfully targeting this population for weight intervention. Pediatric providers, adolescents and their parents agreed that having avatars that shared similar external characteristics was crucial to user engagement and adherence.

CONCLUSION

Our findings indicate the need for more culturally appropriate tools when creating interventions. Specifically, these results are important in the development of our mHealth technology targeting behavior change in AA female adolescents in order to achieve healthier lifestyles.

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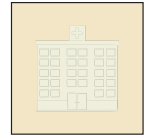
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Female Genital Mutilation/Cutting Survivors' Clinical and Social Needs Based on Health Care Providers' Experiences: A Qualitative Study

INTRODUCTION

In the United States, there is no toolkit that assists female genital mutilation/cutting (FGM/C) survivors address their clinical and social needs. However, health care providers (HCPs) who have served and treated patients who have undergone FGM/C are potential sources of determining FGM/C survivors' needs. By using the HCPs' experiences with FGM/C survivors, the study aimed to determine the FGM/C survivors' needs and consequently what HCPs recommend should be included in the toolkit for FGM/C survivors.

METHODS

The study conducted in-depth, semi-structured interviews with 25 HCPs in the greater Washington, DC area who gave their informed consent to participate and had experience with FGM/C survivors. The interviews were digitally recorded and transcribed verbatim. By using the analytical software QSR International NVivo, the interviews were coded and themes were developed in a grounded theoretical approach.

RESULTS

FGM/C survivors had several clinical complications related to FGM/C including negative mental health such as trauma, local complications such as scarring, pain associated with sex, general discomfort, and issues with childbirth, menstruation and the urinary tract. HCPs also encountered patients who wanted to be re-infibulated after surgery and/or childbirth due to their community's norms. FGM/C survivors that the HCPs treated did not know the consequences of FGM/C and its relation to their health status. In addition, HCPs recognized the following social needs of FGM/C survivors: employment, housing, health insurance, legal support, and social support.

Based on these identified needs, a toolkit will be developed for FGM/C survivors to use in order to improve their clinical experience and health in the greater Washington, DC area. HCPs stated that the tone and communication style of the toolkit should be noninflammatory, understanding and easy to read. Through the toolkit, FGM/C survivors should gain a better understanding of what FGM/C is, how FGM/C can affect them and what they can do to avert or address complications that arise due to FGM/C. HCPs also suggested referral lists of HCPs and social workers experienced with FGM/C, lists of FGM/C resources and support groups, and lists of questions that FGM/C survivors can ask their HCP or should anticipate from their HCP.

CONCLUSION

The toolkit will be a resource for FGM/C survivors and serve as a foundation for a national toolkit to be developed in the future. By empowering FGM/C survivors with the information they need, they can take control over their lives and enhance their health outcomes.

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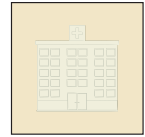
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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Understanding the Health Care Needs of Women who Have Undergone Female Genital Mutilation

INTRODUCTION

Female genital mutilation/cutting (FGM/C) is a human rights issue, with far reaching negative health outcomes, and is therefore a global health concern. The practice is rooted within many cultural traditions worldwide, and is not limited to any one region or religion. It is estimated that over 500,000 women and girls living in the U.S. are at risk or have undergone FGM/C. Despite this, little attention has been dedicated towards understanding how these women interact with the US health system to meet their health care needs. Using the voices of FGM/C survivors, this study aimed to describe the overall health service needs of FGM/C survivors in the Washington, D.C. Metropolitan area (DMV).

METHODS

The study employed a qualitative phenomenological approach where face-to-face individual interviews were conducted with 25 FGM/C survivors over the age 18 residing in the DMV. Enrollment utilized snowball recruiting techniques through outreach to cultural and faith based communities, while extra caution was taken maintain the anonymity of these women. Thematic analysis centered on women's narratives of the FGM/C experience as well as how women experience health care and communicate with their health care providers.

RESULTS

For women, the FGM/C experience functions as an adverse childhood event which manifests in various expressions of lifelong physical and psychological trauma that are compounded by: stigma around FGM/C within the American context; women's misunderstanding of sexual health; language and cultural barriers; lack of training among health care providers on FGM/C; negative interactions with health care providers; and the lack of communication on FGM/C both within health care encounters and within women's communities. Consequently, FGM/C related needs are systematically not addressed within such encounters.

CONCLUSION

These women's experiences communicate their perspective and determine to what extent the current health system is meeting their needs, and inform efforts to improve services for women who have undergone FGM/C. The results highlight the potential role of medical education; communication strategies and changing social norms can have on the quality of life and provision of appropriate health care services of FGM/C survivors.

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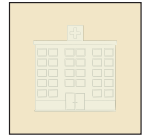
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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Active and Passive Stress Management Mechanisms in Physically Active Young Adults

BACKGROUND

Physical activity and stress are common factors that affect the health and wellness of young adults worldwide. Higher levels of stress in students can lead to increased blood pressure and decreased immune system defenses. Previous studies have found that students who report more physical activity also report lower levels of stress. Perceived stress is subjective, however, and therefore the amount of physical activity that affects stress levels could vary. Additionally, extensive research has yet to be conducted on the different coping mechanisms that physically active students use to relieve stress. These mechanisms may include physical activity as a stress reliever, as well as more passive methods, such as sleeping, eating unhealthy foods, and watching television.

PURPOSE

The purpose of this study is to investigate the relationship between physical activity, stress levels, and active and passive stress management mechanisms. Through this research we will first examine how stress levels among young adults who are overweight and obese compare to a normative sample. The primary research question we hope to answer is whether young adults ages 18-35 years who are more physically active cope with stress using active mechanisms more than those who are less physically active? Two supplemental questions to follow include: (1) Do physically active undergraduate students manage stress differently than physically active graduate students, and (2) Do physically active males manage stress differently than physically active females?

METHODS

Data analysis will be conducted using baseline measurements collected for the Healthy Body Healthy U Study. Data from Actigraphs, the International Physical Activity Questionnaire, the Perceived Stress Scale, and the Stress Management questionnaire, as well as demographic data will be included.

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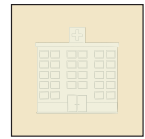
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Teenage All-Terrain Vehicle Crashes: Helmet Non-Compliance and Traumatic Brain Injury

BACKGROUND

All-terrain vehicle (ATV) crashes are a source of childhood injury, especially traumatic brain injury (TBI). Children have differing influences on behavior at different ages; age-group assessment of safety practices is important in designing prevention programs. Helmet use is one of the proven injury prevention practices for ATV drivers. The primary objective was to identify which age groups had the highest odds for traumatic brain injury and exhibited lack of helmet wearing practices, to target a group for health prevention education.

METHODS

After IRB approval, a retrospective cohort study of medical records at a level one trauma center was completed for years 1998-2012. Variables included presence of TBI, helmet use, crash month, and age. Chi-square analysis was used for categorical variables. Cases categorized into age groups corresponding to school levels. SPSS version 25 was used for analysis.

RESULTS

349 out of a total 750 were younger than 18 years. Cases/age group: 65 ages 0-10, 90 ages 11-13, 194 ages 14-18. Peak admission months were: 11-13-year-olds in September (15), August (11) and January (10); 14-18-year-olds in July (24).

190 had TBI, age categories: 27(41%) of 0-10 years, 51(56%) of 11-13 years, 112(57%) of 14-18 years. Comparing proportions in age groups of those with TBI, the 14-18-year-old group had the highest percentage at 58.9% ($p = .068$). 349 had helmet data, 17% used helmets. Eighteen (11%) persons out of the 163 with acute brain injury were wearing a helmet, 145 (89.0%) were unhelmeted ($p = .004$). Relative risk of unhelmeted patients for TBI was 1.6. Odds ratio for unhelmeted to have TBI compared to helmeted was 2.656, $p = .004$. Relative risk of TBI for unhelmeted compared to helmeted to have TBI in the 0-10, 11-13, 14-18 age groups respectively was 1.5 ($p = 0.47$), 2.7 ($p = .21$), 1.75 ($p = .009$).

CONCLUSION

Overall odds ratio for unhelmeted children admitted after ATV crash was significantly higher than for helmeted crash victims. OR for TBI was significantly elevated in unhelmeted 14-18-year-old ATV crash victims admitted to the hospital, the largest age group category with the highest proportion of TBI. Since July had the highest incidence of TBI, the 14-18 year-old group should be targeted prior to July for a helmet-wearing ATV safety education intervention.

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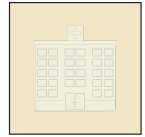
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PREVENTION AND COMMUNITY HEALTH



SCHOOL OF MEDICINE AND HEALTH SCIENCES

District of Columbia v. Heller: A Time Series Analysis on the Impact of Legislation on Gun Violence in Washington, D.C.

The purpose of this analysis was to investigate whether the 2008 landmark court case District of Columbia v Heller had an impact on gun violence. The case ruled in favor of Heller, and stated that Washington, D.C.'s handgun ban and requirement that lawfully-owned rifles and shotguns be kept "unloaded and disassembled or bound by a trigger lock", violated the Second Amendment. Our preliminary analysis involved comparing the prevalence of firearm related encounters in D.C from 2002-2008 and 2008-2015. Our initial investigation used the CDC WONDER database, which provided the number of firearm related encounters that resulted in mortality. We were able to stratify by intent of firearm use, gender, year, and level of urbanization. However, the data excluded firearm related encounters that did not result in mortality. Given the incomplete data from the CDC, we used the FBI UCR database to track the number of aggravated assaults involving firearms instead. Using a time series analysis, we compared the aggravated assaults involving firearms in the District of Columbia with the aggravated assaults found in the state of Pennsylvania as a way to account for confounding variables. However, due to the rapidly changing political, economic and social environment in the District of Columbia from 2002-2015, we were unable to capture the true impact of the District of Columbia v Heller case on gun violence.

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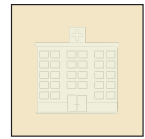
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Vaccine Associated Subacromial Bursitis

Intramuscular injection into the deltoid muscle of the upper arm is a common method of delivery for a variety of vaccines. Potential for injury exists if the vaccine is given in an incorrect location due to the proximity of nearby anatomical structures such as the subacromial bursa, long head of the biceps tendon, and axillary nerve among others. Within the past decade, there have been multiple reports of shoulder injury associated with vaccine administration.

This report details a case of a 34 year old woman who presented with acute left shoulder pain and limited range of motion following the administration of a Tdap vaccination into her left upper arm. The patient indicated that she thought that the vaccine injection had been given abnormally high in the shoulder. Subsequent MRI imaging showed an increased T2 signal in the subacromial/subdeltoid space suggesting an inflammatory process in the subacromial/subdeltoid bursa consistent with subacromial bursitis.

A guidance document provided by the Immunization Action Coalition indicates that intramuscular deltoid vaccines should be given “in the central and thickest portion of the deltoid muscle—above the level of the armpit and approximately 2–3 fingerbreadths (~2”) below the acromion process.” The CDC’s Vaccine Administration Pink Book recommended a 1” to 1 ½” needle based on our patient’s female gender and weight.

A 2006 study by Bodor and Montalvo found that the subdeltoid bursa extends distally from the acromion with a range of 3.0 to 6.0 cm (1.2 to 2.4 inches) and that its depth from the skin ranged from 0.8 to 1.6 cm (0.3 to 0.6 inches). Thus, the potential exists to inject vaccine into the subdeltoid bursa even with the recommended vaccine administration protocol detailed previously. Therefore, when evaluating a patient with complaints of shoulder pain and/or dysfunction, vaccine associated shoulder injury should be added to the differential diagnosis if the history reveals a recent upper arm intramuscular vaccination.

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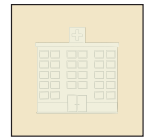
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MILKEN INSTITUTE SCHOOL OF PUBLIC HEALTH

Caring for Diverse Cancer Patients: What Roles Can Patient Navigators Play in Facilitating Challenges?

BACKGROUND

As the cancer patient population in the U.S. becomes increasingly diverse, cultural competence in healthcare has become a pressing issue for health equity. This study aims to: (1) describe oncology provider perspectives on challenges interacting with diverse patient populations; (2) describe provider-identified facilitators and barriers to the provision of culturally competent care; and (3) describe patient navigator perspectives on roles that they play in supporting the provision of culturally competent care.

METHODS

Similar web-based surveys were administered to convenience samples of multidisciplinary oncology clinicians and to patient navigators. In open-response fields, providers were asked to describe a difficult cross-cultural interaction, and to identify facilitators and barriers to culturally competent care in their practice settings. Meanwhile, navigators were asked to describe the role of a navigator in providing culturally sensitive cancer care. Qualitative content analysis of all text responses was conducted to generate codes summarizing common challenges, facilitators, barriers, and navigator roles, which were also enumerated.

RESULTS

Out of 406 oncology clinician survey respondents, 49.3% were physicians and 41.9% were registered nurses. Providers identified 22 distinct cross-cultural challenges, most commonly mentioning situations involving language barriers (n=143), alternative religious or cultural health beliefs (n=52) and refusal or non-adherence to care (n=46). Most frequently mentioned facilitators of cultural competence included interpretation services (n=29), staff attitudes (n=26) and support services (n=25). Knowledge and training (n=31), time constraints (n=25) and staff attitudes (n=20) were common barriers. Meanwhile, patient navigators (n=149) described 11 interrelated navigator roles in supporting cultural competence. Most frequently mentioned were: assessing and understanding the patient (n=51), tailoring care (n=44) and building rapport (n=38).

CONCLUSIONS

Multidisciplinary oncology providers face numerous complex challenges in assessing and tailoring care for diverse patients. Patient navigators, with their patient-centered orientation, are well-equipped to fulfill multiple functions in supporting the healthcare team in providing culturally competent care.

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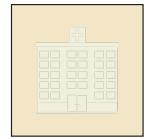
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Toolkits to Help Women Who Have Experienced or Are at Risk of Female Genital Cutting: A Review

In recent years, written guidance and other tools to assist professionals in multiple sectors has been issued to increase their awareness about female genital mutilation/cutting (FGM/C), knowledge of how to respond appropriately, and means of delivering optimal care to women who have undergone FGM/C. A long-standing human rights-framed issue, FGM/C is a global health concern and is most often carried out on young girls. Apart from practicing origin countries, increased international migration has given rise to FGM/C in countries in the Americas, Europe, and Oceania, and compelled domestic legislation to outlaw FGM/C. This prohibition makes FGM/C an area in which the emergence of operational guidance and educational materials in the form of toolkits is a relatively recent intervention phenomenon. This project sought to evaluate existing toolkits and formulate recommendations for future toolkits.

METHODS

This review sought to examine Internet accessible toolkits and other web-based resources, regarding issuance, derivation, distribution format, scope of delivery/content, and target audience. Each toolkit was assessed as to the country of origin, date of issuance, format, target audience, content, and evidence underlying the content, using the following search terms: FGM online resources in other countries, toolkits FGM survivors and health care professionals. These search terms were used as key words in Google with no limit on date published.

RESULTS

A total of 44 toolkits were included in the initial review and evaluation of these toolkits found 30 were geared toward women with FGM/C and health care providers. The majority of the toolkits were produced outside the United States. Toolkits were issued by international organizations, non-governmental organizations, and government agencies in many countries, including the United Kingdom, The Netherlands, Australia, and New Zealand. The toolkits were found to be variable in quality of content and timeliness of information presented. They were found to communicate epidemiological and legal information, but lack the provision of skills development or a presentation of evidence-based practices in working with women who have experienced FGM/C.

DISCUSSION

While some of the toolkits addressed prevention efforts in connection with FGM/C, others aimed to inform care practices for affected women and girls in accord with applicable laws. However, there is a need for skills development and tools that can be used by health care providers to ensure effective best practices are implemented when working with women who have experienced FGM/C.

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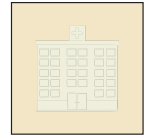
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PREVENTION AND COMMUNITY HEALTH



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Piloting CareStart™ Rapid Diagnostic Test (RDT) to Promote Glucose-6-Phosphate Dehydrogenase (G6PD) Screening in Malaria Endemic Community in Cambodia

BACKGROUND

Primaquine (PQ) is the only FDA-approved drug for radical cure of *Plasmodium vivax* (*P.v*) malaria, but treatment can result in life-threatening hemolysis if given to a glucose-6-phosphate dehydrogenase deficient (G6PDd) patient. Therefore, the G6PD status of the patient with *P.v* must be known prior to prescribing PQ. However, a patient's G6PD status in rural malaria endemic settings is generally unknown, illuminating the need for reliable point of care G6PD diagnostic tests as a prerequisite to safely administer PQ. To increase community PQ access in Cambodia, performance of CareStart™ G6PD rapid diagnostic tests (RDTs) needs to be evaluated in healthcare workers (HCWs) and village malaria workers (VMWs).

METHODS

Training materials on G6PD and PQ were developed for HCWs and VMWs, and each trainee performed G6PD RDT test on 8-12 adult male volunteers, with pre- and post-training questionnaires completed by trainees and volunteers. The performance of CareStart™ RDT for G6PDd screening was assessed against a quantitative G6PD test (Pointe Scientific, Inc. MI, USA). Descriptive and inferential statistics were used to analyze the data.

RESULTS

94 trainees and 960 G6PD volunteers were recruited in Oddar Meanchey province, Cambodia from December 2017 to February 2018. Of the 960 volunteers, 146 (15%) were G6PD deficient based on a quantitative test activity threshold of 30%. The sensitivity, specificity, PPV and NPV of CareStart™ RDT were 96.8%, 95.5%, 80.2%, 99.4% for HCW/VMW trainees vs. 96.2%, 97.2%, 86.7%, and 99.3% for trained study staff in the field and 94.2%, 98.8%, 93.6% and 98.92% for experienced laboratory staff, with no statistical difference among the groups. The mean knowledge score pre-training was 33.9% (VMWs) and 56.4% (HCWs), with improvement to 89% and 90% post training ($p < 0.001$). The improvement in knowledge scores was independent of the years of experience, profession and education level.

CONCLUSIONS

With minimal training, CareStart™ RDT seem highly specific, feasible and a practical option for the identification of G6PDd male patients and its use may enable safer prescribing of PQ to decrease the burden of *P.v* relapse.

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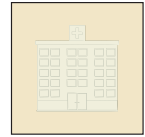
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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Increasing the Completion Rate of Anemia and Lead Exposure Screens for At-Risk Population of Infants in D.C.: A Quality Improvement Initiative

BACKGROUND

Iron deficiency anemia and lead exposure create serious implications, especially for infants around 1 or 2 years old. These implications are far-reaching and affect these youths for the rest of their lives. It is well known that these exposures can cause very deleterious developmental and cognitive impairments. The full effect and true public health burden is not yet known. Inner city populations of children are at high risk for these conditions. The American Academy of Pediatrics recommends and the District of Columbia Department of Health requires that infants are screened twice for anemia and lead by the age of two. In this study, two interventions were implemented at Mobile Health—Children’s National Hospital. Baseline statistics showed that 47% of anemia and lead tests were incomplete for 60 well-child checks. Root analysis determined that 60% of incomplete well child checks were due to inaccessibility of the e-Clinical Works medical record, 30% were due to failure in lab handling of blood specimen, and 10% were due to unsuccessful venipuncture.

INTERVENTION 1

After baseline and root analysis, the first intervention included Quality Improvement (QI) methodologies through: reminders to staff to streamline well-child-checks by completing the registration process prior to placement of patient orders, and retraining staff to ensure proper specimen handling. Result analysis of 135 patient charts yielded a 21% increase up to 74% in completed hemoglobin and lead screens from baseline. However, these results conclude that still three out of ten children were not completing screens.

INTERVENTION 2

The second intervention included integration of point-of-care (POC) technology. This technology eliminates the aforementioned issues by excluding the need to access e-Clinical Works EMR and a lab for specimen analysis. These tasks would all be completed at POC testing. Analysis of 45 patient charts from the period of POC implementation yielded a 93% completion rate for anemia and lead screening tests, a 19% increase from the previous intervention and a 40% increase from baseline.

CONCLUSION

Integration of QI methodologies and POC interventions proved to be significant boons in increasing anemia and lead screens for infants and young children. Given the severe implications of anemia and lead exposure at an early age, it is imperative that these conditions are screened early. Results from this study aim to ensure that anemia and lead exposure are screened early so appropriate action is taken in order to prevent the negative sequelae due to anemia and lead.

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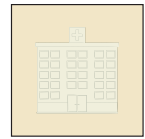
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PREVENTION AND COMMUNITY HEALTH



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Engaging PCPs in HCV Management with a Resource-Based Provider Toolkit

Nationally, an estimated 2.7-3.9 million people are living with chronic hepatitis C infection, a liver disease which can lead to cirrhosis, liver failure, and liver cancer. In addition to the 700,000 deaths per year from hepatitis C-related liver disease, rising rates of advanced liver disease complications and health care costs contribute to the growing burden of Hepatitis C Virus (HCV). Traditionally, HCV treatment with interferon drugs was poorly tolerated and ineffective for patients, and difficult for physicians to manage. More recently, new and well-tolerated treatments called direct-acting antiviral (DAA) agents have revolutionized HCV management with reported cure rates approaching 100%. While the notoriously high price tags on these DAA agents are a predominant barrier for patients, those with Medicaid health insurance fortunately receive coverage for these medications.

As the cure for HCV becomes more accessible, the D.C. Department of Health's HIV/AIDS, Hepatitis, STDs, and Tuberculosis Administration (DOH HAHSTA) is now mobilizing to create a five-year HCV Elimination Framework to eradicate HCV as a public health threat in the District. We first studied the eligibility criteria for Medicaid coverage of HCV DAAs among different D.C. Medicaid programs (AmeriHealth, Trusted, and Medicaid Fee-for-service) to better understand the restrictions for these patients. We found that while Medicaid programs previously restricted patients to treatment by specialist physicians, programs are now relaxing restrictions so that patients may be prescribed by primary care providers (PCPs). Allowing prescriptions by PCPs prevents more loss to follow-up with patients who are tested to be HCV positive, as patients on Medicaid health insurance often face difficulty receiving specialist care. HAHSTA is currently focusing on encouraging more PCPs to manage their patients' HCV as a mode of increasing overall treatment rates and thus, cure rates in D.C. After assessments on PCP comfort and knowledge in HCV management, we developed a HCV Management Provider Toolkit, with resources including medication guidelines, prior authorization protocols, HCV treatment-to-cure algorithms. After finalization, this toolkit will be published on the D.C. DOH website and printed and distributed to local PCP offices.

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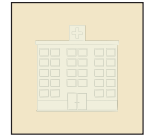
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Driven to Succeed: Improving Adolescents' Driving Behaviors through a Personal Narrative-Based Psychosocial Intervention in Serbia

OBJECTIVES

Road traffic crashes continue to be the leading cause of death among adolescents. While males are more vulnerable to crashes than females, driver education interventions are less likely to succeed among males than females. Some studies suggest that stronger optimistic bias and overconfidence bias in males may be the reason for this.

METHODS

In a quasi-experiment conducted in Serbia, forty schools were stratified by size and randomly assigned to watch a road traffic safety presentation utilizing personal narratives or to a control arm. Surveys were administered before the intervention (N=1,449) and again six months later (N=1,072). Data was analyzed by gender in order to investigate gender differences.

RESULTS

Risk perceptions improved for both males and females, and injunctive norms improved for females ($t= 1.87, p < .05$ for males and $t= 2.0, p < .01$ for females). Improvements in overconfidence bias and descriptive norms were predictive of improvements in high-risk driving behaviors ($\beta= .21, p < .001$ for males and $\beta= .25, p < .001$ for females; $\beta= -.15, p < .001$ for males and $\beta= -.11, p < .01$ for females, respectively). A significant interaction between improvements in injunctive norms and the intervention revealed that males whose injunctive norms improved were significantly more likely to be affected by the intervention, compared to the other groups ($\beta= .13, p < .05$).

CONCLUSIONS

Interventions targeting road traffic safety behaviors in adolescents should utilize a gendered approach. For males in particular, influencing perceptions of injunctive norms is important for intervention efficacy.

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The Effect of Brief Psychotherapy in Alleviating Anxiety and Depression in Cancer Patients Referred to a Psycho-oncology Clinic: Preliminary Study

This poster will present preliminary findings from a recent research study conducted at the George Washington University Medical Faculty Associates Department of Psychiatry. Psychological distress and morbidity (including loneliness, anxiety, depression and PTSD) may be triggered or exacerbated by cancer diagnosis (Swartzman, et al 2016). Depressed cancer patients show worse treatment adherence and worse survival compared with non-depressed cancer patients (Hartubf et al, 2017). Cancer survivors in the United States reported using medication for depression and anxiety at twice the rate of the general public (Hawkins et al 2017). Childhood cancer survivors may experience post-traumatic stress symptoms as young adults or adults. Psychiatrists and resident trainees are not normally trained to deal with special needs of cancer population, and this training takes place within the GW psychooncology clinic. Given the high prevalence of mood disorders and adjustment disorders among oncology patients, this study will aim to assess if our current intervention is beneficial in addressing the client's target symptoms. The study will examine the effectiveness of brief psychotherapy for oncology patients. Currently, patients are referred to the psychooncology clinic from various oncologists and social workers with the oncology center. Resident psychiatrists provide 5-8 sessions of brief psychotherapy to address issues of anxiety, mood changes and adjustment to diagnosis. This study aims to examine if therapy sessions achieve the goal of helping to decrease anxiety and mood changes and changes patient's outlook on life. Patients will be administered surveys assessing for depression, anxiety and well-being prior to and following therapy sessions and the results will be compared. The hypothesis is that patients will score significantly lower on the anxiety (GAD-7) and depression (PHQ-9) questionnaires and higher on the WHO 5 measure Quality of Life Scale, indicating that the several sessions of brief psychotherapy were effective in helping them to develop positive coping skills to adjust to their diagnosis and how it impacts their lives.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Implicit Attitudes about Mental Illness in Saudi Arabia

ABSTRACT

Most people in Saudi Arabia have negative perspective towards psychiatrists and patients who seek help from them. This attitude makes people who affected by mental illness and their families hesitate before seeking help from psychiatrists and may prefer seeing Faith Healer instead of that. Properly, having a stigma and general lack of understanding of mental illness are the main reasons behind their decision.

In our study, we are looking for assess people's knowledge and attitudes toward mental illness, psychiatric professionals and psychiatric symptoms, by utilizing methods that allow us to examine implicit vs. explicit attitudes toward mental illness and mental health professional, and measuring general knowledge of the symptoms of mental illness and as well as the role of mental health professionals.

The purpose of this study is to determine the effect of this attitudes about mental illness and mental health professionals on making the decision to visit a psychiatric professional among Saudis who are living in Saudi Arabia vs. Saudis who are living in the United State.

We hypothesize that people living in Saudi Arabia will exhibit higher levels of explicit and implicit negative attitude and Saudis who are living in the United State will exhibit lower levels of explicit negative attitudes, but a similar level of implicit negative attitudes toward mental illness and mental health professionals. The consequence of acculturation on explicit attitudes will be moderated by the length of time in the United States, levels of knowledge of mental health symptoms and the roles of psychiatric professionals.

METHOD

The implicit-Association test (IAT), is a measure within social psychology aim to recognize traces of past experience that mediate favorable or unfavorable feeling, thought, or reaction toward social objects. The IAT may help the researchers to get around the difficult problem of social desirability bias and for that reason, it has been extensively to assess people's attitudes towards commonly stigmatized groups. A computer-based measure, the IAT requires that participant rapidly categorize two target concepts with an attribute (e.g. the concepts "male" and "female with the attributes "logical"), such that easier pairing (faster responses) are interpreted as more strongly associated in memory than more difficult pairings (slow responses).

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Resilience of Children with Chronic Health Conditions: The Impact of Neuropsychiatric Comorbidities

BACKGROUND

Resilience, the ability to overcome adversity and effectively recover from stressful experiences, is a complex theory with many contributing factors. Previous studies have shown that condition-specific summer camps for children with chronic health conditions increase resilience and adaptive coping skills, change attitudes toward the illness, and improve quality of life. The aim of this study was to determine how neuropsychiatric comorbid diagnoses such as attention deficit hyperactivity disorder (ADHD), learning disability, and anxiety disorder influence the resilience of children with chronic health conditions.

METHODS

Children with chronic health conditions including autism, epilepsy, cerebral palsy, Tourette's syndrome, sickle cell anemia, neurofibromatosis, congenital heart disease, and type 1 diabetes attended Brainy Camps of Children's National Health System and participated in this study between 2010-2016. Sixty-seven participants ages 7-17 completed the Connor-Davidson Resilience Scale (CD-RISC) questionnaire pre- and post-camp. Parents of participants reported presence of comorbidities including ADHD, learning disability, and anxiety disorder. Averages for pre- and post-camp CD-RISC scores were taken for participants with ADHD, learning disability, or anxiety disorder, and were compared to scores for control participants without each comorbidity.

RESULTS

Averages for all groups indicated an increase in resilience scores. The increase was 10.27 points on the CD-RISC for the 35 participants without ADHD, and 7.95 points for the 32 with ADHD. The increase was 7.61 points for the 30 participants without learning disability, and 5.98 points for the 37 with learning disability. The increase was 8.36 points for the 47 participants without anxiety disorder, and 6.38 points for the 20 with anxiety disorder.

CONCLUSIONS

These findings demonstrated a positive shift in resilience for all participants with chronic health conditions who attended Brainy Camps. However, the results indicated larger improvements in resilience for participants without comorbid diagnoses of ADHD, learning disability, or anxiety disorder. Therefore, children with chronic health conditions who also have these neuropsychiatric comorbidities have more challenges developing resilience. One limitation of this study is possible false reporting of comorbid diagnoses from parents. Further research is needed to explore how interventions such as residential summer camps can also impact self-management and health outcomes of children with chronic health conditions.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Mental Health Care in Bolivia

Although Bolivia has come a long way in the last decade, about 64% of the country still lives in poverty and it has an illiteracy rate of about 14%. Bolivia implemented a universal health care system in 2007, but because of the levels of poverty and education it is estimated that 77% of the population has been excluded from health services.

For two months, I had the opportunity to volunteer at an inpatient mental health Hospital in Sucre, Bolivia called Instituto Nacional de Psiquiatria Gregorio Pacheco. It was founded in 1884 and named after the president of the time who supported its construction. It is the oldest mental hospital in Bolivia and for a long time, it was the only. There are about 350 patients ranging from acute to chronic, although the majority of patients are chronic and live there indefinitely. They have acute wards for both men and women with a capacity of about 20 beds each. Working there allowed me to see the conditions these patients were in as well as some alternate therapeutic tools implemented by these facilities.

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A Review of Depression in Patients After Thyroidectomy

BACKGROUND

The association between a hypothyroid state and depression has been well documented in the literature, but few studies have measured rates of depression among patients after a thyroidectomy. Some observational data suggests that suboptimal thyroid replacement therapy may result in depression despite normal TSH levels, which has significant implications for monitoring patients after a thyroidectomy. This literature review will provide an overview of the existing research on depression in patients after a thyroidectomy.

METHOD

The research was produced through a literature review using PubMed with search terms "Thyroidectomy" and "Depression." Of the 191 search results, studies ranging from 1965-2017 published in English looking specifically at psychological depression among human subjects who had undergone a thyroidectomy were included. All studies or case reports of patients with a history of mood symptoms prior to the thyroidectomy were excluded, as were studies looking exclusively at perioperative depression and anxiety during periods of induced hypothyroidism. Eight articles were included with a total of 87 patients.

RESULTS

Three case reports were reviewed that documented psychotic depression and depression among hypothyroid patients after an average of 1.5 months without a thyroid. Among these cases, 100% had resolution of mood symptoms with thyroid replacement. In three other studies, investigators measured depression in the hypothyroid state versus euthyroid state in patients after a thyroidectomy. Investigators observed greater rates of depression and anxiety in hypothyroid patients. One case report documented a euthyroid MEN2A patient after a total thyroidectomy who presented with anxiety and depression found to be due to bilateral adrenal pheochromocytomas. One study looked at patients with thyroidectomy for Graves Disease and hypothyroidism secondary to Hashimoto's Thyroiditis and found that adding carbimazole to levothyroxine (LT4) increased free triiodothyronine (FT3) and improved depression.

DISCUSSION

The existing literature on depression in patients after a thyroidectomy is limited. Case reports show psychotic depression and depression among patients with uncontrolled thyroid levels. No formal research has been done to study the prevalence of depression in euthyroid or subclinical hypothyroid patients after thyroidectomies over an extended time period. Given the observational data suggesting that current replacement therapy may not serve as a fully functional replacement for psychological well being, there may be a population suffering from mood symptoms after a total thyroidectomy. Further research is needed to determine whether physicians should monitor for mood symptoms after thyroidectomy and whether physicians should modify the current thyroid replacement regimen to maximize FT3.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Looking at the Major Criticisms Against Global Mental Health and How They Relate to the Real World

Global mental health (GMH) has come under a significant amount of criticism from anthropologists, sociologists, and transcultural psychiatrists who point out that the movement is misguided because of its perceived cultural insensitivity and the power differential between different stakeholders. In order to better understand how the major arguments against GMH apply to a sample of actual programs, this paper conducted a systematic evaluation of GMH programs in light of the anti-GMH criticisms. A literature review helped elucidate salient arguments or criticisms relating to 1) How mental illness is identified, 2) The evidence for GMH interventions, 3) The approach towards social determinants, 4) Power imbalance, and 5) The approach towards stigma. The innovations were taken from a simple random sample of twenty five programs from the Mental Health Innovation Network and systematically evaluated based on the criticisms. The analysis showed that most programs do employ what has been understood as a more “Westernized” or “top-down” approach in defining mental illness. Programs are evidence-based with increasingly comprehensive methods of impact evaluation and tend to utilize more direct treatment approaches rather than targeting innovations from the standpoint of social determinants and stigma (though these constructs are taken into account). As far as power dynamics, the design of most interventions does seem to permit diverse stakeholder involvement but how this plays out in practical terms is unknown in most cases. The evaluation sheds light on the complexity of the issues underlying the GMH criticisms, and the majority of GMH interventions can speak for themselves in terms of “counterarguments.” At the same time, it may not be possible to have a program that would satisfy all of the criticisms and the value of such an approach is unknown.

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Sustainable Development Goals and Mental Health Knowledge Among First Year Medical Students

INTRODUCTION

The United Nations Sustainable Development Goals for 2030 highlights the global impact of mental health illnesses by including goals for the prevention and treatment of behavioral, developmental, and neurological disorders. In order to facilitate the advancement of mental well being, it is important to monitor and evaluate the baseline of mental health knowledge. Current scientific literature is limited in identifying the baseline mental health knowledge among medical students. This study aims to look specifically at first year medical students to determine their mental health knowledge prior to and after a targeted program intervention.

METHODS

Fifty-nine first year medical students were surveyed with the Mental Health Knowledge Schedule (MAKS) prior to and after the intervention. The program intervention was composed of an hour session that introduced students to negative health outcomes such as demoralization, burnout, depression, and dependency. The intervention also introduced students to the different strategies to specific to addressing the different negative health outcomes.

RESULTS AND CONCLUSION

Preliminary results from the MAKS survey indicates that first year medical students vary in what negative health outcomes they consider to be mental illness. Preliminary results also indicate that after the intervention, students have an increased understanding of what situations merit mental health attention. In conclusion, the combination of the MAKS survey with the program intervention demonstrates a positive trajectory in mental health knowledge among first year medical students.

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Sweet Care: Improving Diabetes Outpatient Quality Measurements with Implementation of EMR Based “Macros”

Diabetes Mellitus (DM) is an endemic chronic medical condition that requires a multispecialty approach, which much of the time is led by a primary care provider. Management of DM can be challenging due to the widespread effect of the disease on multiple organ systems in addition to the high level of morbidity that can result. Due to increased demands of seeing more patients, primary care physicians have ever decreasing time with their patients, yet patient’s disease state remains complex. Thus, it may not be difficult to overlook certain guidelines when managing patients with DM.

A set of quality measures has been established for the treatment of DM by the Ambulatory Care Quality Alliance [1]. The GW MFA currently tracks these diabetic quality measures for each resident’s panel of patients. To improve our quality measure compliance, we were interested in implementing a checklist to remind residents of the guidelines when seeing diabetic patients in clinic. We developed a macro within the EMR which would allow for proper documentation and checklist during diabetic clinic visits. The aim of this study was to increase quality measure reporting by 20% over 3 months through the initiation of macros.

Baseline data was obtained from our clinics quality measure data which included goals for the following: HgbA1c, blood pressure, cholesterol, immunizations, eye exam, and nephropathy laboratory work. Macros were created in the electronic medical record with national guidelines for screening and management of diabetics from the American Diabetic Association. These macros were shared with a sample of residents.

The response to the use of macros was positive from the participating residents as they found it helpful in reminding themselves of the guidelines which are occasionally overlooked. The results of the intervention were favorable with 14% increase in quality measure reporting. Although we did not meet our initial goal of increase in 20%, the results were favorable. The next steps in this project are working closely with physicians who oversee the electronic medical records to extend the use of the macro to all physicians in the practice who manage diabetes. Lastly, we hope to streamline the macros in order for the quality measures to automatically be uploaded in order to provide easier documentation.

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Improving 23-Valent Pneumococcal Polysaccharide (PPSV23) Vaccination in Pediatric HIV Patients

BACKGROUND AND OBJECTIVES

Children living with HIV are at increased risk for invasive pneumococcal disease. The American Academy of Pediatrics recommends all children with HIV infection receive 23-valent pneumococcal polysaccharide vaccine (PPSV23) after receiving the 13 valent pneumococcal conjugate (PCV13) vaccine series. Despite this recommendation, the rate of PPSV23 vaccination in children with HIV remains low. This quality improvement project aimed to increase the rate of PPSV23 vaccination rate among pediatric and adolescent high risk population attending Special Immunology Services (SIS) HIV specialty clinic at Children's National.

METHODS

Eligible patients included children and adolescents receiving care at SIS clinic. A baseline assessment of PPSV23 vaccination rate was performed in April 2015. Interventions included proactive acquisition of updated vaccination records from primary care providers, determining need for PCV-13 vaccine series and PPSV-23 during clinic visits, and requesting primary care providers to administer required vaccinations or providing PPSV-23 at subsequent SIS appointments. A REDCap database was created to track documentation of PCV-13 and PPSV23 vaccination.

RESULTS

In April 2015, 184 children and adolescents were enrolled in care at SIS. Fifty-seven patients (40.0%) had immunization records available, and only 17 (9.2%) had documentation of completion of PCV-13 series and none (0.0%) had documentation of PPSV-23. After 2 Plan-Do-Study-Act cycles over a period of 8 months, there was an increase of total patients with immunization records to 95 (51.6%). Thirty-six (19.6%) had documentation of completion of PCV-13 series and 16 patients (8.7%) had documented PPSV-23 vaccine. 3 (18%) PPSV-23 vaccines were administered in SIS clinic.

CONCLUSIONS

Obtaining patients' current vaccination records from primary care providers and lack of prior administration of PCV-13 are two barriers to completing PPSV-23 vaccination in children with HIV receiving care in a specialty setting. Dedicated SIS staff time is required to consistently operationalize procuring updated immunization records and administering PCV-13 and PPSV-23 as recommended by national guidelines.

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Reducing Readmissions through Patient Engagement Prior to Discharge

INTRODUCTION

Hospital discharge follow-up with primary care providers is essential to ensuring patient safety between the inpatient and outpatient settings and in reducing readmissions to the hospital. Indeed, one in five patients suffers an adverse event during the first several weeks after hospital discharge and up to half of Medicare patients readmitted within 30 days were not seen in the outpatient setting after discharge. These findings highlight the importance of ensuring prompt primary care follow up. Two explanations for lack of follow-up are patients leaving the hospital without critical post-discharge appointments, or appointments that are scheduled do not align with patients' schedules. Our project's focus was to empower and facilitate patients scheduling their own appointments prior to hospital discharge.

AIM

Increase the proportion of patient-made follow-up appointments for patients admitted to the general medicine service from 0% to 50% by June 2018.

METHODS

Patients were educated on the intervention and provided a checklist one to two days prior to the anticipated hospital discharge. The checklist described the rationale for the intervention, provided phone numbers to make appointments, and included a section for the patient to record appointment information. Patients who had appointments too important to be left to chance, who could not understand the intervention, refused to participate, or who were not being discharged to home were excluded from the intervention group.

RESULTS

Three PDSA cycles were conducted focusing on improving the form layout, wording, and communication of the intervention. 41 patients were included in our analysis. 44% of patients met our entry criteria, and of these, 72% succeeded in scheduling their appointment with the use of the instructional checklist. Each PDSA cycle resulted in an increase in the number of patients who were successfully able to make follow-up appointments.

CONCLUSION

In this pilot study, we determined that for an appropriate subset of patients, a self-made post-discharge follow-up appointment is a viable alternative to current approaches and may result in improved transitions for care. While we did not meet our project's aim, the rapid-cycle quality improvement process resulted in significant improvements in our targeted outcome. Our project's future focus includes tracking appointment compliance and assessing patient outcomes such as re-hospitalization, adverse events, and patient/provider satisfaction.

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Reducing Unnecessary Hospital Laboratory Testing

BACKGROUND

Healthcare expenditures in the US account for 17.9% of the national GDP, or nearly \$10,000 per person per year. Of this, waste has been estimated to represent approximately 1/3. This cost burden creates financial stress on the patient, care providers, and the system of care which attempts to allocate scarce medical resources. Several previous studies have shown that excessive or unnecessary clinical laboratory testing in the inpatient setting may be an opportunity to reduce waste without resulting in changes to care quality, patient or physician satisfaction. In our academic medical center, "morning labs" have become a culturally ingrained on the medicine wards despite little evidence that testing actually results in a change in patient management for patients who are otherwise stable. Here we test a "goal-triggered" (i.e., will checking this laboratory test result in a change in management?) approach to routine inpatient laboratory testing.

AIM

Reduce unnecessary laboratory testing by 20% from baseline by July 2018.

METHODS

We identified seven basic laboratory tests which are routinely included in morning laboratory draws, but could potentially be omitted in stable patients, where these labs would not change management. These included CBC, Differential, BMP, Liver Function Tests, Coagulation studies, Magnesium level, and Phosphorous level. A chart review was performed to identify all patients on a specific resident internal medicine team at a large university urban hospital throughout two months of 2017-2018. We first gathered baseline data on laboratory draws per patient without any intervention. The second PDSA cycle was composed of attending and resident education reminding care teams to only request laboratory testing if it would change the management for the patient. The third PDSA cycle included the use of laboratory cost sheets which were posted on the workstations of residents. Data regarding number of laboratory draws on each patient was obtained. A Microsoft Excel database maintaining subject confidentiality was created.

RESULTS

Reducing unnecessary laboratory testing was well received by both the hospital housestaff as well as attending physicians. During the two testing phases, only once was an intentionally unrequested laboratory test subsequently ordered due to clinician or patient preference. Despite qualitative acceptance, overall laboratory testing did not see a decline from our baseline in PDSA cycle #1 (2.9 to 3.2 tests per patient per day), in PDSA cycle #2 (2.9 to 3.5 tests per patient per day), or between PDSA cycles (3.2 to 3.5 tests per patient per day). Subgroup testing did show a significant reduction in certain laboratory tests, specifically the complete blood count differential (21% reduction overall).

DISCUSSION

Despite appropriate interventions, laboratory testing on a per-patient per-day basis increased during our study period. Possible reasons for this increase include increased awareness placed on laboratory testing (with subsequent increase in laboratory ordering), variations in housestaff team composition, variations in patient acuity, and ineffectiveness of our intervention. While our results do not convey a great change in the amount of laboratory testing that was ordered by internal medicine, it does bring to light an important focus of our healthcare spending that further research would be able to bring to light. Future quality improvement activities will focus on different interventions to reduce unnecessary laboratory ordering including ongoing physician education, changes to the electronic medical record order sets, and potential interventions by nursing and phlebotomy to ensure appropriateness of clinical testing.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES
CHILDREN'S NATIONAL MEDICAL CENTER

Improvement in Investigator Satisfaction After Implementation of Changes in the Clinical Research Unit: A Quality Improvement Initiative

BACKGROUND

The Clinical Research Unit (CRU), within the Clinical and Translational Science Institute at Children's National (CTSI-CN), provides specialized services to support clinical researchers at Children's National (CN) and George Washington University (GW). CRU services include biorepository, nursing, study coordinators, nutrition, behavioral testing, and laboratory processing. The CRU predominantly serves CN investigators and would like to increase collaboration with investigators from GW. A 2016 survey provided information about CRU usage by CN investigators and assessed satisfaction with services. In response to CRU user feedback, processes were implemented as standard operating procedures including: new processes for scheduling, PK studies and protocol implementation budget development, billing, and revision of the cost structure.

OBJECTIVE

We aim to determine if process improvements have increased investigator satisfaction.

METHODS

Frequent, occasional, and non-users of CRU services received a REDCap survey in July 2016 (n=115) and December 2017 (n=131) assessing satisfaction with overall services, scheduling, billing, and CRU staff. Twelve questions used a 5-item Likert scale ranging from "Not Satisfied" to "Extremely Satisfied" and two questions allowed free text responses. Survey data was extracted and categorical responses were assigned a numerical value in increasing order of satisfaction (1=Not Satisfied, 5=Extremely Satisfied), reported by year as mean and standard deviation. Differences in the mean response over time were identified using Student's t-test. Investigators collated free-text responses to identify salient themes.

RESULTS

In 2016, 28.7% of CRU users (n=33) completed the survey compared to 34.4% (n=45) in 2017. Indicators of satisfaction improved among CRU users between the two survey time points. The greatest increases were found in areas where process improvements were implemented in the previous year, including responsiveness, scheduling, and communication. Of the 12 satisfaction areas, 9 had statistically significant increases in mean values ($p < 0.05$) including the desire to recommend CRU use. Reasons for non-use and low satisfaction were primarily related to factors outside the CRU's purview, or lack of knowledge about CRU services.

CONCLUSIONS

The process improvements implemented within CTSI CRU increased investigator satisfaction, and the survey results offer opportunities for continued improvements. These results indicate that GW investigators could also benefit from our services and we are hoping to increase collaborations with GW investigators.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Challenges to Lung Cancer Screening: Increasing Screening In Ambulatory Setting

Lung cancer remains the leading cause of malignancy related death in the United States. A significant component of this mortality is late diagnosis and recognition as earlier diagnosis offers more definitive treatment options. There is evidence that early detection of lung cancer by screening high risk patients with annual low-dose CT scans can improve the survival rate by 20%, and is now recommended by the USPSTF. However, low dose CTs are not ordered by primary care physicians as routinely as other screening tests such as mammography. Previously, in the resident clinic at the Medical Faculty Associates at George Washington University Hospital, only 4.3% of physicians documented whether or not a patient met criteria for lung cancer screening. Documentation and ordering of the exams remained low despite re-education about recommendations and making the ordering process simpler.

The year prior, our colleagues surveyed attending physician, which showed multiple reasons that added to the low rate of screening. A few of the core reasons for poor documentation and ordering, including lack of knowledge of the guidelines, obtaining insufficient smoking history, and poor documentation and ordering habits. With this data we undertook a quality improvement project to compare ordering of low dose CT scans for screening before and after direct email messaging with information on proper screening and directions on how to order. In addition, we compared appropriate documentation of those that both qualified or did not qualify for screening process at annual physical exams before and after the designated targeted interventions.

Targeted interventions included email prior to the start of the residents outpatient ambulatory week and direct communication with printed-out material. Our aim was to increase the rate of residents documentation of both qualifying and non-qualifying screening of patients, and appropriate ordering of low-dose CT scans, by 25% after initiation after each targeted interventions. Further strategies include finding barriers that caused poor gathering of smoking history, quicker or more efficient EMR documentation techniques, and continued education of current evidence based practices.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Reducing Stress and Burnout: Interventions to Improve Resident Wellness

BACKGROUND

Resident wellness has been an increasingly important topic in residency programs across the United States. Increasing social isolation, decreased work satisfaction, and feelings of depression have led to unexpectedly high and rising rates of resident self-harm. Several initiatives have been attempted to minimize resident burnout and depression at the George Washington University Hospital but have not been measured in the past.

AIM

This project aimed to decrease resident feelings of burnout by 25% by April, 2018.

METHODS

Using a standardized questionnaire, several initiatives were attempted at our home institution to improve resident wellness and to measure the response. After assessing what residents deemed would best improve wellness and quality of life, a series of Plan-Do-Study-Act (PDSA) cycles were launched to improve baseline scores. These interventions included a daily joke sent out to all residency classes intended to boost morale, scheduling regular social after hours events open to the entire residency cohort, and educating the residency class about resources aimed at resident wellness.

RESULTS

Our wellness interventions were generally well received by the residency cohort; however, we were unable to assess repeat wellness scores after our three PDSA cycles. Qualitative responses to our interventions are as follows. During PDSA cycle 1 (daily joke) we noted that several residents unsubscribed to the mass text list as it interrupted daily workflow; however, many residents commented that this was a welcome addition to their busy day. The best time of day to send these messages was during lunch, though even this proved an interruption for some. PDSA cycle 2 (social hours) was also well received with a number of residents offering to help coordinate future events.

DISCUSSION

We identified that there are many different avenues available to improve residency wellness, and that there is benefit to offering a variety of interventions that mirrors the diversity within a residency class. While most residency wellness interventions were well received, there were obstacles to delivering wellness opportunities including funding constraints and potential conflicts with residents' busy schedules. Future projects can focus on expanding the variety of interventions, engaging the program leadership to invest financial resources, and creating a blueprint that can be expanded to other residency programs outside of our home institution.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Getting Patients to Clinic: Project to Increase Follow-Up After Hospitalization

INTRODUCTION

Hospital discharge follow up appointments are critical in making the care transition from the inpatient to the outpatient setting. However, the number of patients who are discharged from our hospital with follow up appointment(s) is low, partly due to the difficulty of navigating the healthcare system. This responsibility often falls on the housestaff, which is an onerous administrative burden. Our resident-led quality improvement (QI) project had three aims: (1) to increase the percentage of discharged patients who left with at least one follow up appointment by 50%, (2) to decrease the time that residents spent obtaining appointments by 50%, and (3) to discharge patients from the hospital earlier by improving the discharge appointment process.

METHODS

We implemented a clinic phone directory in the inpatient medicine team rooms, with direct line numbers for various subspecialty clinics, in order to reduce residents' phone times. Our project utilized the IHI Model for Improvement with various plan-do-study-act (PDSA) cycles. We started with 1 inpatient resident medicine team, and expanded our project to include all inpatient resident medicine teams in a step-wise fashion. Our primary measure was the percentage of patients leaving the hospital with at least one discharge appointment in place. Secondary measures included the time of discharge, the amount of time spent on the phone making follow up appointments, and resident satisfaction with the directory.

RESULTS

The percentage of patients who left the hospital with at least one follow up appointment in place increased from 28.5% (baseline) to 35.9% (PDSA cycle 3), with a maximum of 48.2% during PDSA cycle 2. The average time of discharge did not change significantly. The average phone time decreased from 18.5 minutes (baseline) to 9.7 minutes (PDSA cycle 3), with a low of 6 minutes during PDSA cycle 2. Residents who used the phone directories found them to be helpful in obtaining follow up appointments.

CONCLUSION

We improved the discharge appointment process by creating a phone directory. This decreased the time spent making follow up appointments and increased the percentage of patients who left the hospital with at least one follow up appointment in place. Leaving with scheduled follow-up aided in the transition of care upon discharge. However, patient discharge times did not change, likely because the actual time of discharge is dependent on several other variables which are independent from discharge follow-up appointments.

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Improving Admission Medication Reconciliation Completion at GW Hospital

BACKGROUND

Medication errors represent a major cause of adverse events in hospitalized inpatients. 27-83% of hospitalized patients will have at least one discrepancy in their medication history at admission, with 11%-59% of errors having clinical importance. Current processes for completing admission medication reconciliations are ill-defined, further increasing the risk of errors. Implementation of a standardized medication reconciliation process has led to a reduction in medication errors.

AIM STATEMENT

To increase the number of admission medication reconciliations completed within 48 hours of admission to GW Hospital by 25% over three months.

METHODS

From September 2017 until December 2017, an educational intervention was delivered to internal medicine residents rotating on the wards at GW Hospital and refined over three PDSA cycles. The intervention included an educational presentation on proper completion of an admission medication reconciliation, given at resident noon conference and to the night float team, a video by hospitalists reinforcing principles of proper medication reconciliation, and creation of a signoff checklist to assess interns for proper completion of medication reconciliations. The number of properly completed admission medication reconciliations within 48 hours of admission for patients admitted to one general medicine day team and to the night float team was assessed. Completion was denoted by green checkmarks next to "Document Medications by History" and "Medication Admission Reconciliation" in Cerner. Data was collected for all new admissions every post-call day and was expanded to an additional daytime team with PDSA Cycle 3.

RESULTS

Baseline data revealed that admission medication reconciliations were completed on 20% and 77% of new admissions to the daytime and night float teams, respectively. Completion rates by the day team varied from 16% to 100%, but with a clear trend towards improvement with over 50% completed on the days reviewed. Little change was observed on the night admission team. Expanded data from the additional daytime team showed improved completion rate.

DISCUSSION

Our study demonstrated that early provider education, adherence to a standardized process, and reinforced education are ways of improving admission medication reconciliation completion. There was an overall increase in admission medication reconciliation completion in the daytime medicine team, but not in the night float team, likely owing to the more frequent turnover of night float residents. Data collection was expanded to a second daytime medicine team and is ongoing with possible extension to all medicine wards teams. Limitations include provider turnover throughout our interventions, the inability to assess accuracy of completed medication reconciliations, and the varying experience with admission medication reconciliation completion among providers. Future interventions include education at intern orientation, reinforced with successful completion of a signoff checklist, and involvement of pharmacists.

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SCHOOL OF NURSING

A Single Center Retrospective Study on the Use of Perioperative Stress Dose Steroids in Preventing Adrenal Crisis in Surgical Pediatric Patients

BACKGROUND

Adrenal crisis is a rare and fatal complication of adrenal insufficiency (AI) caused by inadequate release of cortisol during periods of increased physiologic stress. Current endocrine clinical practice guidelines recommend the use of perioperative stress dose steroids (SDS) in patients with AI to prevent adrenal crisis related hypotension or electrolyte imbalances. Although SDS are essential and can be lifesaving, there is evidence that the proposed glucocorticoid coverage for surgical procedures is excessive resulting in inconsistencies and ambivalence in the use of perioperative SDS.

OBJECTIVES

The purpose of this study was to investigate the administration of perioperative SDS to prevent pediatric patients between ages 0–18 years with or at risk of AI from developing adrenal crisis during surgical procedures or postoperatively.

METHODS

A retrospective chart review was conducted to compare signs and symptoms of AI in surgical pediatric patients who did or did not receive perioperative SDS from January 2007 to December 2016.

RESULTS

64 sedated surgical procedures met study's inclusion criteria. Patients had similar demographic characteristics except for primary diagnosis. 21 patients received SDS and 43 patients did not. Adrenal crisis did not occur in either group. However, 14% of patients in non-SDS group displayed postoperative symptoms that may have been consistent with AI.

CONCLUSIONS

Study findings revealed that there is the potential for adrenal crisis in at risk patients. Perioperative strategies including but not limited to identifying patients at risk, administering SDS per clinical guidelines and monitoring patients closely perioperatively should be implemented to avert this potentially fatal complication.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Optimizing Nurse-Physician Communication During Morning Rounds

INTRODUCTION

The Joint Commission found that communication problems were the third most frequent root cause of reported sentinel events in 2015. Research on interdisciplinary rounds and protocols to improve communication has been limited. Structured communication tools have been shown to enhance collaboration between nurses and physicians. This study aims to analyze the impact of a combination of Trio Rounding - a collaborative rounding approach between nurses, physicians, and patients—and a structured communication protocol on interdisciplinary communication.

METHODS

To elicit existing gaps in communication, a free-text questionnaire was randomly administered to nurses and physicians in the Department of Medicine at George Washington University Hospital, a tertiary care center in the District of Columbia. Results were used to outline the satisfaction surveys and the structured communication protocol, which highlights plan for the day, preventative measures and placement plans (the “3 Ps”).

Nurses and physician assistants (PAs) in the Department of Medicine enrolled in this before-and-after study. Trio Rounding and the structured communication protocol were implemented for 5 weeks. To assess satisfaction with communication, 5-point Likert Scale surveys were administered pre- and post-intervention to nurses and PAs, with a score of 5 indicating complete satisfaction and a score of 1 indicating complete dissatisfaction.

RESULTS

8 nurses and 9 PAs completed the pre- and post- intervention surveys. For nurses, although paired T-tests revealed slightly increased satisfaction with combined communication aspects (plan of care, safety measures, discharge planning, and nurse-physician relationships) from pre- to post- intervention, these results were not statistically significant (11.88 vs. 12.13, $p=0.8489$). For PAs, paired T-tests revealed increased satisfaction with nurse-physician relationships from pre- to post-intervention (1.89 vs. 3.33, $p=0.0117$) and increased satisfaction with combined communication aspects from pre- to post-intervention (10.00 vs. 14.89, $p=0.0254$). Consistently pre- and post-intervention, majority of nurses and PAs believed that overlap of nursing duties was the greatest barrier to communication during rounds.

CONCLUSIONS

Based on these results, our intervention had a significant impact on PA satisfaction with interdisciplinary communication. Limitations included the short duration of intervention and small sample size. Our study highlights that implementation of Trio Rounding in conjunction with a structured communication protocol improves satisfaction with interdisciplinary communication, and thus has the potential to mitigate communication problems that commonly lead to medical errors.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Improving the One Call Inter-Hospital Transfer System to Improve Patient Safety and Efficiency of Care

INTRODUCTION

As a tertiary care health center, George Washington University Hospital accepts transfers of care from regional hospitals for patients who need a higher level of care. Due to the high level of care that these patients require, they are often at increased risk of bad outcomes or even death due to their clinical state. However, since these patients are admitted directly to GW Hospital under inpatient status, they bypass the well-developed triaging systems that are in place in the emergency department. Given the relatively high proportion of patient safety concerns surrounding this admission system, a project was undertaken with a goal of expediting time-to-evaluation by the general medicine admitting physician teams.

METHODS

Key stakeholders around the One-Call Hospital transfer system were engaged, including the internal medicine medical residents, nurses, charge nurses, nursing administration, and bedboard. A first PDSA cycle was attempted with the goal of creating an order-set protocol to be executed by floor nurses. This PDSA was unsuccessful and attributed to difficulty identifying individuals who could easily lead such changes as well as concerns about educating all floor nurses about this potential process change. A second PDSA cycle was attempted in which BedBoard associates were given a TigerText account and instructed to text the Medicine Admitting On-Call Officer once patients arrived by ambulance (in contrast to the original system of having the floor nurse call the admitting team once the patient had been situated floor). During the PDSA cycle, the original system of having floor nurses notify the admitting teams was kept in place.

The primary outcome will be the difference in time from arrival at GW Hospital to the time of initial admission order placed by the internal medicine admitting teams by review of the electronic medical record.

RESULTS

Final data on this PDSA cycle will be available by March 2018. Preliminary verbal reports from admitting residents physicians suggests that they have received notifications from BedBoard about the arrival of transfer patients an estimated 30 minutes before receiving notifications from floor nurses in some instances. Admitting resident physicians had a highly positive subjective view of this process change.

CONCLUSIONS

Preliminary evidence suggests that the second PDSA is successful and will facilitate earlier evaluations of transferred patients by internal medicine resident teams. Since these patients occasionally arrive from their transferring facilities with poor or deteriorating clinical conditions, this apparent decrease in time-to-evaluation is viewed as a tremendous success. Exploration of expanding this process to other departments may be warranted.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Adult Reconstruction Hip and Knee Fellowship Program Content and Accessibility

BACKGROUND

To assess the accessibility and content of accredited adult reconstruction hip and knee fellowship program websites.

METHODS

Using the online database of the American Association of Hip and Knee Surgeons (AAHKS), we compiled a list of accredited adult hip and knee/tumor reconstruction fellowship programs. A full list of adult reconstruction hip and knee fellowship programs was gathered from the AAHKS website. The program website links they provided were evaluated. A google search was conducted to identify program websites, and analyzed for accessibility and content in three domains: program overview, applying/recruitment, and education.

RESULTS

At the time the study was conducted, there were 78 accredited adult reconstruction hip and knee fellowship programs identified through the AAHKS program directory. Three of the 78 programs identified had a functional link on the AAHKS fellowship program directory; however, Google search identified 60 websites. 18 programs did not have a website and were not evaluated for content. Data analysis of content in the domains of program details, application process/recruitment and education revealed that most websites included a program description and director name with contact information. However, they were not as comprehensive in the application process/recruitment and education domains.

CONCLUSIONS

AAHKS provides a reasonable method of identifying programs. Yet, most programs can readily be identified using a Google Search (76.9%). Although most fellowship program websites contained program details, there is still paucity of information for fellowship candidates.

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Improving Show Rates for Mental Health Appointments in an Integrated Pediatric Primary Care Clinic

BACKGROUND

Integrated mental health (MH) is relatively new in pediatrics but shows promise for increasing access to MH services. Barriers for families engaging in MH care are well described for traditional settings and include stigma, logistical barriers (e.g., child care), socioeconomic status, and parental MH problems. Families may face similar barriers when accessing MH care in the primary care setting. Little is known about ways to improve family engagement in an integrated setting.

OBJECTIVE

1) Determine the current show rate for psychology appointments at two academic health centers within Children's National Health System: the Children's Health Center (CHC) and Adolescent Health Center (AHC). 2) Improve the psychology appointment show rate through creation of a pre-appointment, personal phone call reminder. Design/Methods: We used QI methodology with a PDSA cycle to implement a phone call reminder system one business day prior to a week's worth of psychology appointments. A retrospective chart review allowed us to determine appointment show rates and no-show rates pre- and post-intervention.

RESULTS

At baseline, the psychologist saw 176 patients April-May, 2017, which reflects a combination of same-day and scheduled appointments. The show rate over this time period for scheduled appointments was 48%, the no-show rate was 43%, and 9% canceled/rescheduled. For context, the average show rate for medical visits is ~70%. The average interval between scheduling date and MH appointment date was 14.02 days (± 8.49). The length of this interval did not impact attendance. There was also no difference in show rates for new consults vs. follow-ups. We were able to reach 54% of the families we attempted to contact to remind them of their scheduled MH appointment. The subsequent show rate for the following week was 33%, the no-show rate was 38%, and 29% canceled/rescheduled. Although the show rate did not improve, the no-show rate decreased as patients were able to reschedule appointments during the reminder phone calls. This intervention shows promise for improving utilization of the integrated psychologist by affording increased flexibility to provide same-day consultations during known cancellations.

CONCLUSION(S)

Families do seem to face barriers to attending MH appointments even in an integrated setting. This PDSA cycle laid a foundation for regularly collecting data on show rates for the psychologist and for future interventions to increase family engagement in MH care.

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Discharge Summaries: An Intervention to Improve Standardized Requirements

Medical doctors write discharge summaries every day, documenting a summary of the hospital encounter of patients. Despite the critical role that these documents play in transitions of care, whether it is to a nursing facility or home, they are often times missing crucial information and physicians get little to no training in the creation of discharge summaries during medical school or residency. The existence of Joint Commission standards mandating discharge summary components has made it such that all discharge summaries should include six pieces of information and missing even one component can jeopardize patient safety. This was addressed in a prior study at the University of Wisconsin where Dr. Smith, et al. reviewed the Joint Commission Standard Requirements for discharge summaries, particularly studying discharge summaries for subacute rehabilitation facilities. In their study, they found that the patient's discharge condition was often omitted. Although the impact on patient safety is not clearly known, it is safe to assume that when patients leave hospitals and are unable to verbalize their medical condition, it is of utmost importance to have documentation of discharge condition in the only paperwork that often follows the patient to their next place of care. The purpose of our quality improve project was to assess whether providing a training session to internal medicine interns at the start of their residency improved those measures as outlined by the Joint Commission. By comparing discharge summaries from September/October 2016, prior to any training session, to those of September/October 2017, after training, we found that there was a roughly twenty percent improvement in inclusion of all the criteria. Our study shows that one teaching session during orientation, particularly for interns who have often times had no exposure to discharge summary writing, can be vital in promoting patient safety. This may serve as a foundation for all residency programs to provide such sessions dedicated to discussing the Joint Commission Standard Requirements for Discharge Summaries, and will also provide ground to create more specific components within discharge summaries that are crucial for transition of care.

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An Evaluation of the Ottawa Ankle Rules as Applied via Telemedicine: A Preliminary Analysis

Despite the increasing use of telemedicine, information is still lacking on whether clinical decision rules (CDR) and guidelines have similar validity when applied via telemedicine compared to in-person. A commonly used and well validated CDR is the Ottawa Ankle and Foot Rules (OAR), used to determine the need for x-rays in acute injuries. The rule is highly sensitive for detecting malleolar fractures when applied by physicians; however, a study of layperson application of the rule demonstrated poor agreement with clinicians.

Our study, launched in July 2017, aims to assess the application of the OAR as applied by in-person ED physicians as compared to telemedicine physician assessment through guided patient self-exam. Preliminary analysis of 64 encounters indicates that in-person and telemedicine physicians have high rates of concordance in their assessments and recommendations for ankle and foot x-ray orders (Cohen's Kappa > 0.9). Additionally, telemedicine providers ordered fewer x-rays than in-person providers, reducing the number of unnecessary scans in patients who did not have a fracture.

Remarkably few studies assess the validity of current CDR as practiced via telemedicine. Preliminary results from our study indicate high agreement between telemedicine and in-person providers for OAR recommendations. As telemedicine grows, these studies will become increasingly important in improving both patient and provider confidence in the quality of telemedicine services.

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Quality Improvement: How Bridge to Care Achieved a 115% Increase in Patient Volume

The Bridge to Care Clinic was started in March 2015 by the George Washington School of Medicine & Health Sciences, the GW Healing Clinic, in partnership with the Prince George's County Health Department. The clinic was originally modelled after GW Healing Clinic's previous partnership with Bread for the City, a FQHC in nearby Shaw, where we ran a smaller operation in coordination with their staff. Unlike at Bread for the City however, at Bridge to Care our operations from patient scheduling, patient check-in, phlebotomy, lab processing, prescription placement, follow-up care, triage, referrals, social services are entirely student run. With increased responsibilities we found over the course of our first year open that patient visit lengths were too long, lab errors occurred frequently, our follow-up with patients was documented inconsistently and our student leadership were overworked. Simultaneously during 2016 we noticed an overall rise in patient volume from 8-9 patients/night to over 13-15 patients/night, and an increase in referrals from the Health Department. So with the joint goal of improving patient care and improving capacity to be able to expand we embarked on a project to quantitatively and qualitatively assess the quality of care at Bridge to Care by: (1) assessing patient satisfaction and the quality of patient care received at Bridge to Care using an anonymous patient survey, (2) assessing clinic workflow by process mapping and looking at clinical operations more critically, and (3) creating tools to improve clinic workflow and adjust clinic protocol accordingly. Literature review and patient testing were utilized to optimize a patient survey for our diverse patient population. Process maps were utilized to outline the workflow for clinic lab and prescription processing. A combination of literature review and quality improvement methods were used to devise new tools, actions and objectives for the clinic. Improvements from the summer included a medication education tracking sheet, a new clinic space, assigned managerial roles and a new leadership plan. As a result, the Bridge to Care clinic expanded from one night to two nights per week, experienced a 115% increase in patient volume, and a 90% increase in blood draws. With our new expanded leadership, workflow, and capacity Bridge to Care is looking forward to continuing quality improvement and furthering expansion of our services to continue to better reach the needs of our community. Our current objectives include introducing specialty nights, incorporating undergraduate volunteers and furthering sustainability for our role in the community.

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The Effect of PGY Status on Rates of Postoperative Complications in All Orthopedic Surgeries – A study on the National Surgical Quality Improvement Project Database

BACKGROUND

The influence of residents' participation on patient morbidity has been thoroughly studied across all specialties in the field of medicine. The focus of these studies was on residents as a whole relative to a control (i.e. attending only). The present study assessed the influence of resident involvement on patient morbidity, but stratified the data among residents based on level of experience.

METHODS

The present study utilized the 2005-2014 NSQIP dataset to assess rate of complications in 36,020 patients after all orthopedic surgeries between two tiers of residents by PGY status. Only residents with PGY value of 1-6 were included in the study. Orthopedic training was separated into two groups: PGY 1-3 and PGY 4-6, signifying first and second half of orthopedic surgery training.

RESULTS

Univariate analysis for operative complications showed higher rate of organ space infection in PGY 4-6 group (0.4% vs. 0.3%, p-value: 0.042). Once controlling for comorbidities on multivariate analysis, these differences disappeared (p-value: 0.111).

On univariate analysis for non-operative complications, PGY 4-6 group had higher rates of pulmonary embolism (0.5% vs. 0.3%, p-value: 0.006), requiring transfusion (9.0% vs. 7.7%, p-value: <0.001), and myocardial infarction (0.4% vs. 0.2%, p-value: 0.009).

On multivariate analysis, pulmonary embolism (Odds ratio: 1.74, p-value: 0.004), post-operative transfusions (Odds ratio: 1.12, p-value: 0.007), and myocardial infarction (Odds ratio: 2.35, p-value: 0.001) were shown to be higher in the more experienced residents, even after controlling for pre-operative comorbidities.

CONCLUSION

We found no significant difference between inexperienced residents (PGY 1-3) and more experienced residents (PGY 4-6) in rates of operative complications. However, it was found that there is a greater risk of non-operative complications in the group of more experienced residents, signifying a discrepancy exists in medical management post-operatively as orthopedic residents advance through training.

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IPASS These Patients to You

Quality, standardized sign-out between medical providers is integral to patient safety on an inpatient service. It has become increasingly important with restrictions to resident work hours. The IPASS handoff structure (i.e., illness severity, patient summary, action items, situational awareness and contingency planning, synthesis by receiver) has previously been established to reduce verbal and written miscommunications and errors when used and implemented within an education bundle (Sectish et al, Pediatrics 2011). Our aim was to utilize the IPASS structure to standardize the written handoff process between day and night teams in the internal medicine residency.

We performed seven PDSA cycles. The first PDSA cycle was sending an email to the interns on a single team explaining IPASS and how to use it. Uptake was the main barrier with the interns reporting it was burdensome. Handoffs were scored on a numerical scale correlated to incomplete, partially complete and complete. During the second cycle the resident on a single team interactively provided ongoing education on IPASS. The interns were more receptive to implementation in this cycle and furthermore the sign-outs were more complete (19% improvement). The next PDSA was to explore the impact of IPASS compared to the traditional handoff method on the night float interns, who completed a survey. The night float interns did not notice a large difference between traditional method and IPASS. Our next step was exploring resident uptake through asking two residents on different teams to implement IPASS. They received an email explaining IPASS and were asked to incorporate it into handoff of all new patients to the team. They successfully passed this message onto their interns. However, night float reported it was confusing to have mixed formats on the same team. We next attempted to implement it into the electronic system to reduce barriers to implementation but found this was not readily possible in discussion with IT. Next, in an effort to further justify IPASS, we completed another PDSA cycle of timing verbal handoff which averaged approximately 1 minute per patient. The last completed cycle was implementation of IPASS on an entire team with night float feedback which garnered good responses from the program.

In conclusion, these results are promising for the uptake of the validated IPASS sign-out format however implementation into current workflow remains the greatest barrier. Future work is focused on IT incorporation for IPASS.

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Understanding Nurse, Family, & Interpreter Involvement in Family-Centered Rounds at Children's National Medical Center

Family-Centered Rounds (FCR) is a model that emphasizes bedside rounding with intentional inclusion of the patient and family in partnership with physicians, nurses, and staff. Challenges to conducting successful FCR include language barriers and a lack of a reliable notification system for all parties. These barriers can be overcome through the development of a FCR mobile application to improve communication and coordination between the stakeholders involved in a child's care.

This study analyzed data on nurse, interpreter, and family inclusion in FCR. Objective observations of daily FCR - measures of medical team communication with nurses, stakeholder presence, and licensed interpreter use for limited-English proficiency (LEP) families - were recorded using REDCap. REDCap was also used to survey physicians and nurses for a subjective measure of team communication and nurse presence at FCR.

Physicians self-reported contacting nurses 80% of the time for FCR. However, objective measures showed that they contacted nurses only 59% of the time. When contacted before rounds started, more nurses were present for the entire duration of FCR. Additionally, their presence any time during FCR increased by 31% compared to nurses who were contacted at/ after the start of rounds. This indicates the importance of early notification, a task which can be better facilitated by a mobile app. The most common barrier reported by physicians is nurses not answering their phones. The leading reason nurses self-report for missing FCR is patient care duties, which could explain their inability to answer their phones at all times. The mobile app will resolve this dilemma by providing a text notification option, a method which more than 55% of nurses and doctors are willing to use.

Language is another barrier to conducting successful FCR. Although LEP families were present more often than English proficient (EP) families, they were offered FCR less frequently. Also, a licensed interpreter was only offered 58% of the time. This study demonstrates a need to better facilitate FCR among doctors, nurses, families and interpreters at Children's National. The data shows low nurse attendance, disparities in FCR being offered to LEP vs EP families, and a lack of licensed interpreter use.

We propose that technology such as a mobile app notification system can facilitate better communication and coordination between all parties, ultimately improving patient care.

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Intervention to Improve Residents' Medication Reconciliation Accuracy at Hospitalization Discharge

BACKGROUND

Medication reconciliation is an effective tool to reduce discharge medication errors, which are a major patient safety concern. At the Washington DC VA medical center, medication reconciliation is performed largely by internal medicine residents. Previously, education on medication reconciliation has been successfully provided to residents at our institution. However recently, the curriculum, in addition to formal training, has largely been abandoned.

OBJECTIVE

We aimed to improve the accuracy of medication reconciliation at discharge via an educational intervention for internal medicine residents.

METHODS

The intervention was run from August 2017 to December 2017 and delivered to internal medicine residents from four academic institutions rotating at the Washington DC VA medical center. The educational intervention featured a pocket card outlining the discharge medication reconciliation process, a discharge instruction guide in the orientation booklet, and once weekly or biweekly educational seminars delivered at resident conference. The seminars were led by a chief resident or a faculty member and focused on teaching both quality improvement principles and our institution-specific medication reconciliation process. An effort was made for the seminars to be interactive including time for residents to practice medication reconciliation or assess their own performance using a self-evaluation rubric. The intervention was refined over the course of three PDSA cycles. The accuracy of 50 post-intervention discharge medication lists was compared to that of 50 pre-intervention lists. Accuracy was assessed using a rubric to review the medication list on the patient's discharge instructions compared to the data in the progress note on the discharge date.

RESULTS

The patients included in the pre-intervention chart review were discharged on average with 11 medications while the patients in the post-intervention group received 10. Between the two groups, the number of duplicate medications (26% vs. 9%), extraneous medications (20% vs. 14%), medications sorted by disease or indication (64% vs. 72%), and necessary medications that were omitted (26% vs. 14%). All improved via the intervention.

CONCLUSION

Our educational intervention targeting internal medicine residents is effective in improving the accuracy of medication reconciliation at hospital discharge. However, the challenge remains in making this intervention multidisciplinary, time-effective, and sustainable. We hope that the success of this QI project will help promote future institutional support and stakeholder participation in continuous efforts to ensure patient safety via accurate medication reconciliation.

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A Cross-Sectional Study of Emergency Preparedness in a Tertiary Care Pediatric Emergency Department

OBJECTIVE

To evaluate the culture of emergency preparedness at a tertiary-care Pediatric Emergency Department and the perceived ability to respond to an emergency evacuation order.

METHODS

We performed a cross-sectional survey of emergency providers in an urban tertiary-care pediatric emergency department. A 20-question survey was distributed to providers after participating in a table-top simulation of an ED evacuation scenario. Participants were asked about prior training, importance of disaster training, and feelings toward personal and institutional emergency preparedness. Likert Scales were used to evaluate participants' attitudes towards emergency preparedness training and self-evaluated preparedness. Participants were asked to respond to statements on a scale from 1-5 (Strongly Disagree-Strongly Agree). Median scores were reported.

RESULTS

51 ED providers were surveyed over a six week period. 49% (25) of respondents reported working in the department for >5 years, while 31.4% (16) and 19.6% (10) responded 1-5 and less than 1 year, respectively. 41.2% (21) of respondents had participated in an emergency preparedness drill within the prior year, and 72.5 (37) had undergone prior disaster training. 11.8% (6) of respondents reported having participated in a live evacuation during their career.

The median response score for the statements "Disaster Preparedness is an important part of my continuing education" and "Disaster Preparedness improves my ability to treat patients during a disaster" were 5 and 5, respectively. The median score for "An Emergency Evacuation seems likely to occur in my workplace," was 4, however the median for "the Emergency Department is adequately prepared to respond to an evacuation order" was 3.

The majority of respondents had not read the evacuation plan [78.4% (40)] and were unsure where to find it [60.8% (31)]. 49% (25) of respondents were confident in their role during an evacuation, and 41.2% (21) were confident in their unit's level of emergency preparedness.

CONCLUSION

The goal of this study was to evaluate the emergency preparedness culture and the evacuation capability in a pediatric emergency department. The literature contains very little discussion about the opportunities or challenges unique to evacuating a pediatric emergency department. The results of our survey show that providers value the importance of disaster preparedness and training, particularly focused on evacuations. This value, however, did not correlate with confidence in evacuation preparedness. This lack of confidence in the context of an otherwise robust preparedness culture highlights an opportunity for future improvement. Future directions for this work would be to conduct this table top exercise and survey at different times of the year with variations in seasonal conditions. Considering the challenging environment of the ED, this table top and evaluation format could be a feasible model to implement for training in evacuations.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Impact of COPD on Peri- and Post-Operative Comorbidity and Complications in Patients Undergoing Revision Total Knee Arthroplasty

BACKGROUND

Total knee arthroplasty (TKA) is currently one of the most prevalent orthopedic procedures in the United States used to treat a wide variety of orthopedic conditions and is increasingly more popular among aging Americans. Chronic obstructive pulmonary disease incidence has been steadily rising over the past few decades and it is currently one of the leading causes of death worldwide. Given the increased prevalence of COPD among the aging and elderly, the disease is becoming more common in TKA surgical candidates. Because of this, it is important to understand the impact and relationship of the disease on a broad array of peri- and post-operative comorbidities and complications so that surgeons may more appropriately assess pre-operative risk.

METHODS

A retrospective cohort study was conducted using data collected through the American College of Surgeons National Quality Improvement Program Database. All patients who underwent revision TKA between 2007 and 2014 were identified. These patients were stratified into groups based on the presence or absence of COPD (without COPD = 9370 [94.4%]; with COPD = 551 [5.6%]). The incidence of adverse events following surgery was evaluated with univariate and multivariate analyses where appropriate

RESULTS

This study used 9,921 subjects who underwent revision TKA. A total of 551 patients had COPD [5.6%] and 9,370 did not [94.4%]. Patients with COPD were found to have increased risk of 8 of 9 peri-operative comorbidities and increased risk of 14 of 18 independent post-operative complications as well as increased risk of all-cause post-operative complications. COPD was also found to be an independent risk factor for unplanned return to the OR.

CONCLUSION

Patients with COPD undergoing revision TKA have greater risk for peri- and post-operative comorbidity and complications than those without COPD, with a 28% overall risk for all-cause complications. While risks for independent complications remain relatively low, consideration of COPD status is an important factor to consider when selecting surgical candidates.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Pushing the Limits: Perinatal Outcomes Beyond Prolonged Second Stage

INTRODUCTION

Evaluate whether extremely prolonged second stage of labor in nulliparous women affects maternal and neonatal outcomes.

METHODS

We performed a retrospective cohort study of term, nulliparous women with singleton gestations, epidural anesthesia, who reached 10 centimeters of cervical dilation. Exclusion criteria were intrauterine fetal demise, planned cesarean delivery or major fetal anomaly. Women were compared by length of second stage: 0-179 minutes (normal second stage), 180-299 (prolonged second stage) and ≥ 300 (extremely prolonged second stage). Primary outcome was incidence of spontaneous vaginal delivery (SVD). Secondary outcomes were maternal and neonatal outcomes.

RESULTS

In total, 662 women were evaluated: 115 extremely prolonged second stage (EPSS), 116 prolonged second stage (PSS) and 430 normal second stage (NSS). Incidence of SVD was 93.3% in the NSS group, 86.2% in the PSS group and 50.4% in the EPSS group. The PSS group had a higher incidence of 3rd degree laceration. The EPSS group had a higher incidence of postpartum hemorrhage compared to the NSS group, 3rd degree laceration, neonatal CPAP use and composite neonatal outcome.

CONCLUSIONS/IMPLICATIONS

In nulliparous term women who reached 10 centimeters, the chance of SVD decreased by 55% after 3 hours and by 97% after 5 hours. However, most women delivered vaginally, with 70.4% delivering by SVD after 5 hours. The PSS group had similar maternal and neonatal outcomes as the NSS group; whereas the EPSS group had significantly worse outcomes. Risks and benefits of PSS vs EPSS should be weighed during clinical decision-making on the length of labor during the second stage.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Physical Activity After Delivery: A Pilot Feasibility Study

INTRODUCTION

Enhanced Recovery after Surgery, focuses on decreasing factors associated with prolonged hospital stay. These factors are: pain control, ileus, and immobilization. Although ambulation is a recognized key element for recovery, and a known method of mechanical prophylaxis against deep venous thrombosis (DVT), this variable is rarely objectively measured immediately post-partum.

METHODS

In this pilot study, we evaluated the physical activity after vaginal (VD), and Cesarean delivery (CD), of 24 and 10 parturients respectively, by using a research validated accelerometer (Actigraph GT3X). We examined the effects of age, gestational age, BMI, race, ethnicity, mode of delivery, pain score at rest and with movement, and satisfaction with analgesia over steps taken. The noted variables and number of steps were assessed at 6, 12, 24, 36 and 48 hours after delivery. A 2-tailed- t-test or chi-square were used to analyze the data, with $p < 0.05$ considered significant.

RESULTS

Demographic data analysis is summarized in Table 1. Based on unadjusted, univariable analysis, statistical difference in steps taken between CD and VD patients was noted at 12, 24 and 36 hrs with $p = 0.049$, 0.017 and 0.02 respectively. Satisfaction with pain management was higher for VD at all times; CD patients were significantly less satisfied with their pain management starting at 24hrs post-delivery. After adjusting for pain satisfaction, static maternal age, BMI and race, mode of delivery remained associated with number of steps taken, averaged across time points ($p = 0.03$). On average, after adjustment of covariates, CD and each additional year of maternal age were associated with 2198 (95% CI 237-4159), $p = 0.03$ and 159 (95% CI 23-295), $p = 0.024$ fewer steps respectively.

CONCLUSION

Monitoring patients postpartum with an accelerometer was easily accomplished. Fewer steps were taken with advancing maternal age and after CD. Accelerometer data should be further studied to assess outcomes, and to evaluate the efficacy of educational efforts and multimodal pain management strategies.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Urinary Tract Infection in Children with Spina Bifida and Spinal Cord Injury

INTRODUCTION

Urinary tract infections (UTI) are one of the most common bacterial infections (Schappert & Rechtsteiner, 2008; Litwin et al., 2005). Data from the National Ambulatory Medical Care Survey estimated that UTI caused 8.1 million physicians visits (Schappert & Rechtsteiner, 2008). Children with spina bifida (SB) and spinal cord injury (SCI) are at high risk for UTI (Ouyang et al., 2010; Nair et al., 2005). The purpose of this study was to examine the organisms associated with UTI in the population of children with SB and SCI who were treated in out-patient and in-patient settings at the Kennedy Krieger Institute (KKI).

OBJECTIVE

To examine the organisms and antibiotic resistance patterns that cause UTI in SB and SCI in the population of children who are treated in out-patient versus a sub-acute hospital setting.

METHODS

The Retrospective record review linked SB and SCI with UTI. Data acquisition included the identification of the organism, the antibiotic resistant patterns, medication and diagnosis. Data were obtained from medical records and a pre-existing data base of KKI in inpatient and outpatient with SB and SCI who have UTI from the year 2010-2013. Descriptive statistics summarized the organisms causing UTI by patient diagnosis and inpatient status.

RESULTS

Participants (N = 31) were approximately equally distributed (male = 52%; n=16). The mean age of the population was 16 years with a standard deviation (SD= 7.8). The majority of participants are: 55% white (n= 17), 32% African American (n= 10), 10% American Indian (n = 3) and all respondents were 6% non-Hispanic (n=1, Hispanic n = 1). Medical condition/ diagnosis (SCI = 22, SB = 13) medication(s), organism (s) responsible for UTI, organism (s) antibiotic resistance, hospital status (inpatient = 23, outpatient = 0) were obtained. Data presented on infectious organisms and antibiotics susceptibility for participants with spinal bifida and spinal cord injury.

CONCLUSION

There were no statistically significant differences in the organisms infecting children with SCI compared to SB. E. coli is the leading cause of UTI in our study. Contrary to the studies of hypothesis, the susceptibility of the bacteria to commonly used antibiotics is good. It is also recommended that proper sensitivity testing of Urinary tract infection causing organisms should be undertaken.

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Where She Lives: The Impact of Neighborhood Location and Violent Crime Exposure Risk on Maternal Mortality in the United States—A Case Study of Baltimore, MD

Maternal mortality continues to remain a public health crisis, especially in the United States. Between 1990 and 2013, the maternal mortality ratio (MMR) for the US rose from 12 to 28 maternal deaths per 100,000 births, higher than most developed nations. This issue is even more concerning when discovering that more than 50% of said maternal deaths in the USA have been deemed preventable. Equally as concerning is the increasing racial disparity that persists in the US regarding maternal mortality. According to the CDC, Black mothers are 3-4 times more likely to die in child birth as compared to white mothers. In seeking to address this disparity and the maternal mortality crisis in general, public health leaders in the US have largely focused on viewing the narrative of birth outcomes and racial disparities as a binary of lack of access and utilization of resources at appropriate stages in the pregnancy process and poor maternal health behaviors due to factors largely influenced by income and education.

This focus on maternal behaviors however misses the mark in addressing however a rising and ever-present concern for those taking care of pregnant and postpartum women, how where one lives and the risk of violence plays a role in their lives and health outcomes.

Through a review of the current literature, national health databases, and state specific maternal mortality review annual reports over the last three decades, this paper aims to answer to show that pregnant and postpartum patients are not only at increased risk of mortality, specifically homicide and suicide due to their situational circumstance but that where they reside, their specific neighborhood, may also play a statistically significant role in increasing their risk of being victims of substance abuse, violence and trauma. Through unmasking how place and crime intercede and impact maternal health outcomes, specifically through a case study of Baltimore City, Maryland, this paper hopes to illuminate a more refreshed way of viewing maternal mortality and offer more tailored solutions than previously presented or publicly acknowledged.

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Secretomic Analysis of Spent Embryo Culture Media

OBJECTIVE

Pre-implantation genetic screening (PGS) with euploid blastocyst transfer has facilitated the selection of embryos most suitable for replacement and the optimization of in vitro fertilization (IVF) outcomes. Non-invasive determinants of embryonic competence could be used independently or in conjunction with PGS for embryo selection. Promising methods for evaluating embryonic implantation potential include the evaluation of substrates or byproducts of embryo metabolism, such as metabolite utilization and the assessment of secreted proteins or metabolites in spent embryo culture media (secretome). Using tandem mass spectrometry (MS), we sought to investigate the embryonic secretome in spent embryo culture media in relation to embryo development and quality. After validation of the technique, the embryonic secretome in relation to aneuploidy and IVF outcomes will be investigated.

DESIGN

Prospective cohort

MATERIALS AND METHODS

Patients undergoing IVF with comprehensive chromosome screening (CCS) at Shady Grove Fertility Center were eligible to participate. From fertilization until day 3 of development, embryos were cultured in Continuous Single Culture Medium supplemented with Serum Protein Substitute. From day 3 of development until the blastocyst stage (day 5 or 6), embryos were cultured in Blastocyst Medium supplemented with human serum albumin. Embryos were co-cultured in groups of 3 or 4 from fertilization until the blastocyst stage was obtained. An immunoaffinity depletion strategy was used to deplete high abundant serum proteins (i.e. albumin) from media samples. The remaining proteins secreted into the media were digested with trypsin using pressure cycling technology and peptide digests were analyzed by nanoflow liquid chromatography (LC) coupled with a high-resolution Orbitrap Fusion Lumos mass spectrometer. Tandem mass spectra were searched against a SwissProt human protein database and the relative abundance of proteins were determined by comparing the number of peptides identified per protein across all samples (spectral counting).

RESULTS

Albumin and high abundant proteins were successfully depleted from the embryo culture media, as evidenced by the low peptide-to-spectrum matches of albumin after the Multiple Affinity Removal System protocol. There were no significant differences in the secretome of spent embryo culture media between control samples and those in which embryos were cultured. This may be a limitation related to depletion of albumin and associated bound proteins.

CONCLUSIONS

The use of a Multiple Affinity Removal System protocol resulted in successful depletion of albumin and high abundant proteins in embryo culture media, which may facilitate the detection of low abundance proteins. After albumin depletion, no differences in the secretome between control and sample embryo culture media droplets were detected.

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An Exploration of Global Women’s Health: Findings from a Pilot Online Course Elective for Health Sciences Studies at GW

In 1995, 189 countries endorsed the *Platform for Action*, designed to address issues of gender equality, including health. Despite this 23 year old initiative, women’s health issues continue to be a global crisis (WHO, 2015). The SMHS piloted an 8-week online 1-credit course in Fall 2017 to educate GW students on the top ten issues for women’s health delineated by the World Health Organization (WHO). Each of the eight weeks covered a core women’s health WHO issue while tying in a global human rights perspective. Issues included but were not limited to reproductive health, STIs, violence against women, to name a few. This course was designed to address two key gaps at GWU: 1) there is currently no other course at GW focused on Global Women’s Health offered to undergraduate students, and 2) this is the first 1 credit hybrid elective course, in Health Sciences, to be offered to undergraduate residency students. The teaching platform adopted for this course offered an “inter-school” student body. Enrollees included 7 students from the Elliott School of International Affairs, 6 from the Columbian College of Arts & Sciences, and 1 had a major from the Milken Institute School of Public Health. Course evaluations revealed that students wanted to delve deeper into covered topics and expand to additional topics if we had more time. 90% of students said they would recommend it to others. Qualitative feedback was categorized to indicate that students enjoyed the types of course assignments, the range of topics that were covered throughout the course, as well as the online resources that were provided to supplement the reading material of the course textbook. About half of the students who took this course indicated they would enroll in the course regardless of the delivery platform, face-to-face, blended or online. Pilot course assessment findings also suggest that this course could be expanded into a 3-credit course, could be taught in person, and could be offered as an elective that could count for credit towards other majors within different departments in order to increase its reach. It is imperative to raise awareness within our student body of the importance of addressing women’s health issues worldwide, so that they too can be a part of the commitment to achieve gender equality that began at the 1995 Beijing Declaration and Platform of Action.

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Medical Diagnoses and Associated Characteristics of Neonatal Intensive Care Unit Infants Enrolled in the Giving Parents Support Study

BACKGROUND

Children's National Health System (CNHS) has a number of research studies being performed in the Neonatal Intensive Care Unit (NICU), including Giving Parents Support (GPS), a randomized controlled trial of parent navigation after NICU discharge. As a Level IV NICU, CNHS provides care to the sickest infants with a wide range of medical complexity.

OBJECTIVE

To describe the medical diagnoses and associated characteristics of NICU infants enrolled in GPS.

METHODS

Participants in the GPS study were enrolled from January 2016 to February 2017, and no infants were excluded due to diagnostic criteria. Approximately 300 infants were enrolled, and medical diagnoses were collected from the Children's Hospitals Neonatal Database and classified by organ system; data was provided on 86% of GPS infants (n=257). Associated characteristics, such as infant sex and gestational age (GA), were obtained via chart review. Diagnoses belonging to preterm (<37 weeks GA) and term (37+ weeks GA) infants were categorized separately.

RESULTS

Most infants were male (68%), full-term (55%), and diagnosed with at least one respiratory condition (58%); the majority of those in the latter group (83%) had respiratory distress syndrome (RDS). Of the 115 premature infants reviewed, 12% were diagnosed with bronchopulmonary dysplasia (BPD), 9% were diagnosed with intraventricular hemorrhage, 2% were diagnosed with periventricular leukomalacia, and 13% were diagnosed with necrotizing enterocolitis. Of the 142 term infants reviewed, 5% were diagnosed with hypoxic-ischemic encephalopathy (HIE) and 11% were diagnosed with seizure. Less than 1% of term infants received extracorporeal membrane oxygenation.

CONCLUSION

Medical diagnoses among GPS infants were variable, although most had a respiratory diagnosis of RDS. The most common diagnosis among preterm and term infants was BPD and seizure, respectively.

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Acute Care Long Acting Reversible Contraceptive Placement: A Compare and Contrast Study

BACKGROUND

Improving access to effective contraception and reducing rates of unintended pregnancy are national public health objectives. Long Acting Reversible Contraceptives (LARCs) are safe, well tolerated and the most effective means of reversible contraception. Unfortunately, the requisite clinical pathway leading to LARC placement can dissuade women from obtaining care, as this process is often unfamiliar, time-consuming and expensive. LARC counseling and placement in the Acute Care setting is a novel strategy intended to minimize these logistical barriers. In the present study, we hypothesize that women will express interest in an Acute Care based LARC placement program and that an "expedited referral to a Gynecologist" (ERG) will fail to capture a significant proportion of women interested in obtaining a LARC.

METHODS

This study consists of a 21-question cross-sectional survey, a brief contraceptive counseling video (BCCV) and an optional ERG for contraceptive counseling and placement. A convenience sample of women ages of 18 and 50 were approached at a freestanding urgent care center (UC) (N=146) and an emergency department based urgent care center (ED) (N=144). The study was powered to an N of 288 participants and data analysis completed with chi-squared and t-tests.

RESULTS

Of 439 women approached, 290 (66%) met eligibility criteria and enrolled. 152 participants (52%) reported using their preferred method of contraception. This number decreased to 117 (40%) after viewing the BCCV. 154 (53%) of participants expressed interest in returning to an Acute Care setting for LARC placement. Only 28 of the 114 (25%) participants requesting ERG scheduled a visit when contacted by an office manager. There was no statistical difference regarding responses recorded at the ED vs. UC.

CONCLUSION

Nearly half of reproductive age women presenting to the ED and UC are not using their preferred method of contraception. Most women felt comfortable discussing contraception in the Acute Care setting and many expressed interest in an Acute Care based LARC placement program. Moreover, an ERG program failed to link a significant proportion of women interested in obtaining a LARC to care. Acute Care LARC counseling and placement is a novel and potentially viable strategy to supplement existing healthcare infrastructure and improve access to effective contraception.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Effect of COPD on Postoperative Complication Rates for Laparoscopic Hysterectomy

OBJECTIVE

The purpose of this study was to evaluate the impact of COPD on postoperative complication rates for laparoscopic hysterectomy.

BACKGROUND

Hysterectomies are one of the most common procedures done in the United States. The incidence of COPD particularly in women has been steadily rising over the past few decades. There has also been very limited research on COPD and its association with morbidity and mortality after laparoscopic hysterectomies. In this study, we examined the following: (1) What demographics and comorbidities are most likely to present concurrently in patients with COPD? (2) Are patients with COPD undergoing laparoscopic hysterectomy at increased risk for development of postoperative complications within 30 days? (3) Do patients with COPD have a higher propensity for extended hospital stay or unplanned return to operating room? (4) Does COPD act as an independent risk factor for development of particular postoperative complications within 30 days?

STUDY DESIGN

This was a retrospective cohort study using data collected from 2005 to 2013 from American College of Surgeons National Surgical Quality Improvement Program Database. All patients who underwent laparoscopic hysterectomies were identified by CPT codes and stratified based on their COPD status. Univariate and Multivariate analyses were done to determine the incidence and frequency of postoperative complications within 30 days of a laparoscopic hysterectomy.

RESULTS

This study included 42,674 patients that underwent laparoscopic hysterectomies (COPD=479 [1.12%]); (no COPD=42195 [98.8%]). Patients with COPD were found to develop more postoperative complications, including pneumonia, reintubation, renal insufficiency and sepsis. COPD was found to be an independent risk factor for the development of these complications. Of note, patients with COPD were found to have extended length of hospital stay.

CONCLUSION

Our study found that patients with COPD who undergo laparoscopic hysterectomies have a greater risk of developing postoperative complications including pneumonia, reintubation, renal insufficiency and sepsis. The overall occurrence of postoperative complications is low. Gynecologists should take into consideration the COPD status of patients when evaluating their preoperative risk. Overall, the complication rates are relatively low and so the procedure is safe.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Cesarean Delivery Prevention: The Vaginal Breech Initiative at the George Washington University Hospital

INTRODUCTION

Reducing the cesarean delivery rate is a national priority. Performing vaginal breech deliveries can be one important component of a cesarean reduction strategy. Scientific evidence, professional recommendations and consumer demand have all shifted to support vaginal breech delivery as an option to routine cesarean delivery for breech presentations. At the George Washington University Hospital (GWUH), we have established a Vaginal Breech Initiative to increase access to vaginal breech delivery. We are currently studying deferred, attempted and successful vaginal breech deliveries performed at GWUH after the institution of the Vaginal Breech Initiative. We hope to identify the components of successful and unsuccessful vaginal breech deliveries, as well as look at the outcomes of these deliveries. This interim analysis aims to describe our vaginal breech success rate and identify which breech vaginal deliveries were conducted as a part of the Initiative and adhered to our protocol.

METHODS

This is an observational report and interim data analysis of the vaginal breech labors and deliveries managed by a Breech Vaginal Team at GWUH. Electronic medical record (EMR) query identified all charts with relevant ICD-9 codes. A retrospective chart review of planned, attempted, and deferred vaginal breech deliveries at GWU Hospital from 2014-2017 was conducted.

RESULTS

This is an interim analysis based on review of 398 patient charts. Preliminary outcome data from patients attempting a breech vaginal delivery (n=50) at GWUH demonstrate a 76% vaginal breech success rate. Of the total attempted vaginal breech deliveries, 70% (n=35) occurred in the context of the Vaginal Breech Initiative. Of these, provider adherence to the established protocol was demonstrated in 91.4% (n=32) of cases.

CONCLUSION

Improving access to, and training in vaginal breech at GWUH has contributed to a reduced cesarean delivery rate and increased patient satisfaction. It has also provided critical training and skills for our health care providers. Through careful diagnosis, patient selection, counseling, and collaboration, breech vaginal deliveries performed in the context of a Vaginal Breech Initiative are feasible in an academic medical center. This ongoing project requires continued review of patient charts to further evaluate our vaginal breech processes.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Perioperative Complications and Impact of Diabetes Mellitus Severity on Laparoscopic Hysterectomy

BACKGROUND

Hysterectomy is the second most common surgery performed on women and is commonly utilized in the treatment of several common gynecological complaints. With the advance of surgical techniques, the laparoscopic approach has become the standard of care in most cases. Diabetes mellitus (DM) has been shown to increase a patient's risk of postoperative complications for several procedures. However, the current research in the field gynecological surgery is minimal. This project seeks to identify an association between severity of DM and risk of postoperative complications following laparoscopic hysterectomy.

METHODS

The American College of Surgeons National Surgical Quality Improvement Program database was utilized to identify patients who underwent laparoscopic hysterectomies from 2007 through 2013. Patient cohorts were non-insulin-dependent DM (NIDDM), insulin-dependent DM (IDDM), and no DM. The incidence of postoperative complications within 30 days of the procedure was evaluated utilizing univariate and multivariate analysis.

RESULTS

After inclusion criteria, 42,674 patients who underwent laparoscopic hysterectomy were included in the study. The no DM cohort was comprised of 39,245 patients (92.0%), the NIDDM cohort included 2,493 patients (5.8%), and the IDDM cohort included 936 patients (2.2%). Overall, DM increased a patient's risk of developing postoperative complications. NIDDM patients had an increased risk of 8 of 21 evaluated postoperative complications compared to patients without DM. IDDM patients had an increased risk of 12 of 21 postoperative complications studied compared to patients without DM.

CONCLUSION

Although rates of complications following laparoscopic hysterectomy are relatively low in non-DM patients, patients with DM have an increased risk of experiencing a complication compared to a non-diabetic patients. Furthermore, patients with IDDM have a greater risk of experiencing postoperative complications. With this information, gynecological surgeons can better evaluate diabetic patients' risk of developing postoperative complications following laparoscopic hysterectomy and counsel them appropriately.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

Low PAPP-A Levels and Pregnancy Outcomes

INTRODUCTION

Pregnancy-associated plasma protein A, or PAPP-A, is a high molecular weight glycoprotein used as an analyte for first trimester aneuploidy screening along with hCG. There is a significant association between low PAPP-A and adverse pregnancy outcomes, such as: preterm birth, intrauterine growth restriction, stillbirth, and preeclampsia. A recent retrospective study further supports an association of low PAPP-A with aneuploidy and adverse pregnancy outcomes. A systematic review also suggested an association between low serum PAPP-A and adverse pregnancy outcome, but indicated that the predictive values of low PAPP-A remain poor and that further studies should focus on PAPP-A as a prediction model. Because PAPP-A affects placental function, it may affect labor. The objective of this study was to determine if low PAPP-A is associated with labor dysfunction.

METHODS

This is a retrospective study of pregnant women who gave birth at GW Hospital between July 2013 and July 2016. Women with PAPP-A in the 5th percentile (5thile) were compared to women with PAPP-A less than or equal to the 1st percentile (≤ 1 ile). The primary outcome examined was cesarean delivery (CD) rate and the secondary outcomes were indication for CD and perinatal outcomes. Women with fetuses with known or suspected aneuploidy were excluded from the study.

RESULTS

139 women were included in the study; 91 women with PAPP-A in 5thile and 48 women with PAPP-A ≤ 1 ile. Demographics were similar except for gestational age at delivery (38.6 ± 3.6 weeks in the 5thile group vs. 35.9 ± 7.4 weeks in the 1stile group, $p = 0.004$). There was no difference in CD rate (27/91 (29.7%) vs. 12/48 (25%), $p = 0.6$), fetal indication for CD (8/27 (29.6%) vs. 4/12 (33.3%), $p = 0.8$). Birth weight was significantly higher in the 5thile group vs. the 1stile group (3264.6 ± 580.8 grams vs. 2935.4 ± 715.3 grams, $p = 0.004$). Neonatal morbidity composite score was different between groups; (18/91 (19.8 %) in the 5thile group vs. 18/48 (37.5%) in the 1stile group $p = 0.02$).

CONCLUSION

PAPP-A levels less than or equal to the 1st percentile does not seem associated with delivery mode or indication for cesarean delivery in comparison to PAPP-A levels in the 5th percentile. However, PAPP-A levels less than or equal to the 1st percentile may be associated with increased neonatal morbidity during labor, as well as lower birth weight and preterm birth in comparison to PAPP-A in the 5th percentile.

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

An Analysis of the Influence of Provider on the Development of Intraamniotic Infection

INTRODUCTION

Intraamniotic infection affects 2-5% of term deliveries, and is associated with acute neonatal and maternal morbidity. It is not known how midwifery care influences the development of intraamniotic infection.

METHODS

This is a retrospective case control study of term, singleton pregnant patients who delivered at George Washington University Hospital from January 2012 to December 2015. Cases of intraamniotic infection were identified by billing codes and controls were the next two patients who delivered without an intraamniotic infection. Data collected included: demographics, provider type, BMI, number of vaginal exams, medical comorbidities, rupture of membranes status, labor induction/augmentation methods, GBS status, and delivery type. A univariate analysis with a chi-square test identified quantitative confounders. Multivariate logistic regression model evaluated if provider type is independently associated with intraamniotic infection.

RESULTS

Data analysis pending. It will be available during the poster presentation at GWU Research Day.

CONCLUSION/IMPLICATIONS

This study is a novel look at risk factors for developing intraamniotic infection. Our findings will be more thoroughly fleshed out in the poster.

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