SURF | POSTER PRESENTATION LIST

Denman (UC 2.01.28)
1:00PM - 2:00PM

POSTER #1
Effects of Peripheral and Spinal Administration of Mu-opioids on Postoperative Anti-hypersensitivity in Aged and Adult Mice
Jennifer Mecklenburg and Armen Akopian

POSTER #2
Retrospective Analysis of the Post-operative Changes in Higher Order Aberrations: A Comparison of the WaveLight® EX500 to the VISX® S4 Laser in Refractive Surgery
Donovan Reed, Douglas Apsey, Walter Steigleman, James Townley and Matthew Caldwell

POSTER #3
Impact of Teaching Institutions on Socioeconomic Aspects of Chest Pain in the United States
Lindsay Euers and Ali Seifi

POSTER #4
Diabetes in Combat: Effect of Military Deployment on Diabetes Mellitus in Air Force Personnel
Irene Folaron, Mark True, Jana Wardian and Tom Sauerwein

POSTER #5
Genomic Analysis of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis
Brittany Lenz, Thomas Beachkofsky and Patrick Brown

POSTER #6
Development and Characterization of a Preclinical Model Recapitulating Battlefield Stress
Natasha Sosanya, Thomas Garza, Robert Christy and Bopaiah Cheppudira

POSTER #7
3T UPC EBP Retrospective Analysis of Bundle Compliance in MICU Patients
Cassandra Bullock

POSTER #8
Gerardo J. Pacheco, Laura Miller, Rose C. Grimm, Judson C. Janak, Nicole A. Dierschke, Jean A. Orman, Mary Ann Spott and Janice Baker

POSTER #9
En Route Intraosseous Access Performed in the Combat Setting
Sheila Savell, Alejandra Mora, Crystal Perez, Avery Kester, Vikhyat Bebarta and Joseph Maddry

POSTER #10
Emergency Airway Management at San Antonio Military Medical Center: A 12-Month Descriptive Analysis
Michael April, Joseph Maddry, Steven Schauer, Jessie Fernandez, Kimberly Medellin, Daniel Sessions, Shane Summers, Robert Barnwell, Avery Kester, Michael Hilliard and Mark Antonacci

POSTER #11
Healthcare Affordability and Complexity of Medical Visits
Jennifer Daniels and Sandra Burge

POSTER #12
Traumatic Knee Injury: How much Knee Effusion on Radiography is Pathologic?
Nathan Cecava, Shane Dieckman, Liem Mansfield and Kevin Banks

POSTER #13
Battlefield Acupuncture for Acute/Subacute Back Pain in the Emergency Department
Kyle Johnston and Timothy Bonjour

POSTER #14
Crisis Intervention Team (CIT) Training: Implications for Military Settings
Kaitlin Duckett

POSTER #15
Evaluating the Impact of a Tobacco Cessation Training for Military Medical Providers in a Primary Care Clinic
Kaitlin Duckett, Chase Aycock, Ryan Kalpinski, Melissa Little, Daniel Cassidy, David Marks, Jillian Bailie, Brittany Russell and G. Wayne Talcott
POSTER #16
Effect of Hypoxia on Porcine and Human Mesenchymal Stem Cells
Ben Antebi, Kerfoot Walker III, Arezoo Mohammadipoor, Andriy Batchinsky and Leopoldo Cancio

POSTER #17
Optimization of Mesenchymal-stem-cell Culture Conditions for use in Clinical Trials
Ben Antebi, Kerfoot Walker III, Arezoo Mohammadipoor, Robbie Montgomery, Andriy Batchinsky and Leopoldo Cancio

POSTER #18
Effects of Human and Porcine Mesenchymal Stem Cell-derived Conditioned Media on Coagulation and T-Cell Function
Arezoo Mohammadipoor, Ben Antebi, Teryn Roberts, Kerfoot Walker, Robbie Montgomery, Andriy Batchinsky and Leopoldo Cancio

POSTER #19
Investigation of Intravenous Hydroxocobalamin Compared to Hextend for Resuscitation in a Swine Model of Uncontrolled Hemorrhagic Shock: A Preliminary Report
Susan Boudreau, Joseph Maddry, Normalynn Garrett, Maria Castaneda, Avery Kester, Kaysie Canellis and Vikhyat Bebarta

POSTER #20
Sodium Azide Associated Acute Hyperkalemia in a Swine Model of Sodium Azide Toxicity
Maria Castaneda, Joseph Maddry, Normalynn Garrett, Susan Boudreau, Avery Kester, Kaysie Canellis and Vikhyat Bebarta

POSTER #21
Regenerative Potential of Craniofacial Tissues: Evidence That Estrogen-Mediated Negative Regulation of the Lubricin Gene Underlies Female Temporomandibular Joint Damage
Louis Perez, Komal Ramzanali, Clyde Phelix and Richead Lebaron

POSTER #22
Efficacy of Albumin in a Rat Model of Hemorrhagic Shock and Trauma with Tourniquet Depends on its Pre-saturation with Fatty Acids
Alexander Penn, Charnae Williams, David Barraza, Thomas Walters, Michael Dubick and Ivo Torres Filho

POSTER #23
Pirfenidone Reduces the Profibrotic Response in an In vitro Model of TGF-β1-Induced Human Dermal Myofibroblasts
Caroline Hall, Adrienne Wells and Kai Leung

POSTER #24
Mitochondrial Pyruvate Carrier: Homology Modeling, Docking, and Dynamic Simulation to Integrate Non-synonymous SNPs into Individualized Patient Metabolic Biosimulations
Clyde Phelix, Robert Renthal, Liao Chen, Stanton McHardy and George Perry

POSTER #25
Metal Organic Framework (MOF) Reduces Clot Strength and Stimulates Fibrinolysis in Ex Vivo Human Blood
Teryn Roberts, Megan Neufled, Leopoldo Cancio, Melissa Reynolds and Andriy Batchinsky

POSTER #26
Extracellular Matrix Composition Alters Cell Survival in Hyperglycemic Conditions
Robert Moritz and Richard Lebaron

POSTER #27
Utility of Quantitative Analysis of Pulmonary CT Scans in Mild-to-moderate ARDS
Mark Espinoza, Andriy Batchinsky, Daniel Wendorff, Brendan Beely, Alexandar Dixon, Micheal Lucas, Logan Leatherman, Bryan Jordan, Corina Necsoiu and Leopoldo Cancio

POSTER #28
An Environment and Multi-gene Risk Interaction Model for PTSD Symptoms Following Combat Exposure
Michael Hossack, Jon Williams and Matthew Brock

POSTER #29
Transport of Critically Ill Non-trauma Patients by Critical Care Air Transport Teams (CCATT)
Kimberly Medellin, Joseph Maddry, Allyson Arana, Lauren Reeves, Crystal Perez, Alejandra Mora, Avery Kester, Shelia Savell and Vikhyat Bebarta

POSTER #30
Making Mock Code Training Burn Specific
Sabas Salgado, Cline Kirt, Brent Sabatino, Nizar Boedwahni, Monica Abbott, Rebecca Potter, Mark Castillo, Elizabeth Mann-Salinas and Sarah Murray
POSTER #31
Sustainment of Decreased Blood Culture Contamination with an Initial Specimen Diversion Device in the Emergency Department
Jody Huss

POSTER #32
Neonatal Resuscitation Simulation: Fostering a Culture of Safety and Improving Teamwork in the Delivery Room
Maria Cristina Gallup

POSTER #33
The Impact of Critical Care Air Transport Team (CCATT) Ventilator Management on Combat Mortality
Joni Paciocco, Shelia Savell, Alejandra Mora, Crystal Perez, Avery Kester and Joseph Maddry

POSTER #34
The Impact of Transport Time on Outcomes Following Evacuation from Point of Injury
Crystal Perez, Lauren Reeves, Alejandra Mora, Jill Lear, Tuan Le, Avery Kester, Vikhyat Bebarta and Joseph Maddry

POSTER #35
Emergent Re-entry Sternotomy Training via SynDaver Simulation
Darlene Deters

POSTER #36
Cuff, Cuffless or Fenestrated: What Do You Know About Tracheotomy Care?
Chayanin Noramuttha

POSTER #37
Pre-Operative Chlorhexidine Gluconate (CHG) Skin Preparation: A Literature Review
Ross Scallan

POSTER #38
Noise Reduction on an Inpatient Surgical Nursing Unit to Promote Healthy Sleep Hygiene
Candice Catlett

POSTER #39
An Evaluation of Navy En Route Care Training Using a High-fidelity Medical Simulation Scenario of Interfacility Patient Transport
Lauren Reeves, Christine Deforest, Virginia Blackman, John Alex, Alejandra Mora, Crystal Perez, Domenique Selby, Avery Kester and Benjamin Walrath

POSTER #40
Metastatic Hypermucoviscous Klebsiella Pneumoniae Infection in a Young Active Duty Male
Alexis Beauvais

POSTER #41
Prevention of Ischemic-reperfusion Injury and Chronic Rejection in a Porcine Vascularized Composite Allotransplantation Model
Nicholas Robbins, Warren Breidenbach, Kevin Wu, Samuel Tahk, Matthew Wordsworth, Vijay Gorantla and Michael Davis

POSTER #42
Resuscitation with Oral Rehydration Salts Improves MOD Biomarkers in a Pig Burn Model
Belinda Gomez

POSTER #43
Role of Acinetobacter Baumannii Thioredoxin in Bacterial Translocation by Modulation of Mucosal Oxidative Homeostasis
Holly May, Jieh-Juen Yu, M. Neal Guentzel, Rishein Gupta and Bernard Arulanandam

POSTER #44
Athletic Trainer Integration in U.S. Air Force Basic Training
Reid Fisher, Shandra Esparza, Mary Pawlak, Nathaniel Nye, Juste Tchandja, Thomas Cropper, Sarah de La Motte and Bryant Webber

POSTER #45
Impact of the Firearms Training System (FATS) on Occupational Performance in a Polytrauma Population
Robert Oliver, Jill Cancio and Kathleen Yancosek
**POSTER #46**
The Dynamics of Risk: Prior Changes in Psychological Inflexibility Predict Subsequent Changes in Posttraumatic Stress Severity
Meghan Crabtree, Willie Hale, Eric Meyer, Nathan Kimbrel, Bryann Debeer, Suzy Bird Gulliver and Sandra Morissette

**POSTER #47**
Fall Prevention on a Medical-Surgical Unit
Arrah Bargmann

**POSTER #48**
Perceptions of Low Back Pain Treatment for Initial Entry Training: A Mixed Methods Study
Cortney Sebolt, Enrique Smith-Forbes, Yvette Woods and Daniel Rhon

**POSTER #49**
Retrospective Evaluation of Pre-injury Statin Use and Post-injury Thromboembolic Events in Acute Trauma
Ryan Mcmahon, Jon Fletcher, James Aden, Seth Holland, Scott Trexler and Lorne Blackbourne

**POSTER #50**
A Multi-media Mobile Medical Application to Support Fresh Whole Blood Transfusion
Tricia Garcia and Elizabeth Mann-Salinas

**POSTER #51**
Status Epilepticus: Simulation-Based Education Combined with Traditional Didactic Curriculum in Early Medical Trainees
Tyler Koehn, Daniel Simmons, John Sladky and Jeffrey McClean

**POSTER #52**
Developing Clinical Leaders in Primary Care: The U.S. Air Force Diabetes Champion Course
Darrick Beckman, Irene Folaron, Mark True, Jana Wardian, Nina Watson, Connie Morrow and Tom Sauerwein

**POSTER #53**
QuikClot TM Combat Gauze Use by Ground Forces in Afghanistan
Jessie Renee d. Fernandez, Michael D. April, Jason F. Naylor, Andrew D. Fisher, Krista C. Wellein, Daniel B. Brillhart, Cord W. Cunningham, Mark A. Antonacci, Steven G. Schauer

**POSTER #54**
Cardiomyocyte Mitochondrial Respiratory Capacity in Severely Burned Swine
Tony Chao, Belinda Gomez, Joshua Little, Michael Dubick and David Burmeister

**POSTER #55**
Nocturnal Oxygen Variability in Home Dwelling Heart Failure Patients
Cubby Gardner and Harry Burke

**POSTER #56**
Comparison of Two Methods of Inducing Traumatic Cardiac Arrest in Swine
Jason Rall

**POSTER #57**
Emergency Department Imaging of Pediatric Trauma Patients in a Combat Setting
Jamie Roper, Michael April, Guyon Hill and Steven Schauer

**POSTER #58**
A Comparison of Surgical Airway Techniques in a Syn-cadaver: A Randomized Cross-over Study
Jamie Roper, Michael April, Jonathan Srichandra, Derek Brown, Jessie Renee Fernandez, Steven Schauer and Kristy Jeffers

**POSTER #59**
Hybrid Sequencing and Phylogenomic Analysis of Rarely Isolated Non-shigatoxigenic Enterohemorrhagic Escherichia Coli (EHEC) O157:H7
Anna Allue Guardia, Sara Koenig, Zaina Irion-Byrd, Peter Feng, James Bono and Mark Eppinger

**POSTER #60**
Characterization of Trauma-related Upper Extremity Amputees and their Occupational Therapy Treatment
Timothy Tu, Enrique Smith-Forbes, Jill Cancio and Kathleen Yancosek

**POSTER #61**
Minimally Invasive ECLS Reduces Minute Ventilation and Delays Development of ARDS in a Model of En-route Critical Care
Andriy Batchinsky, Brendan Beely, Wendorff Daniel, Jae Hyek Choi, Roberts Teryn, Corina Necsoiu, Jeremy Cannon and Leopoldo Cancio
POSTER #62
Utility of Optical Coherence Tomography and Ultrasound for Diagnosis of ARDS
Daniel Wendorff, Jae-Hyek Choi, James Lantry, Teryn Roberts, Brendan Beely, Bryan Jordan, Corina Nescsou, Kyle Sieck, Mark Espinoza, Leopoldo Cancio and Andriy Batchinsky

POSTER #63
A Novel Bioresorbable/Biointegratable/Biocompatible Dressing for Negative Pressure Wound Therapy
Samuel Tahk, Renford Cindass, Kevin Wu, Nicholas Robbins, Vijay Gorantla and Michael Davis

POSTER #64
Reaching Across State Lines: Telehealth Transforms Healthcare For Toddler With Newly Diagnosed Juvenile Dermatomyositis
Maya Antoine, Patrick Reeves, Luis Rohena and Olcay Jones

POSTER #65
Who is Distressed? Applying the Diabetes-related Distress Scale in a Diabetes Clinic
Joshua Tate

POSTER #66
Depression Trajectories and Risk-taking Behaviors among Active Duty and Retired U.S. Military Personnel with HIV Infection
James White, Xiaohe Xu, Thankum Sunil and Jason Okulicz

POSTER #67
The Impact of a Novel Biobehavioral Intervention on Physiologic State, Perceived Stress and Affect
Jacqueline Killian

POSTER #68
Comparison of MEDEVAC Cricothyrotomy, Endotracheal Intubation, and Supraglottic Airway Outcomes for Operation Enduring Freedom
Patrick Ng, Allyson Arana, Shelia Savell, Avery Kester and Joseph Maddry

POSTER #69
Anti-epileptic Drugs and Suicide Related Behavior: Is it the Drug of Comorbidity?
Hari Sagiraju, Chen-Pin Wang, Megan E. Aman, Anne C. Vancott, Hamada Hamid Altabil and Mary Jo V. Pugh

POSTER #70
Predictors of Long-term Opioid Use in Active Duty Military: Psychotropics, Procedures, Pain
William Kazanis, Claudina Tami, Mary Jo Pugh, Don McGearry, Erin Finley, Maj Joseph Maddry, Vik Bebarta, David Carnahan and Jennifer Sharpe Potter

POSTER #71
Purification-characterization of an Acid Phosphatase from Acinetobacter Baumannii
James Chambers, Jieh-Juen Yu, Luke Daum and Bernard Arulanandam

POSTER #72
Differences in PTSD Symptoms Among Post-9/11 Veterans with Blast- and Non-Blast TBI
Clark Ryan-Gonzalez, Nathan Kimbrel, Eric Meyer, Bryann Debeer, Suzy Gulliver and Sandra Morissette

POSTER #73
Quantitative Analysis of Antibodies to Zika Virus Envelop and NS1 Proteins in Vaccinated Rabbits
Imraan Ali, Richard Tamfu, Masarrat Ali and James Chambers

POSTER #74
Prevalence of Wolbachia Surface Protein (WSP) Antibodies in Humans and Animals
Imraan Ali, Richard Tamfu, Masarrat Ali and James Chambers

POSTER #75
Chlamydia Trachomatis Pulmonary Infection Induces Inflammatory Pathology in MicroRNA Deficient Mice
Siena Pangtay, Bernard Arulanandam, Rishein Gupta, Jonathon Keck, Dona Haj Bashir, Aravind Kancharla, Gina Bitar, Katherine Schenkel Schenkel, Kevin Castillo and Neal Guentzel

POSTER #76
Experience and Effectiveness of an Occupational Therapy Based Sleep Enhancement Program on Military Service Members at Joint Base San Antonio
Stephen Turner, Enrique Smith-Forbes and Yvette Woods

POSTER #77
Role of Macrophages During Murine Neurocysticercosis
Victoria Diaz
POSTER #78
Large Scale Screening and Identification of Novel Ebolavirus and Marburgvirus Entry Inhibitors
Manu Anantpadma and Robert Davey

POSTER #79
Vestibular Dysfunction and Dizziness in Post-9/11 Veterans: A Chronic Effects of Neurotrauma Consortium Study
Alicia Swan, Jeremy Nelson, Terri Pogoda, Faith Akin, Krystal Riska, Courtney Hall, Megan Amuan, Kristine Yaffe and Mary Jo Pugh

POSTER #80
Benzodiazepine Use among Low Back Pain Patients Concurrently Prescribed Opioids in the Military Health System between 2012 or 2013
Megan Curtis, William Kazanis, Claudina Tami, Mary Jo Pugh, Don McGearry, Erin P. Finley, Joseph Maddry, Vik Bebarta, David Carnahan and Jennifer Sharpe Potter

POSTER #81
In Vivo Regenerative Response Enhanced In Critical Size Bone Defects Using High Performance Micro Environments
Sergio Montelongo, Teja Guda, Sy Griffey, Laura Gaviria, Joseph Pearson and Sarah Stagg

POSTER #82
Utility of the Simplified Automated Ventilator II as a Transport Ventilator in a Combat-relevant Model of Lung Injury
Brendan Beely, George Harea, Vitali Karaliou, Teryn Roberts, Jae Hyek Choi and Andriy Batchinsky

POSTER #83
Host MicroRNAs Enhance Susceptibility to Chlamydia Trachomatis Pulmonary Infection
Dona Haj Bashir, Jonathon Keck, Arivand Kancharla, Gina Bitar, Siena Pangtay, Kevin Castillo, Katherine Schenkkel, Neal Guentzel, Rishein Gupta and Bernard Arulanandam

POSTER #84
Trajectories of Comorbidity in Iraq and Afghanistan War Veterans: Long-term Health Outcomes Associated with Brain Injury Severity
Mary Jo Pugh, Alicia Swan, Megan Amuan, Carlos Jaramillo, Blesen Eapen, Erin Finley, Catheryn Oriheula, Sandra Morissette and Alicia Trajectories Of Resilience And Complex Comorbidity Study Team

POSTER #85
Spatially Controlled Mechanical Properties for Musculoskeletal Entheses
Joseph Pearson, Paul Dowell, Kayla Sanchez, Joo Ong and Teja Guda

POSTER #86
Low Dose rhBMP-2 Delivery from Hydroxyapatite-collagen Scaffolds Efficacious for Delayed Restoration of Critical Sized Calvarial Model
Laura Gaviria, Teja Guda, Joo Ong, John Decker, David Silliman, Ian Johnson, Sergio Montelongo and Joseph Pearson

POSTER #87
Bone Histomorphometric Assessment of Distant Bones in a Rat Model Following a Created Non-union Defect
Alejandro Morales Betancourt, Sergio Montelongo, Teja Guda and Mark Appleford

POSTER #88
Randomized Crossover Study of Training Benefits of Low-fidelity ECMO Simulation Versus Animal Model - An Interim Report
Francisco Rodriguez

POSTER #89
Regulation of Host MicroRNAs in Chlamydia Muridarum Infected McCoy Cells
Gina Bitar, Jonathon Keck, Dona Haj Bashir, Aravind Kancharla, Laura Henley, Jieh Juen Yu, Neal Guentzel, Rishein Gupta and Bernard Arulanandam

POSTER #90
Optimization of Silk Hydrogels for Cell Driven Extracellular Matrices
Mubeen Sultana and Joseph Pearson

POSTER #91
Validity of Dementia and Cognitive Disorder Diagnoses in a Sample of Iraq and Afghanistan Veterans as Determined Through Review of Medical Chart Evidence
Margaret Wells, Kathleen Franklin, Jason Soble, Janice Marceaux, Justin O'Rourke, Alicia Swan and Mary Jo Pugh

POSTER #92
Phenotype and Transcriptome Analysis of Central Neuonal and Glial Populations in Multiple Sclerosis
Jon Williams, Simon Ritchie and Marcel Daadi
POSTER #93
A Multimodal Screen to Identify Novel Liver Stage Antimalarials
Kirsten Hanson, Javier Mota and Andreu Garcia Vilanova

POSTER #94
Regulation of Interleukin-1 Secretion by Microglia in Experimental Models of Multiple Sclerosis
Charles Garcia, Sandra Cardona, Andrew Mendiola, Astrid Cardona and Kaira Church

POSTER #95
The Protective Role of CXCL11 Against Pulmonary Cryptococcosis

POSTER #96
Candida-streptococcus Biofilms on Titanium Dental Implant Material and its Consequences for Antimicrobial Drug Resistance
Daniel Montelongo, Anand Srinivasan, Anand Ramasubramanian and Jose Luis Lopez-Ribot

POSTER #97
Prevalence of Human Papillomavirus Genotypes among Women with Abnormal Pap Smears in the Military Health System
Christopher Daly, Shana Hansen and Timothy Roberts

POSTER #98
Dissecting the Role of the Fractalkine Receptor During EAE: New Approach Utilizing a Humanized Animal Model
Sandra Cardona, Kaira Church and Astrid Cardona

POSTER #99
The Association of Epilepsy Specialty Care with Patient Reported Outcomes and Satisfaction
Shaila Gowda, Stephen Chan and Mary Jo Pugh

POSTER #100
Using CellProfiler and Automated Confocal Feedback Microscopy to Quantify Plasmodium Liver Stage Phenotypes and Antimalarial Compound Activity
Charleston West, Javier Mota, Andreu Garcia Vilanova and Kirsten Hanson

POSTER #101
The Personal Impact of Epilepsy (PIES) on Veterans
Stephen Chan, Shaila Gowda and Mary Jo Pugh

POSTER #102
Using 3D Hydroxyapatite-collagen Composite Scaffolds and Spatial-Temporal Variation to Promote Vascularized Bone Tissue Regeneration
Rebekah Rodriguez, U-Ter Aondo Jia, Sarah Stagg, Laura Gaviria, Joo Ong and Teja Guda

POSTER #103
Type 2 Diabetic Muscle: Characterization and Tissue Engineering
Francisca Acosta and Christopher Rathbone

POSTER #104
Examining the Relationship between TBI and Movement Disorders in Veterans
Deanna Baldock, Mary Jo Pugh and Sandra Morissette

POSTER #105
Long-term impact of the Columbine High School shooting on survivors.
Jillian Bailie and Cheryl Meyer

POSTER #106
Deployment preparation, PTSD, and family functioning in returning veterans

POSTER #107
A silk-alginate composite for the treatment of craniofacial defects for the masquelet technique
Paul Dowell, Joseph Pearson, Paul Gutierrez, Joo Ong and Teja Guda

POSTER #108
Patterns of Zolpidem Use among Active Duty Service Members: A Retrospective Cohort Analysis
Kangwon Song, William Kazanis, Megan Amuan, Carlos Jaramillo, Blesson Eapen and Mary Jo Pugh

POSTER #109
Protection Against Cryptococcosis is Enhanced Following Engagement of Mincle Receptor

POSTER #110
An Atypical Presentation of Insulinoma
Joseph Kluesner
POSTER #111
Assessing the Impact of Dronabinol on Patient Weight in a Chronic Pain Population
Robert Kennedy

POSTER #112
Pediatric Rapid Response Team: Vital Sign Based System vs. Pediatric Early Warning Score System
Scott Penney

POSTER #113
The Influence of Race/Ethnicity on the Relationships among forms of Distress, Alcohol Use, and Alcohol Related Problems in a Veteran Sample
Jessica Perrotte, Eric Meyer, Bryann Debeer, Nathan Kimbrel, Suzy Gulliver and Sandra Morissette

POSTER #114
The Association of Teaching Institutions and Complications Due to Overdose or Incorrect Anesthesia Medication in the United States
America Revere, Eden Sirak and Ali Seifi

POSTER #115
Detection of Mixed Bacterial Populations by Surface Enhanced Raman Spectroscopy (SERS)
Luis Martinez

POSTER #116
Effectiveness of Antimicrobial Peptide LL-37 and its Homologous Peptides Against ESKAPE Group of Pathogens
Luis Martinez

POSTER #117
Amalgam Separator Testing and Development for Dental Wastewater Regulatory Compliance
Senay Tewolde

POSTER #118
Attitudes about Wearing Scrubs in Public: Healthcare vs. Non-healthcare
Pavela Bambekova, Chirag Buch, Chelsea Mendonca, Amr Arar, Ali Seifi and Ali Reza Mirahmadi

POSTER #119
Usage of Vasopressors in United States during a Decade
Shaadi Abughazaleh and Ali Seifi

POSTER #120
Analyzing the Trends in Hospital Discharges and National Health Expenditures using HCUP National Inpatient Sample Database
Henderson Jones, Janice De Surmont and Ali Seifi

POSTER #121
“ColdClot” an innovative hemostatic wound bandage combined with endothermic reaction
Madeleine Farrer

POSTER #122
Measuring Physician Coordination of Care Using Social Network Analysis and Relational Coordination
Katharine McMillan

POSTER #123
Evaluation of a Nitric Oxide Formulation Against Multi-drug Resistant Bacterial Biofilms
Peter Onyskiw, Dickson Kirui and Nancy Millenbaugh

POSTER #124
Targeted Gold Nanoparticle-assisted Laser Therapy for the Disruption of Methicillin-resistant Staphylococcus Aureus Biofilms
Gregor Weber, Dickson Kirui and Nancy Millenbaugh

POSTER #125
Delayed Onset of Methemoglobinemia in a Patient with Burn and Inhalation Injury
Alisha Jiwani

POSTER #126
Evaluation of a Nitric Oxide Formulation Against Multi-drug Resistant Bacterial Biofilms
Peter Onyskiw, Dickson Kirui and Nancy Millenbaugh

POSTER #127
Targeted Gold Nanoparticle-assisted Laser Therapy for the Disruption of Methicillin-resistant Staphylococcus Aureus Biofilms
Gregor Weber, Dickson Kirui and Nancy Millenbaugh

POSTER #128
Dynamics of Systemic Expression of High Mobility Group Protein Box 1 During ECLS at Ground Level and High Altitude
Jae Hyek Choi, Teryn Roberts, Vitali Karaliou, George Harea, Kyle Sieck, Brendan Beely and Andriy Batchinsky

POSTER #129
Benchmarking CO2 Removal Efficiency During ECCO2R by Hemolung and Novalung
Effects of peripheral and spinal administration of mu-opoids on postoperative anti-hypersensitivity in aged and adult mice

Mecklenburg, J. M., Patil, M. J., Koek, W., and Akopian, A. N.

**Background:** Postoperative pain management in the elderly is challenging. This challenge arises due to the changes in their anatomy, physiology, biochemistry and especially wound healing dynamics, which are negatively affected by aging (Benyamin et al., 2008; Portenoy et al., 2004). In addition, old age could affect plasticity in the nociceptive pathway. These changes in the elderly may alter opioid effects, the main medicine for pain management. Therefore, we have investigated whether old age alters opioid-induced postoperative anti-hypersensitivity.

**Methods:** Postoperative conditions were modeled by plantar incision in mice (Pogatzki and Raja, 2003). To evaluate the effects of a mu-opoid (DAMGO) and a partial opioid antagonists/agonist (buprenorphine) on postoperative anti-hypersensitivity in adult and aged mice, thermal and mechanical nociception was measured using Hargreaves apparatus and Dynamic Plantar Aesthesiometer, respectively. Various doses of each drug were administered via local (surgical site) or intrathecal (spinal) injections and pain measurements were recorded 30 minutes and 120 minutes post opioid injection.

**Results:** Locally injected DAMGO and buprenorphine had a mild effect on postoperative anti-hypersensitivity in adults and aged mice. However, this effect was not peripherally mediated. In contrast, spinal injection of DAMGO and buprenorphine showed very robust anti-hypersensitivity in adults and to lesser extend in aged mice. Importantly, peripheral and especially spinal DAMGO and buprenorphine-induced postoperative anti-hypersensitivity was substantially more effective in adult compared to aged mice. Thus, dose-response curves were leftward shifted in adults compared to aged mice. The dose-response curve for analgesic effects of buprenorphine was bell-shaped. Finally, buprenorphine had a stimulatory side effect in adults, but not in aged mice, that significantly affected the locomotor activity of adult mice.

**Conclusion:** Our data indicates that mu-opiods are less effective for postoperative anti-hypersensitivity in aged as it is in adult mice. Nevertheless, the bell-shaped dose-response curve for buprenorphine analgesic effects and absence of stimulatory side effects at analgesic dosages in aged mice could make buprenorphine a better candidate for postoperative pain management in the elderly.
Retrospective analysis of the post-operative changes in higher order aberrations: A comparison of the WaveLight® EX500 to the VISX® S4 laser in refractive surgery

Donovan Reed, Douglas Apsey, Walter Steigleman, James Townley and Matthew Caldwell

ABSTRACT

Background: Both photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK) have been demonstrated to increase wavefront aberrations of the cornea and alter the comparative contributions of coma- and spherical-like higher order aberrations often inherent to the natural eye. As future advancements in refractive surgery are being directed toward customized ablations to correct not only lower-order aberrations, but also higher-order aberrations specific to the individual eye, it is important to investigate the utility of current excimer lasers in terms of induced higher order aberrations to maximize treatment outcomes.

Methods: A retrospective analysis was performed to investigate the difference in root mean square (RMS) value of the higher order corneal aberrations post-operatively between two currently available DoD laser platforms, the VISX® Star S4 and the WaveLight® EX500 lasers. Data from 240 total eyes of active duty military or DoD beneficiaries who completed photorefractive keratectomy (PRK) or laser in situ keratomileusis (LASIK) refractive surgery at the WHASC Joint Warfighter Refractive Surgery Center was examined.

Results: The mean change in RMS value for PRK utilizing the VISX® laser was 0.00122, with a standard deviation of 0.02583. The mean change in RMS value for PRK utilizing the WaveLight® EX500 laser was 0.004323, with a standard deviation of 0.02916. The mean change in RMS value for LASIK utilizing the VISX® laser was 0.00841, with a standard deviation of 0.03011. The mean change in RMS value for LASIK utilizing the WaveLight® EX500 laser was 0.0174, with a standard deviation of 0.02417. When comparing the two lasers for PRK and LASIK procedures, the p-values were 0.431 and 0.295 respectively.

Discussion: The results of this study suggest no statistically significant difference concerning induced higher order aberrations between the two laser platforms for either LASIK or PRK. After adjusting for pre-operative refractive error via regression analysis, there was still no significant difference between the VISX® and WaveLight® EX500 lasers concerning post-operative change in RMS for either PRK or LASIK. Overall, the VISX laser did have consistently lower induced higher order aberrations post-operatively, but this did not reach statistical significance. Further investigation of visual outcomes between the two laser platforms should be investigated before determining superiority in terms of visual image and quality post-operatively. Thus, additional factors such as cost, availability, patient characteristics, and surgeon preference should be taken into consideration when determining the most appropriate laser to utilize for refractive surgery.
Introduction

Chest pain is the second most common presentation to hospital emergency departments in the United States, leading to millions of hospital admissions. The number of days a patient stays and the tests performed to rule out any life-threatening etiology can be costly for hospitals. In examining the literature, there are few published articles on the socioeconomic aspects of patients hospitalized for acute chest pain and the impact of Teaching (T) institutions, all of which either do not focus on chest pain or include too small a sample size\textsuperscript{1,2}. Given this lack of relative information, we sought to evaluate the socioeconomic aspects of chest pain and the impact of teaching institutions on a national scale in the United States.

Method

Using the Nationwide Inpatient Sample database, we conducted a retrospective study comparing the socioeconomic metrics in adult patients for a diagnosis of chest pain (MS-DRG 313) from 2008-2014 in the United States. The cohort was dichotomized to teaching (T) and non-teaching (NT) hospitals and analyzed with z-test to identify differences in these two institutions.

Results

Over the course of seven years a total of 2,837,696 chest pain discharges were recorded with a significant decrease of 581,537 to 236,690 from 2008 to 2014 (P< 0.0000). The majority of patients were aged 45-64 years old (47.4%), with a mean age of 60 years old, of which 53.69% were female.

During the study period, the hospital length of stay (LOS) increased from 1.734 to 1.871 days (P< 0.0000) with patients at T hospitals staying significantly longer during the entire study period, 1.8 vs 1.7 days (p < 0.01642). Overall mortality increased significantly from 0.06% in 2008 to 0.10% in 2014 (P< 0.0092), with no significant impact of T institutions on this outcome. Regarding the financial aspects of chest pain, the mean cost to hospitals increased from $4,207 to $5,043 and the amount hospitals’ charge increased from $13,793 to $21,810. There was no significant difference in cost in T institutions during this period, however, the mean hospital charges have significantly decreased in T institutions since 2012 compared to NT (P < 0.0009).

Conclusions

Our results indicate that the number of chest pain cases significantly decreased in the studied period of time with an increase in mortality during recent years. We found that T hospitals have a significantly longer LOS, however, they have a nonsignificant and inconsistent impact on mortality, mean
cost and charge. This increased LOS could be associated with T hospitals offering more specialized care, more advanced treatments, and treating populations with greater illness acuity. With medical education and LOS being important factors in the Centers for Medicare and Medicaid payment system, it may be of benefit to teaching facilities for these factors to be adjusted with respect to reimbursement for some of the more common diagnosis related groups including acute chest pain.

References

Background:

The United States Air Force (USAF) restricts military personnel with Diabetes Mellitus (DM) from participating in military deployments due to the uncertainty of healthcare availability in an austere environment. For military providers, it has been challenging to assess the deployment candidacy of a member with DM since no data has been published to date describing the effect of a deployment on glycemic control. We conducted a retrospective analysis on USAF personnel who deployed with DM to examine their response in hemoglobin A1C (A1C) and body mass index (BMI) after a deployment of at least 90 days.

Methods:

Subjects were identified by ICD-9 diagnosis of Diabetes Mellitus through the Department of Defense electronic health record. A1C and BMI were also gathered through the electronic health record. Deployment information was obtained through the Aerospace Information Management System. Medication information at the time of deployment was obtained through the Pharmacy Data Transaction Service database. All databases are maintained by the Defense Health Agency.

Results:

We identified 366 USAF personnel who deployed with a diagnosis of DM between 2004 and 2014. Each subject’s A1C and BMI were obtained before deployment and within 6 months of repatriation. For the entire population, there was no statistically significant difference in the mean A1C before and after deployment (6.5% vs. 6.7% respectively, P=0.17). Likewise, subgroup analyses of gender, rank, and age showed no significant difference in A1C before and after deployment. In subjects taking oral DM medications only or no medications, which represent the ideal regimen in deployment due to cold storage limitations, there was no significant difference in A1C before and after deployment (n=335, 6.4% vs. 6.6% respectively, P=0.09). However, members requiring insulin appeared to have worsened glycemic control before and after deployment (A1C 7.8% vs. 8.4%, respectively), although the census in this category (n=25) was insufficient to accurately calculate statistical significance. Mean BMI for the overall population declined significantly after deployment (28.4kg/m2 vs. 27.8kg/m2, P<0.01).

Conclusion:

A1C appears to remain relatively stable before and after a deployment among AF personnel with DM. However, those requiring insulin demonstrated a concerning pattern of A1C increase. Further studies are needed to determine specific factors in military deployment that affect glycemic control.

Acknowledgements: Dr. Alan Sim, Ms. LeeAnn Zarzabal, and Mr. Alexander Rittel of the Defense Health Agency for assistance with data acquisition.
INTRODUCTION:

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous adverse drug reactions with significant morbidity and mortality. Though the exact pathogenesis remains unclear, targeted genomic analysis has identified relationships with certain immunologic markers and enzymes associated with drug metabolism. HLA-B types in particular have been associated with ADRs; however to date these associations exist for only a few specific drugs and patient populations. We sought to examine whether certain HLA-B alleles were present at an increased frequency in patients with SJS/TEN from our facility and identify potential associations with inciting drugs.

METHODS:

We conducted a retrospective study of SJS/TEN patients admitted to the San Antonio Military Medical Center (SAMMC) Burn Unit between 2001 and 2015. Targeted sequencing of the HLA-B gene was performed on 28 formalin-fixed paraffin-embedded (FFPE) skin biopsy samples from cases with a known offending drug. Typically, HLA-B alleles are determined by sequencing Exons 2 and 3 of the gene, using primers that anneal in a non-variable region of the introns. This was not possible with FFPE samples due to fragmentation of DNA; therefore we used commercial primers designed from the least variable areas of the exons possible. Using the Sanger sequencing method, we identified the potential HLA alleles present in the FFPE samples and evaluated for an association with the offending drug.

RESULTS:

Multiple potential HLA-B alleles were identified in most of our specimens. This highlights the limitations of DNA sequencing using FFPE samples, as the fragments of DNA and non-overlapping sequences limited our ability to determine an exact HLA type for every specimen. Based on these results, we were unable to determine statistically significant associations regarding frequency of HLA type or inciting drugs. However, our data show HLA-B*44 as a potential allele in 9 of the 28 samples, including 5 of 10 cases associated with Bactrim. This is consistent with prior reports of HLA-B*44 associated with SJS/TEN due to sulfonamides and SJS/TEN with severe ocular complications.

DISCUSSION:

Severe cutaneous ADRs remain a significant cause of morbidity and mortality in health care and are often unpredictable. To further investigate potential genetic risk factors, we designed a prospective study using whole genome sequencing and transcriptome studies in patients with SJS/TEN. A secondary goal of this study is to create a tissue repository at the Collaborative Health Initiative Research Program, to aid in future studies examining ADRs.

We are currently enrolling patients at SAMMC through 2018. To date, our study is the first to conduct large-scale, comprehensive simultaneous genome-wide and epigenome-wide studies of SJS/TEN, with the goal of obtaining a better understanding of the pathogenesis of this condition and identifying novel molecular markers for use in individualized medicine.
Background: Sound/noise, physical restraint, vigorous physical activities and extreme temperature are some of the common environmental stimuli to which Service Members are often exposed to on the battlefield. As a result, the exposure to such unique battlefield specific stressors, can affect their normal psychological and physiological functions thus causing stress disorders. Indeed battlefield soldiers develop stress-induced syndromes that include anxiety, depression and body pain. Here we report the development of a protocol to mimic battlefield setting-induced stress disorders in a rat model because such preclinical model will be instrumental to comprehend fundamental mechanisms governing stress induced syndromes and identify molecular targets leading to potential therapeutic opportunities.

Materials and Methods: Male Sprague Dawley rats were exposed to four different types of stressors: (1) sound stimulus for 30 min; (2) restraint stimulus for 4 h; (3) cold stimulus for 4h; and (4) forced swim procedure for 20 min. The order of exposure of rats to stressors was intermittent; one type of stressor was presented per day for 4 days in a week (Monday – Thursday) over 4 weeks. The anxiety level in stressed animals was assessed by defecation rate during forced swim and cold stress tests while depressive-like behaviors were assessed by measuring immobility time in the forced swim test. Additionally, the alteration in nociceptive behaviors of stressed rats was detected by using von Frey and thermal hyperalgesia tests.

Results: Four weeks of intermittent stress protocol exposure in rats increased fecal pellet output and depressive-like behavior. Notably, stressed rats developed significant mechanical allodynia and also tend to develop increased sensitivity to thermal stimuli.

Conclusion: The present study has characterized a novel protocol to model battlefield stress in rats that will aid in the study of the underlying pathological state and also to identify mechanisms of pharmacological agents that can be clinically effective against combat-related stress disorders. Our investigation is quite timely and significant due to the potential to provide a new therapeutic avenue in stress related syndromes that negatively affect Service Members performance in the battlefield and also during post-war lifespan.
3T UPC EBP RETROSPECTIVE ANALYSIS OF BUNDEL COMPLIANCE IN MICU PATIENTS

CASSANDRA BULLOCK

BACKGROUND

The Surviving Sepsis Guideline recommends the routine screening of potentially infected patients for sepsis. The mortality rate for patients diagnosed with sepsis is eight times higher than the average for other inpatient diagnoses. Sepsis is the sixth most common diagnosis, and the most costly. At the time of this proposal, there is not a unit specific, inpatient policy or guideline on the routine screening of potentially infected patients for Systemic Inflammatory Response System (SIRS) or Sepsis. The only protocol based policy or guideline for SIRS/Sepsis identification are in place in the Emergency Department (ED) of San Antonio Military Medical Center (SAMMC). Once activated in the ED, there is no follow through on the protocol in the Medical Intensive Care Unit (MICU), in spite of 10% of MICU admissions being sepsis related. Patient safety can be severely compromised due to missed early identification of SIRS/Sepsis.

ACTIONS

The MICU Unit Practice Counsel (UPC) conducted a retrospective chart review utilizing a computer screening tool to survey the electronic medical record and laboratory interface identifying patient’s meeting SIRS and Sepsis Criteria. MICU patients were audited to include patients who did not have a sepsis related diagnosis upon admission or transfer into MICU. If patients met sepsis criteria and there was evidence of suspected or confirmed infection with end organ dysfunction, their charts were audited for compliance with the Surviving Sepsis Compliance Severe Sepsis Protocol. Data were gathered and compiled, reflecting the standard of care currently being provided in the MICU at SAMMC. Areas for improvement were identified for compliance with the Surviving Sepsis Guidelines. A total of 160 MICU charts were reviewed from OCT 2014 to OCT 2015. Surveys regarding knowledge of sepsis benchmarks were also collected from MICU nurses and SAMMC providers.

RESULTS

Results obtained from chart review, with regards to the seven identified benchmarks; the MICU met only four of the benchmarks 75% of the time or greater. Two of the benchmarks were met 67% of the time, and one benchmark was met 30% of the time. Results of surveys showed that 2% of providers correctly identified the bundle time marks at 3 and 6 hours; 21% of nurses were able to correctly identify them. In regards to the question "Does the MICU have a current sepsis protocol?" 36% of providers and 46% of nurses replied 'yes', when in fact none exists.

IMPLICATIONS FOR MILITARY HEALTHCARE PERSONNEL The results of this unit-based performance improvement project could be beneficial to the organization by serving as a catalyst for revamping early SIRS and Sepsis identification in the inpatient population. Our recommendation is that Surviving Sepsis protocols be implemented in MICU to routinely screen potentially infected patients for SIRS/Sepsis and improve patient outcomes.
CAUSES OF DEATH IN MILITARY WORKING DOGS DURING OPERATIONS IRAQI FREEDOM AND ENDURING FREEDOM, 2001 TO 2013

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Background

Military working dogs (MWDs) are a major asset in the theater of operations. Their unique abilities make them ideal for tasks such as tracking, patrol, and scent detection. MWDs deployed to a war zone are exposed to harsh environments and battlefield dangers that increase their risk of disease, injuries, and death. Although canines have been used extensively in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF), no published studies have reported in detail the causes of death among MWDs deployed to these conflicts.

Materials and Methods

Potential cases were defined as U.S. military-owned MWDs that died while deployed in Iraq (OIF) or Afghanistan (OEF) from January 1, 2001 through December 31, 2013 and identified from both official sources and official online searches. Cases included in this study were limited to MWDs with data on cause of death obtained by abstraction from official veterinary health records from the Department of Defense Military Working Dog Veterinary Service, Joint Base San Antonio Lackland Air Force Base, San Antonio, TX.

Results

We identified 92 MWDs that died while deployed to OEF/OIF from 2001 through 2013 and had cause of death information from official veterinary health records. For both OEF and OIF, the most common training program was Multi-Purpose Canine (36.5% and 51.7% respectively), followed by Improvised Explosive Detector Dog for OEF (34.9%) and Patrol Explosive Detector Dog for OIF (34.5%). Our results show that injuries were the primary cause of death for 77.2% of the MWDs for which we had cause of death data. The most frequent external injuries were gunshot wounds (31.5%), explosion or blast (26.1%), and heat stress (9.8%). The proportion of deaths due to gunshot wounds was similar for OEF and OIF (30.2% vs. and 34.5%, respectively). However, a greater proportion of MWDs died from explosions during OEF than during OIF (30.2% vs. 17.2%, respectively). Diseases were the cause of death in approximately 23% of the MWDs. The most common diseases were gastric dilation and volvulus (GDV, n=3), pleuritis (n=2), and sepsis (n=3). Two deaths were associated with anesthesia-related medical procedures. A total of 8.7% of cases were missing cause of death, 8.7% were missing age, 32.6% of cases were missing data on necropsy, and 14.1% were missing data on final disposition of the body. Other variables of interest including number of deployments and duration of training had a very high proportion of missing values and thus could not be analyzed.

Conclusions

Our study is the most comprehensive to date that reports causes of death of MWDs deployed to OIF and OEF. However, limitations in the available data limit the potential of our results to inform improvements in prevention and medical care. Better documentation in veterinary health records and systematic data collection into an official MWD registry would facilitate further development and evaluation of guidelines to improve care of wounded MWDs in future conflicts.
EN ROUTE INTRAOSSEOUS ACCESS PERFORMED IN THE COMBAT SETTING

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Purpose: The objective of this study was to describe and compare vascular access practices used by military en route care providers during medical evacuation (MEDEVAC).

Background: The treatment of critically ill patients requires vascular access to administer lifesaving fluids, blood products, and medications. Peripheral intravenous (PIV) access can be difficult to achieve in patients who have compromised venous circulation, secondary to cardiopulmonary arrest, shock, sepsis, burns, or major trauma. Insertion of a central venous catheter (CVC) requires special equipment and training and is not feasible in most prehospital environments. Intraosseous (IO) access has become accepted as an immediate option for vascular access in emergent care, when intravenous access cannot be rapidly established.

Materials & Methods: This was a retrospective cohort study. Medical records of US military personnel injured in combat and transported by MEDEVAC teams were queried. The subjects were transported by military en route care providers, in the combat theater during Operation Enduring Freedom (OEF) between January 2011 and March 2014. The authors reviewed 1,267 MEDEVAC records of US casualties and included 832 subjects that had vascular access attempts. The outcome measures for this study were vascular access success rates, including intravenous (IV) and intraosseous (IO) attempts. Subjects were grouped by type of vascular access: None, peripheral intravenous (PIV), IO, and PIV + IO (combination of PIV and IO) and by vascular access (PIV or IO) success (No versus Yes). Survival rate, in-flight events, ventilator, intensive care and in hospital days; and 30-day outcomes were compared among groups. The authors used chi-square or Fisher's exact tests to evaluate categorical variables. Analysis of variance (ANOVA) or Kruskal-Wallis tests were used for continuous variables.

Results: Vascular access was attempted in 832 (66 percent) of the 1,267 subjects transported by MEDEVAC during this study period. The majority (n = 758) of the access attempts were PIV of which 93 percent (706/758) were successful. In 74 subjects, IO was the only access attempted with an 85 percent (n = 63) success rate. The overall success rate with IO placement was 88 percent.

Conclusions: Intraosseous access has been used successfully in the combat setting and accounts for approximately 12 percent of vascular access in this MEDEVAC population.

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EMERGENCY AIRWAY MANAGEMENT AT SAN ANTONIO MILITARY MEDICAL CENTER: A 12-MONTH DESCRIPTIVE ANALYSIS

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Introduction: Emergency airway management is a critical skill for military healthcare providers. We describe the Emergency Department (ED) intubations at San Antonio Military Medical Center (SAMMC) over a 10-month time period. Previous studies analyzing the National Emergency Airway Registry (NEAR 2) report 83% success on the first intubation attempt from September 1996 – June 2001 and from July 2002 – December 2012. The overall intubation success rates were 99.65% and 99.4%, respectively.

Material and Methods: Healthcare providers performing endotracheal intubations in the SAMMC ED completed data collection forms for each intubation event. These forms solicited information on patient demographics, intubation techniques, and intubation outcomes including success or failure, adverse events, and patient disposition. We cross-referenced these forms against the numbers of intubation events reported in the ED nursing daily reports to ensure capture of all intubations. Providers completed forms for every intubation within 6 weeks of the procedure. We analyzed data spanning 28 March 2016-24 January 2017.

Results: During the study time period, providers performed 216 intubations in the SAMMC ED. Indications were medical for 59 patients (27%) and trauma for 155 patients (72%). Emergency medicine residents managed the majority of airways (98%). Devices used for first attempts were direct laryngoscopy for 43% of patients and video laryngoscopy for 54% of patients. Sedative agents most commonly used included ketamine for 127 patients (59%) and etomidate for 45 patients (21%). For paralytic agent, provider used succinylcholine for 40 patients (19%) and rocuronium for 137 patients (63%). Providers achieved first-attempt success in 178 patients (82%). First-pass success was 72% in patients undergoing direct laryngoscopy versus 92% in patients undergoing video laryngoscopy. There were no failed airways.

Conclusions: In the SAMMC ED, emergency intubation has a high success rate comparable to that reported in other ED settings.

Funding Source: AFMS SG Office
HEALTHCARE AFFORDABILITY AND COMPLEXITY OF FAMILY MEDICAL VISITS
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BACKGROUND. Socioeconomic status, one of the social determinants of health, is an important factor in outpatient care due to the existence of health inequities across patient populations. According to the World Health Organization (WHO), social determinants of health are economic and social conditions that influence the health of people and communities. Patients’ socioeconomic status affects the ability to afford healthcare, and contributes to the overall complexity of family medicine visits.

The National Ambulatory Medical Care Survey (NAMCS) provided a way for researchers to examine complexity of family medicine practices using a comprehensive description of visits, including patient demographics, diagnoses, tests ordered, and referrals made. Peek & Baird defined additional factors that contribute to the complexity of family medicine visits, including psychosocial, environmental, and financial factors; these are not specifically identified in the NAMCS data set. In this study, we examine the relationship between patients’ ability to afford care and the complexity of their visits to an outpatient family medicine clinic.

METHODS. Medical student researchers shadowed family physicians in 10 outpatient practices in the Residency Research Network of Texas, and recorded details of 982 visits through cross-sectional direct observations. Complexity was assessed by counting time spent in each visit, reasons for visit, issues and medications addressed, counseling types, medical errors, and counseling. The Peek & Baird Complexity Scale documented healthcare affordability.

RESULTS. Of the 982 visits observed, physicians were aware of socioeconomic status in 610 patients, specifically, their ability to afford healthcare services. In this sample (n = 610), 60% of the patients were female, 50% were Hispanic, and 17% were African American. The median age was 52, with 13% under age 21, and 21% age 65 and older.

Patients were divided into 3 groups by healthcare affordability: can easily afford medications and copayments (n = 288); affordable but it’s a pinch (n = 146); and uninsured, underinsured, or severe lack of resources (n = 176). The group with the best affordability had fewest number of reasons for visits ($x = 5.1$ vs. 5.7 and 5.8, $p = .017$); fewest number of issues addressed ($x = 3.2$ vs. 4.2 and 4.0, $p = .000$); and fewest medical errors ($x = 0.3$ vs. 0.6 and 0.5, $p = .010$). The group with the worst affordability required more time in visit ($x = 35.1$ min vs. 30.1 and 32.1, $p = .020$); and received least amount of counseling ($x = 0.7$ vs. 1.2 and 1.0, $p = .001$). All three groups had about the same number of medications addressed ($x = 5.8$ vs. 4.9 and 5.1, $p = .110$).

CONCLUSION. The strong association between healthcare affordability and complexity of medical visits may play an important role in the health outcomes for those who face socioeconomic disadvantages. Economically disadvantaged patients presented with more reasons for visit and physicians spent more time with them. Their lack of resources may cause them to delay seeking health care, and when they do present for care, their problems are more complex and time-consuming.

REFERENCES


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TRAUMATIC KNEE INJURY: HOW MUCH KNEE EFFUSION ON RADIOGRAPHY IS PATHOLOGIC?

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Background: Traumatic knee injury is a common clinical presentation. Radiography is the initial radiological examination to evaluate knee injury. However, internal derangement of the knee, such as ligamentous tears, meniscal tears, and osteochondral fractures are often not detectable on radiography. Therefore, having an effective means to select patients to undergo knee MRI is helpful since MRI is an expensive resource. We hypothesize that patients with suprapatellar effusion greater than 1 cm have a high likelihood of internal derangement of the knee.

Materials and Methods: Lateral knee radiographs performed for recent knee injury in 198 patients were reviewed. Study inclusion criteria specified patients between the ages of 18 and 40 years and knee MR examination performed within 3 months of the radiograph. Patients with radiographic evidence of fracture, lipohemarthrosis, and dislocation were excluded. Prior to viewing the knee MRI, the greatest anteroposterior measurement of the suprapatellar effusion on lateral knee radiography was recorded. Three radiologists (a musculoskeletal radiology fellow, a fellowship-trained musculoskeletal radiologist, and a nuclear medicine radiologist) reviewed both the knee radiograph and MR exam. The size of the suprapatellar effusion was correlated with the presence of internal derangement on MRI.

Results: Of the 198 lateral knee radiographs reviewed, 93 patients (47%) had internal derangement on MRI. Fifty-one of fifty-five patients (93%) with suprapatellar effusion greater than 1 cm on radiography had internal derangement in the knee joint. Of the 143 patients with suprapatellar effusion less than or equal to 1 cm on radiography, 42 patients (29%) had positive findings on MRI. Using greater than 1 cm of suprapatellar effusion on lateral knee radiograph as a positive diagnostic test, this criterion has the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 55%, 96%, 93%, 71%, and 77%, respectively.

Conclusions: There is a strong direct correlation between the presence of suprapatellar effusion greater than 1 cm on post-traumatic lateral knee radiograph and knee internal derangement on MRI. Health care providers can confidently use this criterion to select patients to undergo knee MRI. Given the prevalence of knee trauma in our society, applying this imaging evaluation algorithm has the potential to decrease delayed diagnosis, initiate early correct therapy, improve patient outcomes, decrease cost-associated disability, and enhance military readiness within our populace.

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Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its Components.
BATTLEFIELD ACUPUNCTURE FOR ACUTE/SUBACUTE BACK PAIN IN THE EMERGENCY DEPARTMENT

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Abstract

Purpose:
To evaluate the effectiveness of Battlefield Acupuncture (BFA) versus standard care (medicinal therapy) in an Emergency Department (ED) setting for acute/subacute back pain using the Visual Analog Score (VAS) and Numeric Rating Scale (NRS). Secondary outcomes included the Back Pain Functional Scale (BPFS), satisfaction of treatment, and the need for further pain medication after discharge.

Design and Methods:
A prospective, randomized control trial, (un-blinded, non-placebo controlled) with convenience sampling based on scheduled clinical shifts in the ED. The population consisted of active duty service members and beneficiaries age 18-55 at San Antonio Military Medical Center ED with acute/subacute back pain as the chief complaint.

Members were screened for pathological back pain then enrolled. Demographics, initial VAS, NRS, and BPFS were collected. Participants were randomly assigned to either treatment arm. Subjects received either BFA or standard care, which was pre-determined medicinal treatment. Participants were reassessed at 30-40 minutes post intervention for pain and satisfaction. A discharge questionnaire was completed determining effectiveness of treatment, and subjects were given further instructions including a follow-up telephone interview between 48-72 hours. At follow-up a repeat NRS, functionality questionnaire, and pain medications used since discharge were obtained.

Data Analysis:
With 26 subjects per group (52 total), the investigator was able to detect a 1.0 SD difference measured by a 13mm change in the VAS or a 2 point change in the NRS.

Results:
The study demonstrated both a clinically and statistically significant difference in VAS scores between pre- and post-treatment with the difference between BFA (mean 34.38, SD 26.61) and the standard care (mean 21.46, SD 12.41). The change in pain score in the VAS difference was (t = 2.18, mean difference 12.92, df 50, p = 0.036). The NRS difference between pre and post-treatment was noted to be statistically significant; BFA (n = 26, mean 3.60, SD 1.82), and the standard care (n = 26, mean 2.27, SD 1.34), p =0.005, difference between groups 1.33. Participants in the BFA group experienced a 45% reduction in pain compared to the standard care treatment group which had a 31% pain reduction. BPFS scores also had a greater improvement in the BFA group compared to that of the standard care group, however did not meet statistical significance.

Conclusions:
We found BFA is an alternative treatment for pain control in subjects with non-pathological back pain. BFA has been shown to have a timely response with improved pain outcomes noted at 30 minutes post-treatment. BFA can be used as a first line treatment alone or in conjunction with current standard care to maximize treatment options, as well as improve pain control without the use of narcotics.

Key Words: Battlefield Acupuncture, Auricular Acupuncture, Alternative Medicine, Complementary Alternative Medicine, Military, Service Members, Emergency Medicine, Back Pain, Acute Back Pain, Chronic Back Pain
Topics:
Acute back pain in an acute care setting.
Use of alternative medicine, Battlefield acupuncture, for treatment of a common musculoskeletal complaint.

Submission category: Poster
Crisis Intervention Team (CIT) Training: Implications for Military Settings

Kaitlin Duckett, M.S.

Purpose: The current study will detail the development, application, and outcomes of CIT training based on the current literature. It will also discuss implications and recommendations for the use of CIT in a military setting.

Conceptual Foundation: Crisis situations involving individuals with mental illness present unique challenges for communities and law enforcement, who are often first responders. CIT training was developed in 1988 and has since been utilized as a means of equipping police officers with specialized knowledge and skills for successfully resolving crisis and other encounters with individuals experiencing mental illness.

Methods: The theoretical framework with which CIT training is based (i.e., crisis theory and the equilibrium model) will be explained to provide an understanding of the tenets and structure of CIT training. A thorough review of the literature regarding outcomes of CIT training, most heavily emphasizing the Memphis Model, will be discussed.

Findings: CIT programs have proven successful in reducing use of force, increasing referral rates to treatment facilities, decreasing arrest rates, increasing self-reported officer comfortability and preparedness, increasing knowledge of de-escalation skills, improving police officers’ knowledge of mental illness, and several other community and training outcomes.

Implications: The current research, demonstrating the effectiveness of CIT training for police officers across a broad range of agencies provides strong support for its use by military law enforcement as well. Recommendations for CIT implementation in military settings, in addition to projected outcomes and barriers (based on current literature), will be provided as well.
Evaluating the impact of a tobacco cessation training for military medical providers in a primary care clinic

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Purpose: This study examined primary care providers’ perceived ability to facilitate a brief conversation aimed at referring patients to effective smoking cessation resources, following a training organized around the principles consistent with Motivational Interviewing (MI).

Conceptual Foundation: Tobacco use is a notable public health problem with unique implications for the United States military. While brief interventions in primary care settings can increase tobacco quit rates, there presently exists little evidence concerning how best to train providers in the delivery of such services.

Methods: Fourteen primary care providers working at a large military treatment facility participated in the 1-hour training. Provider comfort with, confidence in, and inclination toward use of a brief conversational strategy for tobacco cessation were assessed with pre- and post-training assessment.

Findings: The participants were on average 52.9 years old (SD=16.21), 57.1% were female, with 13.1 years of experience (SD=6.7). The majority (85.7%) reported currently providing patients with smoking cessation resources, with a little less than half (42.9%) believing their patients were at least slightly receptive to a conversation about tobacco use. Items (pre- and post-test) concerning provider confidence in facilitating a brief conversation with patients not ready to quit and provider comfort in providing smoking cessation resources were compared through paired samples t tests. There were no significant difference in provider confidence from pre-test scores (M=2.77, SD=1.01) to post-test scores (M=2.69, SD=.75), t(12)=.291, p=.776 or provider comfortability from pre-test scores (M=2.77, SD=.60) to post-test scores (M=2.92, SD=.64), t(12)=-1.477, p=.165.

Implications: Prior to administration of the training, 35.7% of participants were extremely confident in their ability to facilitate a brief conversation with a patient not ready to quit smoking and more than half (57.1%) were very comfortable with providing smoking cessation resources. Following the intervention, participants indicated similarly high levels of confidence and comfortability, which may explain why the t-test resulted in non-significant results. Recommendations will be made regarding future directions for research in light of the findings, as well as strengths and weaknesses of the present study.
EFFECT OF HYPOXIA ON PORCINE AND HUMAN MESENCHYMAL STEM CELLS

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Mesenchymal stem cells (MSCs) play a crucial role in the body’s response to shock and trauma. In the bone marrow, MSCs reside in a hypoxic milieu (1-5% O₂) that is thought to preserve their multi-potent state. Typically, in vitro expansion of MSCs is performed under normoxia (~21% O₂), a process that has been shown to impair their function. Here, we evaluated the phenotypic and genetic characteristics of MSCs cultured under hypoxia versus normoxia. We hypothesized that, when compared to normoxia, dedicated hypoxia will augment the growth characteristics of MSCs. Our goal is to define the culture conditions best suited for preparing MSCs for use in clinical studies.

Human-bone-marrow MSCs (hMSCs) were obtained from fresh mononuclear cells purchased from AllCells (Alameda, CA). Porcine-bone-marrow MSCs (pMSCs) were obtained from anesthetized donor swine. The MSCs were cultured for 10 days in either normoxia (5% CO₂/95% Air; 37°C) or hypoxia (1% O₂/5% CO₂/94% N₂; 37°C) using a dedicated hypoxia station (HypOxystation H35, HypOxygen, Frederick, MD). On days 3, 7 and 10, MSCs were evaluated for their metabolic activity (Vybrant Cell Metabolic Kit), proliferative capacity (Quant-iT PicoGreen kit), and viability (Live/Dead Viability/Cytotoxicity Kit). Additionally, quantitative real-time polymerase chain reaction (qRT-PCR, StepOnePlus, Applied Biosystems, Foster City, CA) was performed on Day-7 samples using TaqMan Assay for the following genes: VEGF, HMGB1, Tissue Factor (TF), OCT-4, Nanog, and hypoxia-inducible factor (HIF-1A). Housekeeping genes used were 18S and β-actin for hMSCs and pMSCs, respectively. All experiments were performed in triplicates using passage-3 bone-marrow MSCs. All kits and reagents were purchased from Thermo Fisher Scientific (Waltham, MA).

Results from the metabolic assay showed significant increase (p<0.0001) in the metabolic activity of both human and porcine MSCs cultured at hypoxia versus those cultured at normoxia (Fig. 1A). In contrast, the MSCs cultured at normoxia exhibited significantly higher proliferative capacity than those grown under hypoxia (Fig. 1B). Furthermore, MSCs cultured in hypoxia had up-regulated expression of VEGF and the stem-cell genes, OCT-4 and Nanog. Interestingly, expression of HMGB1 and TF were elevated in human, but not porcine, MSCs cultured under normoxia.

In this study, we examined the effect of prolonged hypoxia on both porcine and human MSCs. Unexpectedly, we observed an inverse relationship between metabolic activity and MSC growth characteristics. While prolonged dedicated hypoxia may up-regulate specific desirable genes (e.g., VEGF), it proved deleterious for MSC growth. Next step is to examine short-term exposure (i.e., 24-48 hrs.) of MSCs to hypoxia.
Figure 1 - Effect of hypoxia on the metabolic activity (A) and growth characteristics (B) of human and porcine MSCs.

We would like to acknowledge the personnel of the Multi-Organ Support Technology (MOST) Task Area, U.S. Army Institute of Surgical Research.

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OPTIMIZATION OF MESENCHYMAL-STEM-CELL CULTURE CONDITIONS FOR USE IN CLINICAL TRIALS

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Current clinical trials utilize large quantities of mesenchymal stem cells (MSC), which necessitate their prior expansion in vitro. It is well known that in vitro expansion is limited to approximately 40 population doublings (PDs), as MSCs senesce and lose their multipotent properties in extended cultures. In this study, we evaluated various conditions of MSC culture, including different basal media, supplements, and seeding densities, in order to identify the most beneficial process for generating clinically-relevant doses of MSCs for future use in studies of organ failure induced by shock/trauma.

Plastic-adherent porcine bone marrow (pBM)-MSCs were obtained from anesthetized donor swine following concentration and plating of the mononuclear cell population. Evaluation of basal media included minimum essential media-alpha formulation (α-MEM) and Dulbecco’s modified eagle medium (DMEM) of low and high glucose content. Assessment of supplements included different concentrations (0, 1, 5, and 10%) of porcine platelet lysate (PL) versus 10% fetal bovine serum (FBS). Cell plating densities included 60, 100, 1000, and 3000 MSCs/cm². The effect of Dil staining on MSC function was also evaluated. Cellular analyses included flow cytometry (BDFACS Canto II) for MSC markers (CD45⁻, CD29⁺, CD73⁺, CD90⁺, and CD105⁺), colony forming unit-fibroblast (CFU-F) assay, growth kinetics, and viability using a fluorescent live/dead assay. All experiments were performed in triplicates using passages 2-3 pBM-MSCs.

No significant differences were observed in the growth characteristics of the pBM-MSCs across the different media (Fig. 1A). In contrast, supplementation of the basal media with 5% and 10% PL showed a dramatic increase in the proliferative and clonogenic capacity of the pBM-MSCs, as compared to 10% FBS (Fig. 1B). Plating different densities of pBM-MSCs showed a dose-like response on day 7, but plateaued on day 10, with fewer PDs and significantly higher yield of MSCs plated at 1,000 and 3,000 cells/cm² (Fig. 1C). Tagging the MSCs with a fluorescent lipophilic stain did not affect their proliferative capacity or alter their phenotype (Fig. 1D). In all cell culture conditions, MSCs were over 90% viable and exhibited high (>95%) expression of MSC surface markers.

In this study, the optimal cell culture conditions for the in vitro expansion of pBM-MSCs were examined. We found that supplementation with 10% PL using an initial seeding density of 1000 cells/cm² was the most conducive for generating large quantities of pBM-MSCs with minimal number of PDs. Future studies will examine other parameters, such as hypoxia preconditioning, to further augment this process.
Figure 2 - Effect of different culture conditions on the growth of porcine bone marrow mesenchymal stem cells

We would like to acknowledge the personnel of the Multi-Organ Support Technology (MOST) Task Area, U.S. Army Institute of Surgical Research.

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EFFECTS OF HUMAN AND PORCINE MESENCHYMAL STEM CELL-DERIVED CONDITIONED MEDIA ON COAGULATION AND T-CELL FUNCTION

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Systemic administration of mesenchymal stem cells (MSCs) is associated with several potential health risks. MSCs have been shown to protect injured tissue, in part, by secretion of a large variety of bioactive factors and extracellular vesicles (EVs); thus, cell-free products from MSCs are becoming more attractive candidates. In cell culture, these mediators are found in conditioned media (CM). We hypothesized that CM are safe for clinical application by evaluating the thrombogenicity and immunomodulatory potential of CM in vitro.

To obtain CM, human and porcine bone marrow-derived MSCs were incubated with serum-free medium. After 24 hours, supernatant was collected and cells were removed by centrifugation. Thrombogenicity of CM was tested by thromboelastography (TEG). Whole blood from healthy human and porcine donors was mixed with CM at different ratios (CM: blood ratios of 1:1, 1:2.5, 1:5, 1:10, n ≥ 3). To study the immunomodulatory effect of CM, mononuclear cells (MNCs) derived from healthy donors were labeled with a proliferation dye and stimulated to induce T-cell proliferation. MNCs were then plated with MSCs or CM in triplicates. After 72 hours, T-cells were collected and assessed by flow cytometry.

We observed that porcine CM significantly accelerated the initiation of clot formation (R) in a dose-dependent manner. Porcine CM also increased the rate (K; α-angle) of early clot formation related to rapid fibrin accumulation. In addition, porcine CM increased the clot strength (MA). By comparison, only the highest dose of human CM (1:1) significantly reduced the R value. However, neither K, α-angle, nor MA were affected by human CM at any ratio. MSCs reduced T-cell proliferation via cell-cell contact; yet, CM did not generate the same effect.

In this study, we developed an in vitro method to evaluate thrombogenicity of CM. Our results suggest that in a porcine model, but not human, a pro-coagulant effect occurs. However, further studies are required to determine if this response is repeated in vivo. Also, the fraction of CM, EVs or EV-free CM, responsible for this effect remains to be elucidated. While the CM did not inhibit T-cell proliferation, it remains to be seen whether the EV fraction will produce the same results.

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INVESTIGATION OF INTRAVENOUS HYDROXOCOBALMIN COMPARED TO HEXTEND FOR RESUSCITATION IN A SWINE MODEL OF UNCONTROLLED HEMORRHAGIC SHOCK: A PRELIMINARY REPORT

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Objectives: To compare SBP over time in swine that have undergone hemorrhagic shock induced by a lethal groin injury.

Background: Previously we reported that intravenous (IV) hydroxocobalamin is as effective as IV Hextend in improving systolic blood pressure (SBP) in a controlled hemorrhagic shock model. We aimed to compare IV hydroxocobalamin (HOC) to Hextend using an uncontrolled hemorrhage model. Non-compressible wounds are difficult to treat. An ideal resuscitative fluid would be a small volume, portable drug that improves blood pressure and survival.

Methods: 7 swine (45-55 kg) were anesthetized, intubated, and instrumented with continuous femoral and pulmonary artery pressure monitoring. A groin injury was created by surgically exposing a femoral artery and vein then transecting both. A suction catheter connected to a canister placed distal to the wound measured blood loss. After bleeding to a systolic pressure of 40 mmHg, QuikClot was used to pack the wound, followed by 5 minutes of manual pressure. A chest seal was then applied. Animals were randomly assigned to receive 150 mg/kg IV HOC solubilized in 180 mL of saline or 500 mL of Hextend and monitored for 120 minutes. A sample size of 9 animals per group was determined based on a power of 80% and an alpha of 0.05 to detect an effect of size of at least 0.25 difference (1 SD) in systolic blood pressure (SBP) between groups. Data were analyzed using repeated measures MANOVA. Data collection is ongoing.

Results: There were no significant differences between the HOC or Hextend groups at baseline or at shock (SBP 52 vs. 59 mm Hg), nor was there a significant difference in blood loss from the injury (1005 vs. 1100 mL). The overall MANOVA model detected a significant difference by time between groups (p<0.5) after treatment. Post hoc analysis indicated no significant difference in SBP, mean arterial pressure (MAP), or heart rate between groups (SBP 86 vs. 80 mm Hg; MAP 63 vs. 57 mm Hg; HR 158 vs. 170 bpm). However, systemic vascular resistance (SVR) was significantly higher and cardiac output (CO) significantly lower (p<0.03) in the HOC compared to Hextend treated animals (SVR, 1373 vs. 764 dyne-sec-cm-5; CO, 3.3 vs. 5.3 L/min).

Conclusion: IV HOC was as effective as Hextend in supporting SBP in an uncontrolled hemorrhagic shock model. Although CO was statistically decreased in the HOC group, this may have been due to an increase in SVR produced by HOC.

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SODIUM AZIDE ASSOCIATED ACUTE HYPERKALEMIA IN A SWINE MODEL OF SODIUM AZIDE TOXICITY

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Objective: To describe the clinical course of sodium azide poisoning and develop novel treatments for toxicity.

Background: Sodium azide (NaN₃) poisonings are rare but extremely deadly. There is very little in the literature regarding the clinical course of sodium azide poisoning. Virtually all of the information comes from case studies and each of those describe hypokalemia hours after poisoning. Antidotes to cyanide have been used for sodium azide poisonings but have had limited success.

Methods: Twenty swine (45-55 kg) were anesthetized, intubated, and instrumented with continuous femoral and pulmonary artery pressure monitoring. After stabilization, anesthesia was adjusted such that animals would spontaneous ventilate with an FIO₂ of 0.21. Sodium azide, in concentrations ranging from 4 to 160 mg/mL and was infused at doses ranging from 0.8 to 10 mg/kg/min until apnea was confirmed for 1 minute by capnography. This rate was sustained for 1.5 minutes post apnea. Only doses at 10 mg/kg/min at concentrations of 160 mg/mL produced consistent apnea but not sustained apnea.

Results: There were no significant differences in baseline vital signs, chemistries, or arterial blood gases including potassium (mean 4.1 mEq/L) and lactate (1.1 mmol/L) among the animals. Once the NaN₃ infusion began, all pigs became hyperkalemic, acidic and hypotensive. In pigs infused with the highest dose and concentration of NaN₃ (n=14), significant hyperkalemia began at apnea (5.1 mmol/L) and continued to rise (mean 7.7 mmol/L) even after the infusion was discontinued. Swine not treated for hyperkalemia died. Those treated with insulin, dextrose 50%, and calcium survived, but demonstrated elevated T waves on electrocardiogram and continued acidosis (lactate mean 6.7 mmol/L).

Conclusions: NaN₃-poisoned swine acutely develop hyperkalemia. We speculate that the hyperkalemia is due, in part, to the intracellular exchange of potassium ions for hydrogen ions in the face of metabolic acidosis. Pathology findings in the animals demonstrate that hyperkalemia is not caused by excessive muscle breakdown. Model development is ongoing.

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Regenerative Potential of Craniofacial Tissues: Evidence That Estrogen-Mediated Negative Regulation of the Lubricin Gene Underlies Female Temporomandibular Joint Damage

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Introduction: Temporomandibular joint (TMJ) disorders (TMJD) affect over five percent of the US population. Interestingly, more females in their birth giving years report TMJ pain and disorder compared to males of similar age. This sexual dimorphism indicates that there may be a hormonal influence playing a role in the pathology underlying TMJD. The overarching commonality patients experience is pain, and there is not a long-lasting effective treatment, nor is the underlying pathology well understood. An evidence-based model indicates that a defect in the quantity or quality of molecules that lubricate TMJs contribute to development of degenerative TMJD. We have previously discovered that the female sex hormone estradiol negatively regulates the gene encoding an articular joint lubricating molecule called lubricin, possibly explaining, at least in part, the sexual dimorphism seen in TMJD. Although it is known that lubricin maintains a fluid and low frictional environment in articular cartilage, there is limited characterization of lubricin gene expression in TMJ and TMD tissues. The objective of our present research is to advance our knowledge of the role of estradiol in TMJD through evaluating estradiol effects on lubricin gene expression in TMJ disc, synovial and cartilage cells derived from young adult female and male Papio hamadryas anubis baboons. Baboon is believed a good model species due to the size of their TMJ and the TMJ loading stimuli relative to humans.

Materials and Methods: Disc cells, chondrocytes, and synovial cells were obtained opportunistically from female and male baboon necropsies. TMJ discs, synovial membrane and articular cartilage tissues were dissected under sterile conditions. Tissues were processed to obtain sections for H&E staining. Additionally, portions were homogenized and placed in growth medium, or portions were placed directly in culture plates to allow for cell translocation onto the plate surface. Isolated cell populations were frozen until used for experiments. Analysis, detection, and quantification of lubricin was performed using quantitative PCR, Western blots, and cell growth analysis.

Current Results: Quantitative PCR was used to investigate effects of estradiol in TMJ cell types, comparing female and male cells, and identifying the active estrogen response elements in the lubricin gene promoter region. An initial time-trial of estradiol exposure shows a time-dependent, incremental repression of lubricin gene expression in female disc cells. We have also documented cellular morphology consistent with cell type. Our cell proliferation assays, and protein assays for the extracellular matrix molecules lubricin, versican, aggrecan and collagens, will be compared to identical assays performed on human telomerase reverse transcriptase immortalized TMJ cells (hTERT TMJ cells) which will be used in future studies.

Conclusion: The negative regulation of estradiol on lubricin gene transcription can potentially explain the clinically observed gender disproportion in patients presenting TMD. This research is expected to open new pathways to develop clinical therapeutic agents, and engineer cells that can help treat, or cure TMD.
EFFICACY OF ALBUMIN IN A RAT MODEL OF HEMORRHAGIC SHOCK AND TRAUMA WITH TOURNIQUET DEPENDS ON ITS PRE-SATURATION WITH FATTY ACIDS

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Introduction. Fatty acids (FAs) from the ischemic gut and from other sites of injury may contribute to lung and other organ damage in shock. In manufacture, FAs are added to human albumin for resuscitation, which could explain its lack of benefit in clinical trials. In vitro, these FAs decrease the available FA-binding capability of albumin and reverse the protection against hemolysis that albumin provides to blood exposed to exogenous FA. Our objective was to compare albumin-based resuscitation fluids with different amounts of FA-binding capability.

Methods. We used 1) 25% FA-free albumin, 2) 25% FA-saturated albumin or 3) Plasmalyte in a militarily relevant model of shock using anesthetized rats: Laparotomy + 45% hemorrhage + tourniquet; 1 h ischemia, then resuscitation followed by 2 h of Plasmalyte as needed to maintain mean blood pressure at 50 mmHg (hour 1 of resuscitation), then 60 mmHg (hour 2). Blood at baseline and at each hour and Broncheoalveolar Lavage Fluid (BALF) at the end were sampled for measuring hematocrit, protein concentration, free hemoglobin, and plasma FA concentration and binding capacity.

Results. 42 animals were hemorrhaged. 2 rats failed to reach their final hemorrhage volume and died. The only other cause of death was associated with sudden losses of arterial pressure control, unresponsive to fluid administration. This occurred in 3 animals before resuscitation and group assignment. Of 37 rats that survived until resuscitation, 17 died in this fashion (9 of 16 in Plasmalyte group, 7 of 12 in FA-free group, 1 of 9 in FA-saturated group; p=0.027 FA-saturated vs Plasmalyte). In the surviving rats, the FA-saturated group required significantly less fluid to maintain blood pressure than either of the other groups. In contrast, FA-free albumin significantly restored and maintained the most volume to the vasculature (as estimated from hematocrit). Both albumin groups increased plasma protein content after resuscitation, however, while the FA-free group increased volume (lowering protein concentration over time), the FA-saturated group lost volume and retained a higher protein concentration. While hemolysis was not evident in the plasma, free hemoglobin appeared to have collected in the lungs. Elevated free hemoglobin was evident in 4 of 8 samples of BALF in the FA-saturated group vs 2 of 7 in the Plasmalyte and 2 of 8 in the FA-free groups (not significant).

Conclusions. Our findings suggest that FA-saturated albumin does a poorer job of restoring blood volume than FA-free albumin, but that this may provide a survival benefit with regards to preventing sudden pressure loss events.

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PIRFENIDONE REDUCES THE PROFIBROTIC RESPONSE IN AN IN VITRO MODEL OF TGF-β1-INDUCED HUMAN DERMAL MYOFIBROBLASTS

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**Background:** The wound healing processes following a burn injury often result in hypertrophic scarring. This type of fibrosis is characterized by chronic pathological remodeling of the dermal tissue leading to excessive production of extracellular matrix (ECM) and the formation of raised, thick, inflexible scars that are often functionally debilitating. The structural and functional alterations of the dermal matrix involve complex cellular and molecular interactions mediated in part by transforming growth factor-beta 1 (TGF-β1), a profibrotic cytokine that is overexpressed in the wound bed. TGF-β1 induces a fibroblast-to-myofibroblast transition whereby normal fibroblasts differentiate into the alpha-smooth muscle actin (α-SMA) expressing myofibroblast effector cells responsible for the overproduction of ECM and scar formation. Thus, some anti-scarring strategies aim to modulate the profibrotic activity of TGF-β1 during wound healing. Pirfenidone (PFD) is an FDA-approved anti-inflammatory and antifibrotic agent currently used for the treatment of idiopathic pulmonary fibrosis; however, the effects of PFD on dermal tissue are not well understood. We aim to characterize the antifibrotic mechanism(s) of PFD in an in vitro model of dermal fibrosis.

**Methods:** An in vitro model of dermal fibrosis was established using differentiated myofibroblast cultures derived from normal adult human dermal fibroblasts stimulated with the profibrotic cytokine TGF-β1. Myofibroblasts were treated with varying doses of PFD given prophylactically, concurrently with TGF-β1, or as a therapeutic following myofibroblast differentiation. The effects of PFD on the profibrotic activities of TGF-β1-induced myofibroblast effector cells were determined in vitro.

**Results:** An effective in vitro dosage was determined at multiple concentrations ranging from 0.1-1.0mg/mL. While PFD treatment reduced TGF-β1-mediated dermal fibroblast proliferation at each time point tested relative to TGF-β1 stimulation, PFD was found to most significantly reduce growth when administered prior to or concurrently with TGF-β1. No major cytotoxic effects were associated with PFD treatment. Additionally, PFD significantly decreased myofibroblast markers, such as α-SMA protein expression, and was found to modulate kinase activity in several key cell signaling pathways involved in wound healing and fibrosis.

**Conclusions:** PFD is a potent inhibitor capable of reducing dermal fibroblast growth and transformation to a profibrotic myofibroblast effector cell type. The mechanism(s) by which PFD exerts its antifibrotic effects on myofibroblast activity in vitro appears to target multiple cellular signaling pathways, including the profibrotic TGF-β1-mediated pathway. With no major cytotoxic effects detected, PFD has potential as a novel therapeutic agent with both antifibrotic and anti-inflammatory properties for the treatment of hypertrophic scarring following burn injury. Further investigations into the in vitro effects of PFD on resident skin cells are currently underway.

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Mitochondrial Pyruvate Carrier: homology modeling, docking, and dynamic simulation to integrate non-synonymous SNPs into individualized patient metabolic biosimulations

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Our group validated a Transcriptome-To-Metabolome™ biosimulation method used for individualized precision medicine. This report incorporates the genome into this predictive biosimulation approach using homology modeling for non-synonymous SNPs of the MPC1 gene. We can predict the right drug, at the right dose, for the right patient, at the right time, in silico, using only a genome and transcriptome from a patient sample. The mitochondrial pyruvate carrier (MPC) was studied in the 1970s-1990s by two lab groups primarily, Andrew Halestrap and Katarzyna Nałęcz, providing many predictions on the functional protein structure and the mechanism of substrate binding. The two genes for human MPC were identified in 2012. No crystal structure is registered or deposited in a protein data bank (pdb). One homology model of the MPC1-2 heterodimer was reported using the bacterial semiSWEET (4QND.pdb) transporter as a template with residues involved in the ligand binding site. This report describes results for another MPC1-2 heterodimer homology model, a template using the E.coli respiratory complex I membrane domain B (3RKO.pdb), residues 242-366 and rmsd ranging from 3 to 9 Å. The 3RKO(B).pdb template ranked by RaptorX was preferred because of the proton translocation properties of complex I. The MPC1-2 heterodimer pdb model generated by pyDockWeb placed MPC1-Cys60-Cys61 in the top candidate ligand binding – proton translocation site as determined by near match of MPC1 residues 64-71 to the ExxERFxYY motif of members of the major facilitator superfamily (MFS) transporters. Two MPC1 mutations with clinical descriptions, L79H and R97W, as well as one SNP, L36I, were modeled by RaptorX to the 3RKO template. Using DynDom Protein Domain Motion Analysis to compare these three mutations to the wild type MPC1, a His84 kink and Pro75 hinge were identified in the third transmembrane helix (TMH3) of MPC1. We predicted that upon binding pyruvate, near Cys60-Cys61 residues of MPC1, the kink would straighten and the hinge would swing toward the MPC2 TMH1; approximating MPC1-Cys83 and MPC2-Cys54 forming a dimer disulfide-bond proposed by Nałęcz. Using AutoDock-Vina-PyMol-Viewer and Rosie-Ligand-Docking, along with Swiss-PDB-Viewer, LigPlot Plus, and RasMol, pyruvate was shown to form hydrogen bonds with MPC1-Asn33 presenting the C2-carbonyl group to Cys60-Cys61 for reversible reaction with the –SH group as proposed by Halestrap. Docking with a known competitive inhibitor, 2-oxoisocaproate, demonstrated hydrogen bonding to MPC1-Arg54 on the mitochondrial intermembrane space side of the carrier and full spatial overlap with the pyruvate binding at Asn33 more on the matrix side of the carrier. This Arg54 is likely the site of action for phenylglyoxal carrier inhibition demonstrated by Nałęcz. Dynamic simulation for pyruvate in the wild type MPC1-2 heterodimer confirmed the binding site interactions and the kink-hinge effects consistent with predictions of Nałęcz. The alternating-access symporter model is also supported. Docking with pioglitazone revealed hydrogen-bonding with Asn33 consistent with MPC inhibition. Using delta-G values and derivatives for wild type and L36I to modify parameters for MPC in the TTM™ biosimulation for six individual human subjects demonstrated that lower pioglitazone doses would be required for L36I individuals.
**METAL ORGANIC FRAMEWORK (MOF) REDUCES CLOT STRENGTH AND STIMULATES FIBRINOLYSIS IN EX VIVO HUMAN BLOOD**

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**Introduction:** A significant challenge encountered with Extracorporeal Life Support (ECLS) is coagulation management. Contact of blood components with surfaces in the circuitry and shear stress lead to thrombus development, while use of systemic anticoagulants may cause hemorrhage and other complications. Alternatives to inhibit thrombus formation on circuit surfaces without systemic anticoagulation are being investigated, including tethering of NO-releasing agents to the circuitry. NO is an endogenous molecule with a short half-life that imparts reversible platelet quiescence and promotes an anti-thrombogenic phenotype. Metal organic frameworks (MOFs) are a class of crystalline materials capable of generating NO from biologically available NO-donors, such as S-nitrosoglutathione (GSNO). It has been reported by our collaborators that in the presence of GSNO, free particles of a specific MOF, [(CuCl)]₃(BTTri)₈ (CuBTTri), were capable of generating 97±6 nmol NO over 3hr, resulting in a 65-fold increase of baseline GSNO decomposition. Additionally, CuBTTri particles were blended into PVC to mimic incorporation into ECLS circuitry and demonstrated a 300% increase in NO generation in the presence of GSNO over 24hr when compared to baseline GSNO decomposition. Based on the demonstrated potential of CuBTTri to generate NO from endogenous sources, we investigated the bioactivity of this MOF in vitro. We hypothesized that CuBTTri generates NO from endogenous NO-donors and reduces platelet contribution to clot formation.

**Methods:** For this study, donor whole-blood (n=5) was collected in 3.8% citrated vacutainers (BD Biosciences, Franklin Lakes, NJ). A MOF solution was prepared by dissolving 2mg CuBTTri powder (provided by our collaborators at CSU) in 1mL PBS (pH 7.4). 300µL citrated blood was added to either 100µL MOF solution (+MOF group) or 100µL PBS (Control group). 340µL of the mixture was transferred to a standard TEG cup and 20µL CaCl₂ was added. Thromboelastography was performed using the TEG 5000 Hemostasis Analyzer (Haemonetics Corporation; Braintree, MA). The following variables were recorded: reaction time (R), clot formation rate (K), propagation (α-angle), clot strength (MA) and lysis time (Ly30 and Ly60). Statistical analysis was performed with GraphPad Prism version 7.01 (GraphPad Software, San Diego, CA). A t-test was performed with significance accepted at p ≤ 0.05.

**Results:** CuBTTri did not affect reaction time, clot formation rate or propagation when compared to the PBS control. Clot strength was decreased in the +MOF samples, and the rate of clot lysis at 30min and 60min post-maximum amplitude was significantly higher in the +MOF group.

**Conclusion:** In this in vitro study, mixing of blood with a MOF (CuBTTri) exerted anti-thrombogenic effects. The TEG clot strength (MA) measure is associated with platelet contribution to clot. The reduced clot strength observed in this study taken in correlation with the NO-generation data previously reported suggests that CuBTTri produces NO in vitro, which inhibits platelet aggregation and contribution to clot. The accelerated lysis rate observed in the MOF group could be due to NO dissolution of platelet aggregates and promotion of fibrinolysis. Further studies are needed to
observe the interaction of blood with MOFs incorporated into ECLS circuitry in vivo, particularly at various flow rates.

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Diabetes is the seventh leading cause of death in the United States and continues to rise. Compared to individuals in the non-minority population, a greater percentage of minority individuals experience clinical-level diabetes complications in the ocular, renal, and vascular systems, highlighting a health disparity in diabetic disorders. Molecules of the extracellular matrix (ECM) are crucial for healthy tissue homeostasis. Perturbing ECM-specific pro-survival signals induces cell death and tissue damage. In diabetic tissues, an increase in ECM synthesis and diminished ECM turnover largely account for accumulated ECM molecules, including the pro-apoptotic protein called BIGH3. Recently we uncovered evidence of a novel apoptosis pathway called BIGH3-mediated apoptosis (BMA). Our study indicates that TGF-β1 promotes BMA, advancing diabetic nephropathy. We show that in the kidney BMA targets renal proximal tubule epithelial cells (RPTEC) and the mechanistic pathway that kills these cells involves TGF-β1 and the increased synthesis, secretion, and accumulation of BIGH3 protein. Here, we extend these observations identifying cell-death sites in BIGH3 by introducing point mutations into BIGH3 cDNA and using apoptosis functional assays to find the critical amino acid residues operating in BMA. We have also determined that a cellular molecule that conveys BMA is a β1-class integrin receptor. Presumably, this interaction disrupts pro-survival signals needed by renal cells. Conclusion of this research is expected to offer novel therapeutic targets for interventions to block development and progression of diabetic complications.
UTILITY OF QUANTITATIVE ANALYSIS OF PULMONARY CT SCANS IN MILD-TO-MODERATE ARDS

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INTRODUCTION: Computed tomography (CT) presents changes in density distribution specifically in the lung, expressed in x-ray attenuation values called Hounsfield units (HUs). A concern with CT interpretation of pulmonary parenchyma by radiologists is that it is subjective and may not be sensitive to differentiating subtle changes. A promising solution to this problem is computerized quantitative assessment of CT scans (CqCT) which differentiates densities based on objective numerical criteria which describe aeration zones as they relate to various degrees of consolidation in the parenchyma. Here we apply CqCT in a preclinical model of ARDS. We hypothesized that CqCT is useful in assessment of pulmonary CTs and facilitates visual differentiation of density distributions.

METHODS: Anesthetized female Yorkshire pigs (n = 20) were intubated, mechanically ventilated and instrumented, randomized to a Control group (n=4), Treated group (Injury+ Nebulized Epinephrine, n=8) or Untreated group (injury and no treatment, n=8). Injury involved: smoke inhalation injury; 40% total body surface area full thickness burn; a 24hr burn fluid resuscitation protocol; injurious mechanical ventilation until ARDS. After onset of ARDS, the ARDSNet mechanical ventilation protocol was initiated in all groups. Animals underwent monitoring until 72hr post injury. Treated animals received 11.25 mg aerosolized racemic epinephrine every four hours, starting 1hr post-injury. CT scans were obtained at BL, 24, 48 and 72hrs post-injury. Analysis was performed using 3D-Doctor software (Able Software Corp., Lexington, MA). The segmentation process was automatically, utilizing accepted HU ranges for Air (-1000), hyperinflated parenchyma (-998 to -900), normally aerated lung (NORMAL = -900 to -500), poorly aerated lung (POOR = -500 to -100), and non-aerated areas (NON = -100 to +100) and presented as histograms (see picture). \( \text{PaO}_2 \)-to-\( \text{FiO}_2 \) ratio (PFR) was calculated using blood gas analysis. Statistical analysis was performed using SAS 9.3 (Cary, NC) with significance at \( p<0.05 \). One-way repeated measures ANOVA with Dunnett’s adjustment was conducted for within-group comparisons; two-way repeated measures ANOVA with Tukey's adjustment was used for between-group comparisons unless noted otherwise.

RESULTS: CT-scan images showed subtle changes in density distributions between groups. Changes in PFR denote both Untreated and Treated animals developed mild-to-moderate ARDS, without between-group differences in CTs.
HU aeration zones showed a unimodal pattern distribution at BL in all groups with most pixels in the normally aerated lung regions (left shift). At 24hrs the distribution of aeration zones in Control animals remains unchanged whereas in the other 2 groups the density distribution accumulated in the poorly and non-aerated zones showing a bi-modal appearance. A similar shift in the histograms was observed at 48 and at 72hrs. At 72hrs, the Treated and Untreated groups are distinguishable. These differences are not apparent upon examination of the CT-scan by eye.

**CONCLUSION:** In this model of ARDS, computerized quantitative assessment of CT objectively quantified increase in poorly and non-aerated lung at the expense of the normally aerated lung regions after injury. Examination of pulmonary HU histograms visualized qualitative and quantitative changes in ARDS which were not quantifiable by eye. CqCT and is a promising diagnostic tool in ARDS.

**Acknowledgements:** This work was supported by the US Army Medical Research and Materiel Command (USAMRMC) under Grant No. W81XWH-13-2-0005, PI Dr. Andriy Batchinsky. The views, opinions and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation. In conducting research using animals, the investigators adhered to the Animal Welfare Act Regulations and other Federal statutes relating to animals and experiments involving animals and the principles set forth in the current version of the Guide for Care and Use of Laboratory Animals, National Research Council.
AN ENVIRONMENT AND MULTI-GENE RISK INTERACTION MODEL FOR PTSD SYMPTOMS FOLLOWING COMBAT EXPOSURE

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Background: Since 9/11 and the resulting operations Iraqi Freedom and Enduring Freedom, over 1.64 million soldiers deployed with over 50% having experienced a psychologically traumatic event. Of this subset, approximately 300,000 are projected to meet the diagnosis of PTSD. The RAND corporation estimated the direct and indirect cost of caring for these individuals to be as much as $25,757 per individual for the first two years post-deployment. The cost is more than just monetary; individuals with PTSD have increased risk of psychiatric comorbidities, domestic violence, family strain, and homelessness.

Early studies of PTSD risk factors focused upon either environmental influences or genetic influences with the hypothesis that “PTSD genes” existed within neurotransmitter systems such as serotonin, dopamine, CCK, and the hypothalamus-pituitary-adrenal (HPA) axis. A more nuanced interpretation has developed, namely that the PTSD related genes may contribute to a “genetic differential susceptibility.” That is, different alleles of key neurotransmitter systems alter the strength of environmental influences upon an individual and may modulate the effect experience has upon individuals. Recent civilian clinical trials have further demonstrated that rather than specific genes conferring susceptibility, it may be the summation of multiple genetic pathways conferring the overall susceptibility to developing PTSD. Even more importantly, these gene metrics have predicted responses to early treatment following trauma.

We hypothesize that by using a multi-gene marker selected from genes hypothesized to modulate differential susceptibility, we can predict the severity of PTSD symptoms after combat.

Methods: Within the San Antonio Military Health System 275 subjects have been enrolled in the IRB approved ACES study, 55 with PTSD and 235 without PTSD. (Total enrollment goal is 520 subjects.) For each subject environmental risk factors will be measured by validated questionnaires of childhood trauma (ACES) and combat exposure (CES). 15 sensitizing single nucleotide polymorphisms SNPs (identified in the literature) will be tested and for each subject a composite score of the total number of sensitizing SNPs will be computed (maximum score of 30). Outcomes will be measured as PTSD severity – via PTSD checklist – military version (PCL-M).

Results: An early interim analysis showed a significant correlation between CES and PCL-M scores (rho = .3130, p = 0.0493), while correlations between ACE scores, CES scores, and gene scores were all non-significant. A significant gene-environmental interaction was found including CES x gene score for PCL-M (r^2 = 0.115, p=0.0319) as well as (CES + ACES) x gene score for PCL-M (r^2 = 0.118, p = 0.0302).

Conclusion: Preliminary data on a cohort of post deployment service members – mostly without PTSD – is showing both a correlation of PTSD severity with CES and a gene-environmental interaction of both adverse childhoods and severity of combat exposure with our developed gene-risk score. It is possible associations will become stronger as additional PTSD subjects are recruited, but even early data may highlight
the role sensitizing genetics and environment play in the development of subclinical PTSD symptomatology following combat.

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TRANSPORT OF CRITICALLY ILL NON-TRAUMA PATIENTS BY CRITICAL CARE AIR TRANSPORT TEAMS (CCATT)

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Purpose: The objective of this study is to characterize critically ill patients without traumatic injury transferred via CCATT to include a description of in-flight procedures and adverse events.

Background: Multiple studies have evaluated Critical Care Air Transport Teams (CCATT) trauma patients; however, nearly 50% of patients medically evacuated from combat theaters are for non-traumatic medical illnesses to include stroke, myocardial infarctions, overdose, and pulmonary emboli. Published data is limited regarding illness types, in-flight procedures, and adverse events. Historically, non-combat critical illnesses have required greater hospital resources with subsequent higher lost person-days; and thus, confer a greater impact on operational capability. Our study is the first to review the actual CCATT and evacuation medical record and describe the frequency and types of inflight procedures and medications administered.

Materials and Methods: We conducted a retrospective review of the medical records of 673 patients without traumatic injuries transported by CCATT out of theater to Landstuhl Regional Medical Center between January 2007 and April 2015. Demographics, description of current illness, vital signs, labs, in-flight procedures, medications, and in-flight adverse events were collected.

Results: The majority of medical (non-trauma) critical care transport patients suffered from cardiac (52%), pulmonary (13%), and neurological (16%) illnesses. The most common in-flight procedures and medications were supplementary oxygenation (62%), anti-coagulant/anti-platelet medications (46%), analgesics (30%), cardiac medications (20%) and ventilation (21%).

Conclusions: These critically ill medical patients require different interventions and medications than trauma patients and challenge the CCATT nurses in unique ways. Our findings suggest CCATT training and CPGs should include the management of cardiac, pulmonary, and neurological medical illness to include ventilator management in pulmonary patients and continuous vasoactive and anti-dysrhythmic medications in older cardiovascular patients.

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MAKING MOCK CODE TRAINING BURN SPECIFIC

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Introduction

Advances in cardiopulmonary resuscitation (CPR) research have shown that the effectiveness of compressions (depth, rate, and pauses) is key to patient outcomes; many hospitals now track this data and other metrics transmitted wirelessly by special pads placed on the patients’ chest. This data provides units with feedback to improve practice. The pads are not currently used on our unit due to anecdotal reports of slipping off of patients with anterior chest burns or grafted skin during CPR. There is no published data on burn specific code training. Therefore, we sought to determine if other burn units modified their code training, as well as to evaluate our own code training. The purpose of this project in the Burn Intensive Care Unit (BICU) is to understand differences in burn patient code events (cardiac/respiratory arrest that requires resuscitation) from other types of patient (non-burn) wards and modify code training to reflect those differences.

Methods

As part of a PI project, we reviewed code data and performed code training using the SIMMAN 3G patient with anterior chest wounds. A water based jelly was added to the chest to mimic the effect of open wounds or fresh grafts. The training consisted of running through a 10-minute scenario followed by an instructional session then a repeat of the same scenario. Participants completed a 5 point Likert-like pre and post training survey measuring satisfaction of preparedness, opinion on differences between burn versus other patients, adequacy of equipment and medication, and overall confidence. Account was also taken into Nurses experience and scope of practice such as Registered Nurses, Licensed Vocational Nurses, and MDs. Data pre and post training were entered into the software Code Net producing a visual display of how participant’s compression fraction rate improved after the instructional session.

Results 50 BICU staff (Nurses: 46; Physician:2; Medical Assistant: 1;Physical Therapist:1 ) participated in code training. Current Code training prepared me for Code Blue (no sig) Code training surveys revealed improved satisfaction of preparedness (p<0.05), and confidence (p. < 0.001). All staff agreed that there were differences in burn versus other patients (p<0.0001), and that equipment and medication was adequate (p<0.0001) Staff felt that lack of adherence of pads effected their ability to perform adequately. Compression fraction, (mean) pre-code (26.67%). Post-Code (68.59%). A compression factor greater than 60% has increased survivability and increase chance of return of spontaneous circulation (ROSC).

Conclusion

All staff commented on the effect of the jelly applied to the anterior chest as realistically simulating burns on the chest. The jelly applied to the anterior of the chest caused slippage of the code pads potentially effecting quality resuscitation.

Research implications/applications Code training should reflect the patient population. Increasing fidelity through simulation may improve outcomes of burn codes.
Poster #31

SUSTAINMENT OF DECREASED BLOOD CULTURE CONTAMINATION WITH AN INITIAL SPECIMEN DIVERSION DEVICE IN THE EMERGENCY DEPARTMENT

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Description: Blood culture contamination (BCC) in the Emergency Department (ED) is a constant challenge. Accurate blood culture results are critical to timely and targeted antibiotic therapy for patients with septicemia. Contaminated blood cultures often lead to inappropriate antibiotic therapy, extended length of stay, multiple drug resistance, and additional costs.

Objectives: Will the continued use of an initial specimen diversion device (ISDD) for drawing blood cultures in the ED maintain the <2% BCC rate achieved during the successful evidence-based practice (EBP) project?

Background: From September 2015-March 2016, an EBP project was completed, with a decrease (7.46% to 0.77%) in contamination events with the use of ISDD versus standard method (SM). These results lead to facility-wide implementation of the ISDD method in June 2016.

SAMMC has adopted ISDD as standard practice, yet usage must be monitored to keep BCC to a minimum. Partnerships between departments, continued EBP education, and record audits are all critical to maintaining maximum efficacy and compliance. The goal is a sustained BCC rate of less than 2% with the ISDD.

Methods: Authors compared blood cultures collected during the 6 months immediately following the initial EBP project in the ED at SAMMC (N=1654), using SM (n = 675) versus ISDD (n = 979). Standardized skin antisepsis was maintained with both types of specimen collection.

Findings: The standard method of specimen collection resulted in 40 contamination events for a BCC rate of 5.93%. In contrast, cultures collected with ISDD resulted in 13 contamination events, for a BCC rate of 1.33%. Blood cultures collected using the pre-assembled device continued to sustain contamination rates of less than 2%.

Implications for military nursing: Given the beginning BCC rate of 7.7%, the costs of contamination could approach $8.6 million annually in SAMMC alone. Assuming the Military Health System (MHS) draws a comparable number of blood cultures, potential costs of contamination would approach $156 million annually. With the system-wide implementation of ISDD as the standard phlebotomy practice, these cost projections could see a 90% reduction, representing the elimination of nearly 16,000 false positive diagnoses each year within the MHS.

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The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of the Air Force and Department of Defense or the U.S. Government.
Background:

In the largest hospital within the Department of Defense, we identified a vision to deliver quality care to a complex, high-risk neonatal population; highlighting performance improvement opportunities in areas of documentation, organization of equipment, allocation of resources, and team communication. The Neonatal Resuscitation Competency Simulation Program was designed to foster a culture of safety, reduce risks/hazards, and improve teamwork training within the perinatal section during neonatal resuscitation.

Methods:

Simulation is recognized as a transformative tool for culture change and a recommended educational strategy. Facility simulation experts, perinatal clinical experts and education leaders from the organization reviewed previous simulated and actual neonatal resuscitations and determined key areas for improvement. Focus areas included teamwork skills, product acquisition, documentation, communication, and the safe transfer/transport of neonates. An NRP Confidence Survey highlighted areas for improvement in individual neonatal resuscitation skills and teamwork behaviors. Six specific learning objectives and 25 critical actions were identified for training based on ideal neonatal resuscitation performance and in accordance with 2015 Neonatal Resuscitation Program (NRP) guidelines, 7th edition. Two in-situ (labor deck) clinical scenarios using a low-fidelity infant manikin and a Simulation Training Assessment Tool (STAT) were developed. All personnel assigned to the perinatal section who performed newborn resuscitation participated in at least one simulation scenario. Validation of competency was measured by requiring completion of 90% of critical actions listed on the STAT. Two facilitators were present during simulation scenarios to assess inter-observer reliability.

Results:

As part of the NRP Confidence Survey, 98% of those surveyed felt competent in routine newborn resuscitation, however more than 25% of team members did not feel competent in more advanced resuscitation interventions. In a three month period (Sep-Nov 2016) 40 simulation exercises were conducted, totaling 326 training hours, educating and validating 96% of our perinatal staff. Feedback from simulation activity debriefs provided positive feedback regarding individual skillsets, improved confidence in neonatal resuscitation, and enhanced teamwork skills. Simulation exercises allowed our education team to immediately address observed knowledge and performance gaps, later highlighted for ongoing training. Other systems issues were also identified and timely mediated to enhance future simulation/real-world neonatal resuscitation clinical practice.

Conclusion:

The development of a comprehensive, problem-based neonatal simulation training program has been instrumental in creating a safe learning environment for health care practitioners in our facility. The program encourages the application of evidence-based clinical processes, and enhances team skills to continuously improve patient safety. Upon completion of initial staff training and validation, we transitioned into the "sustainment" phase where each person will participate in a simulation at least once
every 6 months. This program continues to demonstrate what "right looks like" when each member of the team understands their role and practices within a safety minded perspective.
Objective: The purpose of this study was to evaluate the impact of ARDSNet compliance during aeromedical evacuation of ventilated combat injured patients.

Background: Aeromedical evacuation platforms such as CCATT play a vital role in the transport of critical military patients. Mechanical ventilation (MV) is used to support patients with failing respiratory function. Inappropriate MV management can worsen or cause lung injury and increase mortality. We hypothesize that subjects whose tidal volumes are ≤8 cc/kg and PEEP to FiO₂ ratios are in accordance with the ARDSNet table recommendations will have less ventilator and hospital days and lower mortality than subjects with non-compliant ventilator settings.

Materials and Methods: We performed a retrospective chart review of combat injured patients transported by CCATTs from Afghanistan to Landstuhl Regional Medical Center (LRMC) in Germany between January 2007 and January 2012. Regression analysis was used to assess compliance and post-flight outcomes. Cox proportional hazard models were used to evaluate associations between the risk factor of Non-compliance with increased number of ventilator, ICU, or hospital days.

Results: Sixty-two percent (n=669) of 1086 patients required MV during transport. Patients (n=650) requiring volume controlled MV were included. Sixty-two percent (n=400) were Non-compliant per tidal volume and ARDSNet table recommendations. The groups were similar in all demographic variables, except the Non-compliant group had a higher ISS compared to the Compliant group. Subjects in the Non-compliant group were more likely to have an occurrence of acute respiratory distress, acute respiratory failure, and ventilator associated pneumonia (7% vs 2%, p<0.0196) and had an increased incidence of inflight respiratory events, more ventilator and ICU days, and a higher mortality rate.

Conclusions: Non-compliance with the ARDSNet protocol is associated with increased adverse outcomes and increased mortality. The initial CCATT Mechanical Ventilation Clinical Practice Guideline (CPG), based upon the ARDSNet protocol, was published in 2012 (revised 2013). The results of this study support the use of the CPG and may be incorporated in pre-deployment training to encourage CPG compliance and improve patient outcomes.

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THE IMPACT OF TRANSPORT TIME ON OUTCOMES FOLLOWING EVACUATION FROM POINT OF INJURY

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Objective: The objective of our study was to determine the impact of transport time on patients with traumatic extremity amputation and non-compressible torso injury.

Background: During combat operations, patients with traumatic injuries require urgent medical attention and evacuation to improve survival. Aeromedical evacuation platforms such as MEDEVAC allow for urgent evacuation to a medical treatment facility (MTF) that provides higher levels of care. While it is accepted that shorter pre-hospital time is associated with improved survival, little is known about the influence of transport time on patient outcomes or the influence of transport time on specific injury types.

Methods: We performed a retrospective review of patient care records for US military and contractors in Afghanistan who were evacuated from the point of injury (POI) to a MTF between January 2011 and June 2014. Data were abstracted from MEDEVAC records and supplemental data was queried from the Department of Defense Trauma Registry. Transport time was stratified: ≤30, 31-60, and >60 minutes. Patients were stratified into three groups: patients with traumatic extremity amputation only (AMP); AMP and non-compressible torso injury (AMP+NCTI); and neither amputation nor NCTI (Non-AMP/NCTI).

Results: A total of 1267 patients were included (AMP, n=106; AMP+NCTI, n=72; Non-AMP/NCTI, n=1089). AMP+NCTI patients were more severely injured (ISS of 33[25-40]), followed by AMP (18[14-26]) and Non-AMP/NCTI (9[5-17]). With a median transport time of 38 (30-51) minutes, there was no significant difference in elapsed time from POI to MTF among the study groups (p=0.30). AMP+NCTI had a longer ICU stay (15[9-24], 7[3-11], and 0[0-5] days, respectively) and longer hospital stay (47[35-66], 37[26-35] and 8[4-19] days, respectively). We did not detect a difference in mortality for AMP (p=0.1614) or AMP+NCTI (p=0.0683) across transport time groups. However, when transport time was >60 minutes, AMP+NCTI had the highest mortality (AMP, 7% vs. AMP+NCTI, 18%; p=0.045).

Conclusion: The knowledge gained from this study may inform triage decision making related to determining order of evacuation of specific injury types.

Disclaimer: The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of Defense.

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Emergent Re-entry Sternotomy Training via SynDaver Simulation

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Background: In providing care to the post-surgical open heart patient who may require emergent re-entry sternotomy, what is the effect of standardized training on the nurse’s perception of ability to perform their roles before and after hands on training with the use of the SynDaver Median Sternotomy Model simulation?

Material/Methods: Simulation training has been used in many avenues such as aeronautics, law enforcement & healthcare, to assist in the training of personnel in learning a new task and also in performing highly technical procedures. It has been shown to be the best training for low use high risk task such as how to land a plane that has complete engine failure, performing reconstructive surgery, and also for emergent lifesaving procedures, such as emergent re-entry sternotomy on the post open heart patient. The challenge was to identify a simulator that could be surgically cut, with simulation fluids (blood) running through the simulator as well as mechanical movement of internal organs. The desire to make the experience as real as possible; while at the same time to not expose the staff to any additional harm (electrical counter shock) lead us to evaluate the use of the SynDaver technology. The goal of this project is to assist the bedside intensive care nurse in their self-perception of being comfortable in assisting the physician in performing an emergent sternotomy on the post-surgical open heart patient. We will take a multi-departmental approach to training and familiarity of procedures and roles that the open heart nurses and the surgical team members on the 3South CCU/CT unit would encounter if needing to perform an emergent re-entry sternotomy.

Results: After receiving funding for the purchase of the SynDaver Median Sternotomy Model simulator. The cardiothoracic surgeons and a select group of nurses performed a simulation of a controlled emergent re-entry. Safety of all staff was achieved; however the Syndaver required modification to the rib cage, so the
device was sent back to the company to build a more secure rib cage, for a more potentially realistic sternotomy re-entry. During the first dry-run it was also discovered that the emergent sternotomy re-entry cart, had more items than was necessary. The cart inventory was streamlined, and will be tested for accuracy and appropriateness to emergent sternotomy re-entry.

Conclusions: The use of the SynDaver Median Sternotomy Model to simulate emergent post open heart re-entry training with intensive care unit nurses was attempted and achieved. Further examination and training will occur once the SynDaver returns with modifications.

References:


Poster #36

Cuff, Cuffless or Fenestrated: What Do You Know About Tracheostomy Care?

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Department and Institutional Affiliation: Brooke Army Medical Center, Orthopedic Trauma Surgical Unit

Focus Areas/Learning Tracks: Inpatient/Outpatient Care Presentation Format:

Poster presentation

Description of the Problem: A tracheostomy care and patient safety knowledge deficit was identified on the Medical Surgical unit after a patient's tracheostomy tube became dislodged. The Medical Surgical staff, voiced concern regarding familiarity with taking care of a patient with a tracheostomy. Tracheostomy tubes are high risk invasive medical devices and lack of knowledge can result in negative patient outcomes. On this unit tracheostomies are a low volume invasive device causing a decrease in staff knowledge on tracheostomy care.

Background: On a busy orthopedic trauma surgical unit the presence of tracheostomies and the care thereof are of low volume. It has been reported that nurses working outside the Intensive Care Unit are lacking in skills, knowledge, and confidence to provide safe tracheostomy care (Yelverton, Nguyen, Wan, Kenerson, Schuman 2015). We identified a need to provide comprehensive education on tracheostomy care with the intention of increasing staff knowledge and confidence.

Materials and Methods: Using the DWA model, a focused question was developed and literature review completed. PICO question: Will tracheostomy care education improve knowledge deficits of nurses and paraprofessionals during a three month period?

Tracheostomy tubes are of high risk of negative patient outcome if not cared for and maintained properly. Nursing and paraprofessional staff must be knowledgeable in the proper care and emergency process of tracheostomy tubes to ensure patient safety.

Pre-intervention data (Pre-Test) was collected to determine the baseline knowledge the staff had in regards to tracheostomy care. An educational platform was then produced. Several in-services were provided by a respiratory therapist regarding tracheostomy tubes and tracheostomy care. Post interventional data (Post-Test) was conducted to
determine if the educational platform was effective in educating the staff. Pre and post test results will be reviewed to see if there will be significant in staff knowledge at the in-service.

Results: Pre-Test results identified knowledge deficits in the following areas: only 3 out of 41 knew how many seconds you can suction a tracheostomy, 19 out of 41 knew how many seconds you should let the patient recover before suctioning again, 8 out of 41 knew what to do if tracheostomy becomes dislodged, 16 out of 41 knew what solution is used for tube care, 14 out of 41 knew that tracheostomy care requires sterile technique, 6 out of 41 knew the differences in types of tracheostomies. After the tracheostomy in-service was implemented, a post-survey was completed in which 41 staff participated.

Results showed all 41 knew how to provide safe tracheostomy care.

Conclusions: This project has significant implications in supporting education and knowledge skill set pertaining to tracheostomy care. Staff must have knowledge on how to care for patients with tracheostomies. Utilizing the most current evidence and preparing an effective in-service significantly increased the staff’s knowledge and confidence with caring for tracheostomy tubes. Continuous education and in-services will be provided to sustain tracheostomy knowledge. A tracheostomy care reference was completed and is available on the unit.
Pre-Operative ChlorhexidineGluconate (CHG) Skin Preparation: A Literature Review

2LT Ross Scallan, BSN, RN; 1LT Stephanie Gerathy, BSN, RN; 2LT Frine Santiago, BSN, RN; 2LT Zane Amrein, BSN, RN; 1LT Kayla Ellmann, BSN, RN; Joyce Price, LVN; SGT Jacob Hetterley; Ann Marie Lazarus, MSN, RN, CNS

Department and Institutional Affiliation: Brooke Army Medical Center, Surgical Telemetry Unit

Focus Areas/Learning Tracks: Inpatient/Outpatient Care Presentation Format:

Poster presentation

Description of the Problem: On a surgical telemetry unit, no standardized preoperative skin preparation exists. Given a higher than expected rate of surgical site infections (SSIs), a team of nurses sought an evidence-based solution.

Objective: Review of the literature to examine the existing evidence and clinical practice guidelines related to the following question: In surgical patients, does bathing with chlorhexidine gluconate (CHG) scrub decrease incidence of SSIs?

Background: Nationally, SSIs are associated with an additional 406,730 hospital days and hospital costs exceeding $900 million (de Lissovoy, 2009). CDC guidelines recommend using a preoperative antiseptic shower or bath to decrease skin microbial colony counts (CDC, 2016). In 2015 our unit had the highest rate of SSIs among the Medical Surgical units at Brooke Army Medical Center (BAMC).

Materials and Methods: We searched Cochrane, CINAHL and PubMed databases with the following key terms: presurgical skin preparation, chlorhexidine skin preparation, surgical site infection prevention and hospital acquired infections.

Results: The review identified five articles, with mixed findings. One systematic review revealed preoperative CHG showers reduce SSIs; however the recommended frequency was inconclusive (Jakobsson et al, 2010). A meta-analysis comparing the use of CHG with providone-iodine for preoperative skin antisepsis supported CHG as more effective (Lee et al, 2010). Three randomized control trials (RCTs) examining use of CHG were examined, with the following findings: (a) CHG 4% bathing was significantly more effective than soap in reducing colony-forming units (Tanner et al, 2012): (b) use of a 2% CHG cloth before shoulder surgery is more efficacious than soap and water at decreasing cutaneous pathogenic bacteria (Murray et al, 2011): (c) CHG 4% pre-operative showers are efficacious in destroying surgical wound pathogens (Edmiston et al, 2015).
Conclusions: We recommend standardizing skin preparation for preoperative patients through use of a pre-surgery cleansing instruction checklist, a step-by-step protocol, staff education and documentation through a "Nurse Initiated Order" within the electronic medical record. Implementation of a standardized skin preparation method is expected to reduce the incidence of SSIs, leading to a decrease in length of stay and improving patient outcomes for patients on a surgical telemetry unit within a military treatment facility.

Keywords: Surgical site infections, chlorhexidine gluconate, preoperative patients, skin preparation

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Air Force, the Department of the Army or the Department of Defense or the U.S. Government.
Poster #38

NOISE REDUCTION ON AN INPATIENT SURGICAL NURSING UNIT TO PROMOTE HEALTHY SLEEP HYGIENE

1LT Candice Catlett, RN; Capt Angel Nwankwo, RN; 1LT Tina Mask, RN; 1LT Liai Vassar, RN; A1C Chayanin Noramuttha, Medical Technician; Mrs. Stephanie James, LVN; Mrs. Ann Marie Lazarus, CNS

Department and Institutional Affiliation: Brooke Army Medical Center, Orthopedic Trauma Unit

Focus Areas/Learning Tracks: Inpatient/Outpatient Care Presentation Format:

Poster presentation

Description of the Project: Current evidence has demonstrated that sleep deprivation is detrimental to the health and well-being, as well as having physical, behavioral and psychological consequences for hospitalized patients. Based on the TRICARE Inpatient Satisfaction Survey (TRISS) and our internal patient satisfaction surveys, patients on our Orthopedic Trauma Unit at Brooke Army Medical Center reported decreased satisfaction with the amount of noise during the night on the ward.

Background: Evidence has shown that sleep is necessary for physiologic restoration and maintaining cognitive and emotional well-being. Noise can alter the treatment care pathway for patients. Noise reduction programs that take a whole system approach, specifically staff education, environmental control and organization of care has demonstrated positively on patient satisfaction and patient healing.

Materials and Methods: Using the IOWA model, a focused question was developed and literature review was completed. A noise survey was developed and distributed from October 15 to November 30, 2016. Patients reported decreased satisfaction with noise levels at night; strongly correlating with the TRISS results. Staff were in-serviced on the effects of noise and the benefits of a noise reduction program for patient healing and behavior modification. Environmental controls, organization of care techniques and "Quiet Kits" were implemented. Visual indicators were displayed on the ward to remind staff, patients and visitors to consider their voice levels at night. Post-noise reduction surveys were collected after the noise reduction program was implemented.

Results: During the time frame of October 15, 2016 to November 30, 2016, 85 patients on 4 West participated in a pre-noise survey to identify level of satisfaction regarding noise at night. Results indicated that 47 patients were unsatisfied with noise levels at night, 40 were awakened by staff conversation, 45 reported that brown lighting was used not used by staff and 46 wanted the staff to be quieter during the night. After the noise
reduction program was implemented, a post-survey was collected from 1 December, 2016 to 15 January 2017 in which 65 patients participated. Results indicated that only 10 patients were unsatisfied with noise levels at night while 52 were satisfied, 6 were awakened by staff conversation while 55 were not, 3 said low lighting was not used by staff while 60 said low lighting was used and 6 wanted the staff quieter during the night while 55 were satisfied. The post-survey results showed increased satisfaction with noise reduction. The noise reduction program and "Quiet Kits" were a success to promoting healthy sleep hygiene and will be continued to be used.

Conclusions: This project has significant implications in supporting implementation of a whole system approach to noise reduction. A noise reduction program has demonstrated that implementing changes enhances the patient experience. Creating a culture of quiet contributes to peaceful, healing and conductive environment that enhances the wellbeing of patients as well as increased patient satisfaction and anxiety. We will also follow up on our TRISS to see if patient satisfaction has improved.

Keywords: Noise reduction, sleep hygiene; night, noise survey

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Air Force, the Department of the Army or the Department of Defense or the U.S. Government.
AN EVALUATION OF NAVY EN ROUTE CARE TRAINING USING A HIGH-FIDELITY MEDICAL SIMULATION SCENARIO OF INTERFACILITY PATIENT TRANSPORT

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5. Navy Medicine Training Support Center, San Antonio, TX

OBJECTIVE: Our study objective was to evaluate and compare performance between SMTs and Navy Nurses in a high-fidelity patient transport simulation scenario.

BACKGROUND: Military pre-hospital and en route care (ERC) impacts patient outcomes. Provider knowledge and skills are critical variables in the effectiveness of care delivered. Simulation technology facilitates a standardized patient encounter to enable complete, prospective data collection while studying the effect of an independent variable; i.e. provider type.

METHODS: A prospective, multi-site, observational study using high fidelity simulation was conducted. Participants completed an ERC scenario caring for a post-operative patient (Laerdal SimMan® fitted with intravenous arm and amputated leg) from collection at a Role II facility through transport in a simulated 20 minute MH-60 “flight,” to hand-off at a Role III facility. Participants were equipped with standardized ERC equipment, medications, and supplies. Blinded expert evaluators observed participant performance. Specific in-flight knowledge and skills evaluated included identification and treatment of both extremity hemorrhage and tension pneumothorax. Completion of task (yes/no), and action performed correctly (yes/no) were recorded by two evaluators with discordant observations reviewed by a third evaluator using recorded audio-visual files. Data were analyzed and compared by provider type. Chi-square or Fischer’s Exact tests were performed and results were reported as percentages.

RESULTS: Participants included 30 nurses and 29 SMTs. At least one intervention was performed by 100% nurses and 93% SMTs (p=0.09). Tourniquet application was performed by 60% of nurses and 72% of SMTs (p=0.31). Of those, 39% of nurses and 86% of SMTs applied the tourniquet correctly (p=0.003). Blood administration was attempted by 79% of nurses and 17% of SMTs (p<0.0001). Needle decompression was performed by 79% of nurses and 33% of SMTs (p<0.01). Of these, 87% of nurses and 67% of SMTs performed needle decompression correctly (p =0.34).

CONCLUSIONS: Based on our findings, we recommend significant improvements to the training pathways for both SMTs and Navy Nurses if they are expected to independently perform critical care patient transport missions.

Funding Support: JPC 6 - Forward Surgical, En-route and Critical Care CITS Combat Casualty Care Research
Metastatic hypermucoviscous *Klebsiella pneumoniae* infection in a young active duty male.

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Introduction: *Klebsiella pneumoniae* has become the most common cause of pyogenic liver abscess in Asian countries, Europe and the United States. Virulence is associated with the capsular (K) types K1 and K2 which predispose to the hypermucoviscous phenotype. These hypermucoviscous phenotypes are more often associated with cryptogenic abscesses in middle aged diabetic males and cause invasive syndromes including metastatic meningitis, pleural empyema and endopthalmitis.

Case Report: A 24 year old Active Duty Navy technical school student was admitted with hepatic abscess and evidence of multi-organ hematogenous embolization. He had been treated as an outpatient for two weeks of abdominal pain, nausea, vomiting, cough, and chest pain. Chest x-ray was normal but he was noted to be febrile with an elevated white blood cell count. He then developed eye irritation and was diagnosed with left eye panuveitis and retinal detachment. CT chest was ordered by outpatient ophthalmologist and showed a large, loculated cystic liver mass as well as multifocal lung and kidney septic emboli. He was admitted to the Internal Medicine service and started on broad spectrum antibiotics. Ophthalmology was consulted for management of endophthalmitis. The patient underwent vitrectomy, phacoemulsification and intravitreal antibiotics. Blood, urine, and vitreous cultures were positive for *K. pneumoniae*. Antibiotic coverage was narrowed to ceftriaxone dosed for central nervous system penetration. The liver abscess was drained and was culture positive for *K. pneumoniae*. The string test of bacterial colonies confirmed the hypermucoviscous phenotype. The patient was re-admitted one week after discharge with worsening headache; on MRI several multifocal rim enhancing lesions throughout the cerebral hemispheres were visualized consistent with hematogenous abscesses. Therapy with IV ceftriaxone was continued.

Discussion: This case illustrates an increasingly common presentation of hypermucoviscous *K. pneumoniae* infection in an atypical, healthy host. K1 and K2 serotypes represent a majority of liver abscess serotypes, are typically cryptogenic and represent a 10% to 45% association with metastatic meningitis and endopthalmitis. Clinicians should be aware of the potential for metastatic complications in patients with *K. pneumoniae* liver abscess.
Prevention of Ischemic-Reperfusion Injury and Chronic Rejection in a Porcine Vascularized Composite Allotransplantation Model

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Aim

Modern body armor, rapid evacuation, and advanced combat casualty care have improved survival after catastrophic extremity and maxillofacial trauma. Restoration using vascularized composite allotransplantation (VCA) is superior to conventional reconstruction in such injuries but requires immunosuppression and long-term outcomes suffer due to chronic rejection (CR). An approach that can improve the functional outcome, reduce immunosuppression load and minimize or eliminate CR would have a substantial impact on VCA and increase the number of war fighters who benefit. To mitigate obligate reperfusion injury and subsequently CR in VCA, we evaluate the efficacy of ex vivo tissue preservation using a novel machine preservation (MP)/hemoglobin oxygen carrier (HBOC) for 17 hours; a total ischemic time of 18 hours.

Methods

A proven porcine myocutaneous heterotopic transplant flap model was performed. Control flaps (n=24) underwent CSP at 4ºC with University of Wisconsin (UW) solution for 3 hours prior to transplant. Experimental group (n=24) flaps were perfused with MP/HBOC for 17 hours at a subnormothermic temperature of 21ºC. Flaps were monitored daily for clinical evidence of viability and biopsied per protocol with an end point of either 17 hours for ex vivo only, 14 days for autotransplants and 60 days for allotransplants. The allotransplanted animals were placed on systemic triple immune suppression and maintained at therapeutic levels for the duration of the study. Histologic analysis was blinded and reviewed by an expert veterinarian pathologist at the conclusion of the study.

Results

Twenty-four porcine myocutaneous flaps are designated to experimental groups, and 24 to the control group. We anticipate results will be similar to our groups previous porcine myocutaneous flaps exposed to 14 hours of CSP (n=4) or MP/HBOC (n=4). Results indicated significantly attenuated markers of IRI, significant apoptosis on TUNEL staining, and endothelial damage in the CSP group when compared to subnormothermic MP/HBOC.

Conclusion

If VCA can be preserved for up to 18 hours or more and be protected from ischemic damage and CR following allotransplantation in the porcine model, then this achievement will have a profound clinical application in VCA as well as solid organ transplantation. Based on the promising preliminary data, we believe efficient tissue oxygenation promoted by subnormothermic (21ºC) MP/HBOC in VCA could (1) extend graft preservation times and improve donor access across geographic spans, (2) enable increased
efficacy of ex-vivo targeted graft manipulation and (3) ensure graft quality and tissue viability prior to VCA transplantation.
RESUSCITATION WITH ORAL REHYDRATION SALTS IMPROVES MOD BIOMarkers IN A PIG BURN MODEL

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DCR, US Army Institute of Surgical Research, Fort Sam Houston, Texas

Background: Severe thermal injuries of greater than 20% total body surface area (TBSA) results in complications such as multiple organ dysfunction (MOD). Resuscitation protocols recommend IV infusion of fluids to maintain organ perfusion however, in austere environments where IV fluid is unavailable oral fluids may be sufficient. Information on the optimal strategy for oral resuscitation is currently lacking. The present study investigated the effects of oral resuscitation with water and oral rehydration salts (ORS) on kidney and liver dysfunction in an established porcine 40% TBSA burn model.

Materials & Methods: Anesthetized Yorkshire pigs sustained 40% TBSA full-thickness contact burns with brass probes heated to 100°C placed in contact with the skin for 30 seconds. Animals were allowed to recover in metabolic cages and randomized to one of three groups: no water access (n=7), ad libitum water access (n=6), or 70 mL/kg/d ORS (n=6) for 48 h. Urine and blood were collected at baseline (BL), 6, 12, 24, 32, and 48 h post-burn for quantification of biochemical markers. After euthanasia, kidney and liver samples were collected for Western blot, multiplex immunoassay, and histopathology.

Results: Urinary and plasma creatinine increased by ~26.8 mg/dL and ~0.6 mg/dL, respectively in all animals. Total bilirubin and liver enzymes alanine and aspartate aminotransferases were also elevated by 6 h post burn regardless of treatment. However, at 48 h plasma creatinine and aminotransferases were reduced to BL levels only in animals receiving ORS or water (p<0.05). Similarly in the plasma, blood urea nitrogen spiked at 6 h and was reduced with oral fluids by 48 h (p<0.01) compared to water-deprivation. Histopathology revealed perivascular edema in all livers, and glomerular nephritis accompanied by tubular atrophy to varying degrees. In the kidney, Western blot demonstrated total NFκB was reduced in water restricted animals, and expression was greatest in animals receiving ORS. In the liver, preliminary multiplex data suggests that the phosphorylated/total ratios (i.e., activation) of both ERK and STAT3 was greatest in water restricted animals (0.19 and 0.52, respectively; n=2) compared to ORS (0.09 and 0.39, respectively; n=3) and ad libitum access animals (0.10 and 0.32, respectively; n=4). Moreover, the ratio of STAT5 phosphorylation was greatest in animals receiving ORS (0.55) compared to water (0.34) and water restriction (0.30).

Conclusions: This study demonstrates that oral resuscitation with 70 ml/kg/d of ORS or ad libitum water access alleviates MOD after thermal injury in the absence of IV resuscitation. Additionally, results support the use of oral resuscitation efforts in burn casualties in prolonged field care scenarios. Future work will focus on different volumes and solutions for oral resuscitation, and further delineate the mechanistic basis of their therapeutic effect.
Role of Acinetobacter baumannii thioredoxin in bacterial translocation by modulation of mucosal oxidative homeostasis

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Despite medical advances, sepsis remains an increasing cause of death in hospitalized patients in the United States. Mortality rates from sepsis range between 30-80% depending on the severity of the disease and those that survive often have long lasting effects on their health. Acinetobacter baumannii is an increasing cause of hospital-acquired infections including pulmonary infections, urinary tract infections, and sepsis. Since 35% of sepsis cases originated from a pulmonary infection, our lab has created a pulmonary model of Acinetobacter baumannii infection that leads to sepsis and death in C57BL/6 mice. This model is dependent on the induction of host oxidative stress induced through supplementary lipopolysaccharide injection. Hospitalized patients are often in states of oxidative stress due to trauma, surgery, or secondary infection. Specifically, LPS induced oxidative stress has a significant impact on mucosal barrier function, leading to enhanced permeability and bacterial translocation. Using this model, our lab has begun to delineate the importance of the bacterial factor thioredoxin in A. baumannii translocation. Thioredoxin-1 (Trx1/TrxA) is a member of the thioredoxin protein superfamily that can be reversibly oxidized and reduced to facilitate reduction of disulfide bonds, as well as for protecting against free-radical damage. Our lab has created a mutant of A. baumannii Clinical isolate 79 (Ci79) that lacks thioredoxin-1 (ΔTrxA). Mice undergoing oxidative stress showed significantly increased translocation of Ci79 via organ burden compared to ΔTrxA. Additionally, when Ci79 is treated with an irreversible thioredoxin blocker (PX-12) before challenge, mice showed an organ burden comparable to that of mice challenged with ΔTrxA. Concordantly, mice which were challenged with the PX-12 treated Ci79 showed significantly increased survival compared to those which receiving Ci79 alone during oxidative stress conditions. This data shows that thioredoxin is playing a vital role in bacterial translocation and virulence. Further research in our lab will focus on the determining the mechanism by which thioredoxin assists in translocation.

Funding: This work was supported by funding from the UTSA Center for Excellence in Infection Genomics training grant (DOD #W911NF-11-1-0136) and the NIH (AI12402)
Athletic Trainer Integration in U.S. Air Force Basic Training

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Background
As the leading contributor to missed military training time and medical attrition from training, musculoskeletal injuries significantly affect operational readiness. Reducing injury morbidity among military recruits could minimize disruptions in the training pipeline, decrease the associated costs, and improve the health and fitness of individuals entering the armed forces. This project was designed to evaluate the operational and cost impact of embedding certified athletic trainers (ATCs) in a U.S. Air Force training squadron.

Methods
An athletic training room staffed by two ATCs was opened near the end of 2015 in the 323 Training Squadron of U.S. Air Force Basic Military Training, Joint Base San Antonio-Lackland, Texas. Musculoskeletal and overall attrition rates, on-time graduation rate, failure rate for final physical fitness assessment, healthcare utilization for injury, stress fracture rates, and per capita injury-related costs were calculated for the intervention squadron and compared to two control squadrons without access to ATCs. This population-based intervention trial profited from extant random allocation of recruits into the three squadrons. Preliminary analyses for the first twelve months of the program (January 1, 2016 through December 31, 2016) were conducted for this abstract.

Results
A total of 7,619 recruits accrued 409,340 trainee-days in the intervention squadron, compared to 11,695 recruits and 634,363 trainee-days in the control squadrons.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention</th>
<th>Control Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal Attrition</td>
<td>1.0%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Overall Attrition</td>
<td>5.4%</td>
<td>6.8%</td>
</tr>
<tr>
<td>On-Time Graduation Rate</td>
<td>88.0%</td>
<td>87.4%</td>
</tr>
<tr>
<td>Fitness Failures</td>
<td>1.5%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Physical/Occ Therapy Rate</td>
<td>9.15</td>
<td>24.2</td>
</tr>
<tr>
<td>Orthopedic Clinic Rate*</td>
<td>0.77</td>
<td>1.37</td>
</tr>
<tr>
<td>Stress Fracture Rate*</td>
<td>2.42</td>
<td>2.87</td>
</tr>
</tbody>
</table>

*Per 1000 training-weeks

The decrease in musculoskeletal attrition garnered a cost saving of $919K, and the decrease utilization of healthcare for musculoskeletal injuries saved $148K of medical costs and 7900 training hours.
Conclusions
Embedded ATCs in U.S. Air Force Basic Military Training significantly reduce out-of-squadron clinical appointments, associated medical costs, and overall attrition. Stress fracture rates and attrition specific to musculoskeletal injury trend towards significance. This program is early in its implementation and analysis should continue to delineate the longitudinal impact of ATCs in a military training environment.

Disclosures
This project is funded by a Clinical Research Initiative grant from the Congressional Directed Medical Research Program (award #DM140461). The opinions expressed here are solely those of the authors and do not represent an endorsement by or the views of the U.S. Air Force, the Uniformed Services University, the Department of Defense, or the U.S. Government.
IMPACT OF THE FIREARMS TRAINING SYSTEM (FATS) ON OCCUPATIONAL PERFORMANCE IN A POLYTRAUMA POPULATION

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Kathleen E. Yancosek, PhD, OTR/L, CHT, LTC, SP, USA, Director, Center for the Intrepid (CFI)

**Background:** The military and the Department of Defense (DoD) have a vested interest in maximizing injured service members (SM’s) occupational performance, function, and quality of life for return to duty (RTD). Rehabilitation to regain independence for RTD in a real-world environment may not always be possible due to safety concerns. Virtual reality (VR) has the benefit of providing real world complexity in rehabilitation without the associated risks. Marksmanship is a key military skill, one which is considered pertinent to military service. The DoD has also placed high value and interest on the potential use of VR training environments. This research aims to evaluate the impact of the Firearms Training System (FATS) on military weapons performance, specifically shot grouping, of injured SM’s.

**Methods:** A retrospective chart review of patients with polytrauma who received FATS training at the Center for the Intrepid (CFI) will evaluate how FATS training impacts the occupational performance of rifle marksmanship. It is hypothesized that FATS training will improve occupational performance as seen in the decrease of shot group size measured in centimeters.

**Results:** Data collection and recruitment into this study is ongoing.

**Discussion:** Improved shot grouping is believed to lead to higher qualification rates. The ability of an injured SM to qualify on small arms weapons systems is one occupational performance metric that may influence a SM’s ability to RTD.

**Conclusions:** Injured SMs, specifically polytrauma injuries, represent a unique rehabilitation population. If FATS training in this population is found to be effective, this study may pave the way for the use of the FATS for RTD decision, in the medical evaluation board (MEB) process, and on a grander scale in rehabilitation specifically occupational therapy. Completion of the study is needed for full data analysis and determination of predicting factors.

There is no funding for this research at this time.

**Keywords:** Polytrauma, Occupational Performance, Military, Return to Duty

**Track & Category:** Technology and Innovation in Healthcare, Poster presentation
THE DYNAMICS OF RISK: PRIOR CHANGES IN PSYCHOLOGICAL INFLEXIBILITY PREDICT SUBSEQUENT CHANGES IN POSTTRAUMATIC STRESS SEVERITY

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Background: According to Bond et al. (2011), psychological inflexibility is characterized by the “rigid dominance of psychological reactions over chosen values and contingencies in guiding actions” (p. 682). As a malleable risk factor, psychological inflexibility is heavily implicated in the etiology of posttraumatic stress symptoms, even accounting for other known predictors (Meyer et al., 2013; Kampula & Varkovitz, 2011; Bryan et al., 2015). While prior research demonstrates psychological inflexibility temporally precedes posttraumatic stress symptoms, the dynamic relationship between the two variables remains unexplored. For example, it is unclear if changes in psychological inflexibility and posttraumatic stress have reciprocal within-person effects on their mutual developmental trajectories.

In the current study, we evaluate the temporal dynamics characterizing the relationship between psychological inflexibility and posttraumatic stress by examining whether longitudinal changes in posttraumatic stress symptom severity are determined not just by initial levels of psychological inflexibility (i.e., degree of inflexibility) as found in previous studies, but also by recent changes in psychological inflexibility (i.e. increases or decreases in inflexibility).

Methods: Participants were 285 combat veterans who served in Iraq and Afghanistan and were enrolled in a larger longitudinal study (N=309). Of the full sample, 24 veterans were excluded from the present analysis because they reported no previous combat exposure. The majority served in the army (85%), were male (67%), and Caucasian (57%) or African American (33%). Veterans completed self-report measures of psychological inflexibility (AAQ-II, Bond et al., 2011) and military-related posttraumatic stress symptom severity (PCL – M, Weathers et al., 1991) at baseline, 4 months, 8 months, and annual follow-up. To examine the dynamic relationship between psychological inflexibility and posttraumatic stress symptoms, we used an extension of the Bivariate Latent Difference Score (LDS) modeling approach, which tests whether prior within-person changes in one variable precede subsequent changes in another variable (Grimm, 2012). The Bivariate Latent Difference Score modeling approach combines features of latent growth curve and cross-lagged regression models to examine both bivariate inter-correlations and growth in change over time (Ferrer et al., 2003).

Results: We tested a series of nested latent difference models examining both the unidirectional and bidirectional impact of initial levels and prior changes in both posttraumatic stress symptom severity and psychological inflexibility on subsequent changes in psychological inflexibility and posttraumatic stress symptom severity. A positive, unidirectional effect was observed for changes in psychological inflexibility on changes in posttraumatic stress severity. Specifically, if psychological inflexibility recently decreased, the model predicts proportional declines in posttraumatic symptom severity during the subsequent follow-up period.

Conclusion: These results demonstrate the importance of estimating the effects of previous change on subsequent changes between variables, as prior declines in psychological inflexibility may be more clinically meaningful than a lower initial state of psychological inflexibility in predicting the developmental trajectory of posttraumatic stress symptom severity. These results have implications for
clinical intervention, and may provide a useful model of dynamical change in posttraumatic stress symptoms predicted by psychological inflexibility over time.

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FALL PREVENTION ON A MEDICAL-SURGICAL UNIT

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Abstract: Falls during hospitalizations are a safety concern, resulting in increased length and cost of hospital stay. Retrospective reviews of the Patient Safety Reporting system and Falls Response Team indicated that the number of falls on a busy 26-bed medical-surgical unit doubled from 2015 to 2016. In 2016, the unit had 12 falls and averaged 3.22 falls per 1,000 hospital days. After reviewing literature and the most current clinical practice guidelines, current evidence suggests that patient-staff safety contracts, in combination with implementation of clinical practice guidelines, can successfully increase patient adherence to fall prevention measures and could reduce the number of inpatient falls. This project aims to increase patient education about falls risk and prevention, which will contribute to a reduction in the fall rate on a 26-bed medical-surgical unit.

A retrospective review of fall reports and fall prevention audits were used to obtain baseline data. After baseline data was obtained, the staff was educated on the multicomponent fall prevention program and the safety contract. The program consists of 1) early assessment of the patient’s fall risk using the Johns Hopkins Fall Assessment Scale, 2) patient and family education on the factors contributing to the patient’s fall risk during the assessment, 3) an educational handout on fall risk factors, 4) implementation of previously existing fall prevention measures (bed at lowest level, non-skid socks, falling star on door, yellow socks and bed alarms for high fall risk patients, etc) and 5) a safety contract. Upon admission to the unit, the Registered Nurse will review the patient’s falls risk factors and present the patient with the educational handout and safety contract. The safety contract serves as an additional teaching strategy for fall prevention as well as an agreement between patient and staff that will promote safety. By signing the contract the patient / family are stating that they understand the education provided. Signing the contract will not be mandatory for patients; however, it does ensure that a fall prevention discussion occurs in a structured fashion. In addition to the contract, staff is encouraged to continue to use the fall prevention measures that correspond with their patients’ falls risk, update the patient board and falls wheel in the room, and continue to re-enforce teaching about falls risk during each nursing assessment. After implementation of the project, data from the Patient
Reporting System and Fall Response Team, will be collected and compared to the baseline data. Currently the project is on-going and completed results are expected at the end of May.

**Keywords:** falls, patient education, patient safety

**Focus Areas/Learning Tracks:** Patient Safety

**Presentation Format:** Poster Presentation

**References:**


**Disclaimer:** The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Air Force, the Department of the Army or the Department of Defense or the U.S. Government.
PERCEPTIONS OF LOW BACK PAIN TREATMENT FOR INITIAL ENTRY TRAINING SOLDIERS: A MIXED METHODS STUDY

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Background: Low back pain (LBP) is one of the leading causes of disability in the United States, accruing billions of dollars in healthcare and work-related costs. It has been well-established that psychological and social aspects play as significant a role as the physical aspects in determining prognosis. These psychosocial factors, termed “yellow flags,” have been able to predict cases of LBP that develop into a chronic condition. These yellow flags include depression, anxiety, fear-avoidance behaviors, and pain catastrophizing. Psychoeducational programs involving components of cognitive-behavioral therapy have been found to be beneficial in improving prognosis for LBP. To date, no studies have investigated the qualitative aspects of LBP experienced by Active Duty Service Members (ADSM) in training, which could improve future educational programs. This study aims to (1) assess the effectiveness of a multidisciplinary treatment program involving occupational and physical therapy on pain, function, and psychosocial symptoms and (2) gain an in-depth understanding of the experience of LBP while in training.

Methods: This was a mixed methods study involving ADSM trainees who participated in a self-management treatment program for LBP. All recruitment took place from one clinic located on Fort Sam Houston, TX. Quantitative data was gathered using the Oswestry Disability Index, STarT Back Screening Tool, Pain Catastrophizing Scale, PROMIS-29 (v2), and the Canadian Occupational Performance Measure at baseline and a six-week follow-up. Following treatment completion, subjects completed a qualitative interview investigating the experience of LBP as a trainee and their perceptions of the treatment received.

Results: Quantitative results reveal relatively low levels of disability, pain, and psychosocial factors at baseline and six-week follow-up assessments. Qualitative data revealed that the tools and exercises provided during the multidisciplinary self-management intervention were effective in allowing subjects to manage their LBP and complete their duties as a trainee. Subjects identified lack of time, support from cadre and unit members, and fears of not completing training as barriers to seeking treatment and completing home exercise recommendations regularly.

Conclusions: ADSM trainees may not exhibit high prevalence of disability, pain, and psychosocial symptoms that predict poor prognosis. However, these subjects may face additional barriers in completing treatment that may not be experienced by civilian counterparts. Completion of this study is needed for full data analysis and results.
RETROSPECTIVE EVALUATION OF PRE-INJURY STATIN USE AND POST-INJURY THROMBOEMBOLIC EVENTS IN ACUTE TRAUMA

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Background: Traumatic injury is well-known to increase the risk of venous thromboembolic events (VTE), shown to occur in up to 58% of trauma patients [1-4]. Current therapies to reduce the risk of thromboembolic events and to treat their occurrence are not benign. Statin medications have significant anti-inflammatory properties and have been shown to reduce the risk of VTE [5-9]. We hypothesized that trauma patients who received statin medication prior to injury would have a lower incidence of VTE post injury.

Materials & Methods: A ten year retrospective review identified all patients admitted to our trauma service with an injury severity score (ISS) >9 and an ICU stay of >3 days. Electronic medical records were queried to identify patients based on the medication administration record. This population was categorized as either “statin recipient” (SR) or “statin naïve” (SN), with subsequent categorical division by occurrence of VTE. The following variables were collected and used as comparisons: age, gender, body mass index (BMI) and presenting ISS, along with intensive care unit length of stay (ICU LOS), ventilator days, central venous line (CVL) and inferior vena cava filter (IVCF) placement as well as time to VTE diagnosis. Our primary outcome measure was the occurrence of documented VTE in both SN and SR subjects.

Results: 2519 trauma patients with a mean age of 51.0 (±21.9) years, a mean ICU LOS of 9.6 (3-246) days and a mean ISS of 22.3 (±10.1) were included. 97 (3.8%) developed VTE: 65 (2.6%) with deep vein thrombosis (DVT) and 38 (1.5%) with pulmonary embolism (PE). Risk factors for VTE with a p<0.01 on univariate analysis included: Pre-trauma statin use, age, gender, BMI, CVL, IVCF, ICU LOS, Hospital LOS and Ventilator days. Following logistic regression only pre-trauma statin use in males remained as an independent predictor of VTE (OR = 2.25, 95% CI = (1.25, 4.04), p<0.01). Additionally the median time to VTE onset is found to be three days longer in statin recipients 10.0 (CI 7.3, 12.7) vs. 7.0 (CI 5.6, 8.4) p<0.05.

Conclusions: Pre-trauma statin use does not appear to have a protective benefit of VTE prevention in trauma patients, as we have shown pre-trauma SR male trauma patients to have a twofold increased incidence of VTE. However, when considering the three day longer median time to VTE onset found in SR’s, we consider the protective benefit of statin use reported in the current literature as likely attributable to this observed delayed onset. Future prospective research investigating whether this impact on VTE is a class effect of statins, if it is dose or potency-related, and if normolipidemic trauma patients derive a greater protective benefit deserve further attention.

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Army or the Department of Defense or the U.S. Government. This study was conducted under a protocol reviewed and approved by the Brooke Army Medical Center Review Board, and in accordance with the approved protocol. There are no conflicts of interest to disclose.

A MULTI-MEDIA MOBILE MEDICAL APPLICATION TO SUPPORT FRESH WHOLE BLOOD TRANSFUSION

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BACKGROUND: Optimal combat casualty care is dependent on the knowledge and skill of medics. Nuances of critical, complex, or high-risk interventions may be lost without sustained education and training. We describe evaluation of a mobile medical application platform that can facilitate knowledge and skill acquisition, retention, and evaluation.

IDENTIFICATION OF THE PROBLEM: Fresh whole blood is the pre-hospital resuscitation fluid of choice. There is a need to streamline complex guidelines into interactive, algorithmic multi-media applications.

PURPOSE OF THE STUDY: Determine if the guideVue™ mobile app is an appropriate platform for teaching and sustaining medical skills for military providers.

METHODS: A Fresh Whole Blood Transfusion (FWB TX) guideVue was developed based on current DoD guidelines. End-users were identified and data, including descriptive statistics, were collected on demographics, from a FWB TX 10 question quiz, and a System Usability Scale (SUS). Greater than 65 represents an acceptable SUS score.

RESULTS: A total of 30 SUS surveys were administered; 29 were completed with a mean score ± SD of 70.1 ± 19 (range 20-100). The 10 question quiz resulted in an average score of 63 ± 30% (range 25-100% correct per question) with 15 - 21 respondents per question.

DISCUSSION: The SUS surveys showed an acceptable score with feedback from users stating the application had useful information/content and was simple to use. Limitations included FWB TX guideVue was not intuitive without some instruction and that it is a complex procedure to place in an algorithm.

CONCLUSION: The use of a FWB TX guideVue seems to provide training benefits and knowledge achievement in a user-friendly, condensed version of extensive technical guidelines.

IMPLICATIONS FOR FUTURE RESEARCH: The guideVue system can support medical skill sustainment for perishable clinical and combat-related interventions in an austere environment. Future research will generate/update guideVues on TCCC/TCMC topics, burn care, and other clinical practice guidelines as well as optimize reporting features to track ongoing training and knowledge achievement.

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STATUS EPILEPTICUS: SIMULATION-BASED EDUCATION COMBINED WITH TRADITIONAL DIDACTIC CURRICULUM IN EARLY MEDICAL TRAINEES

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Background
Status epilepticus (SE) is a medical emergency that requires prompt assessment and decision-making to ensure optimal patient outcomes. Mortality rates for SE are estimated to be 19-26%, and up to 48% in cases of refractory SE. Early treatment and proper drug selection can improve these outcomes. Often, non-neurologists are the first to respond to patients with SE, and the number of SE cases varies significantly at training institutions, resulting in a variable degree of experience with its management. There is debate among neurologists whether simulation-based education confers additional benefit over traditional didactics and clinical experience. Recently, Braksick and colleagues published a paper in which critical care fellows underwent a 3-scenario neuro-critical care simulation course. They found that confidence and knowledge were significantly improved following the course. Here we designed a 2 simulation pilot course using the PARTS structure with pre- and post-assessments of confidence and knowledge.

Materials and Methods
Prior to simulations, participants completed 8-question confidence surveys scored on a 7-point Likert scale, as well as a 10-question multiple-choice knowledge assessment. Participants then received a one hour video lecture regarding the management of status epilepticus. The following day, they completed a status epilepticus simulation designed using the PARTS structure. Real-time rating was performed by a neurology resident and faculty. Upon completion, participants were immediately asked to rate their own perceived performance on the same checklist. Two weeks later, the participants completed a different simulation again designed using the PARTS framework. Following the 2nd simulation, participants then repeated the same confidence surveys and knowledge assessments. Quantitative statistical analysis was performed using t-test with two-tailed distribution. Qualitative feedback was gathered from the participants following the completion of the simulations.

Results
Overall, there were significant improvements in confidence and knowledge. Prior to the course, the average confidence of non-neurology trainees was 2.5 (out of a possible 7) versus 4.9 for the neurology trainees (p=0.03). Confidence increased by an average of 102% in the non-neurology trainees versus 7% in the neurology trainees (p=0.03). As a combined group, knowledge increased from 56% to 70% (p=0.03), but there was not a statistically significant difference between the groups. Participants’ performance was not significantly different between the two simulations, although this may be due to the more challenging nature of the second simulation.

Conclusions
In this pilot, simulation proved to be an effective means of enhancing learner confidence and knowledge, similar to results obtained by Braksick and colleagues. The data suggested that non-neurology trainees have as much, if not more, to gain from such a course, when compared to neurology trainees. While not a substitute for patient encounters, we feel simulation provides an effective educational experience. In the future, we hope to broaden our course to include other departments and potentially
open up to group simulations. Further investigation will be needed to determine whether improved clinical outcomes can be achieved as a result of simulation in neurology.
DEVELOPING CLINICAL LEADERS IN PRIMARY CARE: THE US AIR FORCE DIABETES CHAMPION COURSE


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BACKGROUND:
There are over 150K patients (active duty, family members, and retired) with diabetes treated in over 400 worldwide Military Health System (MHS) clinics. Endocrinologists are located at only 15 MHS medical centers; therefore, the majority of diabetes care is delivered in primary care clinics. The US Air Force Diabetes Center of Excellence, whose mission is to promote excellent diabetes care and prevention across the MHS, designed the 3-day Diabetes Champion Course (DCC) to develop primary care leaders to effectively deliver diabetes care. The DCC includes comprehensive diabetes education on guidelines, resources, and hands-on training in a team-based format of which there have been 9 iterations with about 400 participants. We hypothesized that the DCC improved participants’ knowledge, skills, and intention to change clinical practice.

METHODS:
At the last course with 94 participants, we conducted a 17-question pre- and post-course survey to assess the effect of the course.

RESULTS:
Knowledge based questions showed improvement in basic familiarity with insulin pumps (p<0.01), knowledge behaviors to prevent macrovascular complications (p<0.01), and knowledge of cost-effective methods of utilizing self-monitored blood glucose levels (p<0.01). The majority of providers (97%) reported acquiring new knowledge about initiating and titrating insulin despite 89.5% feeling confident prior to the course. Skills based questions showed improvement in ability to demonstrate glucose meters to patients (p<0.01) and ability to perform a comprehensive foot exam (p=0.01). Intention to change clinical practice was demonstrated by 87.8% of participants reported a need to revise current pre operative processes for patients with diabetes; participants’ likelihood to use online resources presented at the DCC significantly increased (p<0.01); and an improved concept of team-based care noted by an increase in perceived responsibility of technicians (p<0.01), nurses (p=0.01), and disease managers (p=0.02) to ensure a foot exam is performed.

CONCLUSIONS:
The DCC provides an effective way to communicate comprehensive diabetes guidelines to the primary care teams, while empowering Diabetes Champions strategically throughout the MHS. Knowledge, skills, and intention to change clinical practice increased through participation in this 3-day course. More follow up is needed to see the extent by which patient care may be positively affected.

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QUIKCLOT TM COMBAT GAUZE USE BY GROUND FORCES IN AFGHANISTAN

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Background
Hemorrhage is the leading cause of potentially preventable death on the battlefield. The military fielded QuikClot TM Combat Gauze (QCCG) in 2008 to replace previous generations of hemostatic products that had adverse side-effects. Civilian-based studies demonstrate success in hemorrhage control using QCCG in the prehospital environment. To the best of our knowledge, despite nearly a decade of use, there are no published data on use by United States (US) combatant forces.

Objective
We seek to describe the use of QCCG by ground forces in Afghanistan.

Methods
We obtained data from the Prehospital Trauma Registry (PHTR). Joint Trauma System personnel linked subjects to the DoD Trauma Registry (DODTR) for outcome data, when available, upon reaching a fixed-facility.

Data
Out of the 705 subjects in the PHTR during the project time period, 118 (16.7%) had documented use of QCCG. The majority of the subjects (69.5%) were Afghan partner forces. All were male. Lower extremities accounted for the most common (39.2%) anatomical site of application. QCCG administration achieved hemorrhage control in 88.3% of encounters with documented hemorrhage control status.

Conclusion
QCCG appears to have important use on the battlefield as a concomitant intervention for obtaining hemorrhage control. Hemorrhage control success was similar to that reported in other military and civilian settings.
CARDIOMYOCYTE MITOCHONDRIAL RESPIRATORY CAPACITY IN SEVERELY BURNED SWINE

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Background: Severe burn injury covering over 30% of the total body surface area (TBSA) results in chronic hypermetabolism characterized by increased cardiac output. Previous studies have shown severe burns induce cardiac dysfunction. However, mitochondrial function in cardiac muscle after severe burn injury is not fully understood. The purpose of this study is to determine mitochondrial respiratory capacity as a proxy of mitochondrial function in a severely burned pig model.

Materials & Methods: Anesthetized Yorkshire swine (n=3) sustained 40% TBSA full-thickness contact burns with brass probes heated to 100°C placed in contact with the skin for 30 seconds. Animals were allowed to recover in metabolic cages, and blood was collected at 6, 12, 24, 32, and 48 hours. After 48 hours, pigs were euthanized and 10–20 mg of heart tissue was collected from the left ventricle and immediately placed in ice-cold mitochondrial relaxation buffer. Samples were analyzed by high-resolution respirometry (Oroboros Instruments, Innsbruck, Austria). Mitochondrial substrates and inhibitors were added sequentially to determine mitochondrial function. After establishing the leak state, octanoyl-L-carnitine (1.5 mM), pyruvate (5mM), malate (2mM) and glutamate (10 mM) were added to induce uncoupled respiration supported by complex I of the electron transport chain (LeakCI). Saturating levels of ADP (5mM) were then added to determine maximal coupled respiration by complex I (PhosCI). Then 10 mM succinate was added to provide electrons via complex II, thus activating maximal oxidative phosphorylation capacity (Oxphos). Afterwards, addition of 5 μM oligomycin induced maximal uncoupled respiration (state 4o). Finally, FCCP, a protonophore, was added to determine maximal capacity of the electron transfer system (ETS). A non-burned pig served as the control. All values are represented as mean ± SEM.

Results: The heart rate of burned swine increased slightly from 122.7 bpm at baseline to 137.3 bpm 48 hours post-injury. Total creatinine kinase in burned animals increased from 668.3 ± 159.4 U/L at baseline to 5958.7 ± 786.7 U/L at 6 hours, and gradually declined (1356.3 ± 252.0 U/L) by 48 hours. Preliminary data suggests that cardiac mitochondrial respiratory capacity is lower than control heart in all respiratory states. Importantly, severe burn lowered Oxphos (73.12 ± 13.61 vs 192.10 pmol O2/mg/s) and ETS (89.69 ± 15.70 vs 254.97 pmol O2/mg/s) vs control. Additionally, the coupling control ratio (CCR: State 4o/Oxphos) represented ATP synthesis efficiency, and was higher in burned swine (33 ± 1%) than control (27%), suggesting that burn renders the heart less efficient at producing ATP with (67% of Oxphos coupled with ATP synthesis versus 73% in control heart).

Conclusions: For the first time, we were able to determine mitochondrial dysfunction in cardiac muscle by directly measuring mitochondrial respiration in a severely burned swine model. Our preliminary data suggests that severe burn injury may diminish mitochondrial respiratory capacity of the heart, thereby reducing ATP availability to cardiac muscle. This altered mitochondrial function may contribute to cardiac dysfunction following severe burns. Future studies hope to identify cardiac mitochondria as a therapeutic target to improve cardiac function in severe burn patients.
NOCTURNAL OXYGEN VARIABILITY IN HOME DWELLING HEART FAILURE PATIENTS

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Background: Heart failure patients experience a high burden of serious disease-related symptoms; many of which occur at night. Patients with heart failure have difficulty recognizing and responding to these symptoms. Clinicians’ knowledge of such exacerbations is essential for optimal management; yet, inconsistency and variety in tools for patient symptom collection is compounded by the inaccuracy and incompleteness of patient recall as a result of aging and heart failure disease. We hypothesize that patients with heart failure experience extreme night-to-night variability in blood oxygen saturation and heart rate over several nights.

Materials & Methods: This was a retrospective analysis of observational data collected between December 2014 and June 2015, to assess the electronic collection of physiologic and subjective state data by patients with heart failure at home overnight for six nights. Patients were included for consideration if they had a clinical diagnosis of heart failure, were between 21 and 90 years of age, able to operate study devices, and collected data for six consecutive nights. Recruitment, consenting and patient training for device use were conducted during routinely scheduled patient encounters. Patients measured heart rate and blood oxygen saturation using the Nonin WristOx2 model 3150 pulse oximeter, a wrist-worn, battery-operated device with onboard data storage and battery life sufficient to collect 48 hours of data at 1-second intervals when worn. Patients put the device on when going to bed, wore it continuously overnight, and took it off when they got up. The device-collected data were downloaded using device-specific software, cleaned using the R statistical language, and uploaded into the study’s MySQL database. Data were analyzed using R (version 3.3.2, https://www.R-project.org/).

Results: This sample included 26 patients diagnosed with heart failure age 69±12 years, with New York Heart Association (NYHA) functional classifications: Class I (7), Class II (14), and Class III (5). In this group, (10) patients had implantable cardiac devices, (1) was prescribed nocturnal oxygen therapy, and (7) were prescribed continuous positive airway pressure therapy. With desaturation defined as below a threshold of 92% for at least 5 seconds, 85% of patients experienced moderate or many frequency desaturations, and 73% of patients experienced intermediate or long duration desaturations. With threshold defined as below 85% for at least 5 seconds, 50% of patients experienced moderate or many frequency desaturations, and 54% of patients experienced intermediate or long duration desaturations. At desaturation threshold of 75% for at least 5 seconds, more than half of patients experienced at least one severe desaturation event.

Conclusion: Patients with heart failure are at high risk of oxygen desaturation overnight. The frequency and duration of desaturation decreases as the threshold is lowered, but most patients experience extreme desaturation events of 5 seconds or more weekly. Episodes of tachycardia tended to last longer and episodes of bradycardia tended to last shorter durations in this sample. Visually displaying datasets for each night side-by-side shows night-to-night variability. Clinicians need this information, which patients are less likely to report, to better inform clinical decision making.
Acknowledgement: The institutional review board (IRB) of affiliated university and institution for research approved this study, WRNMMC IRB Protocol number 400924-4. The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216_AFI40-402. All devices met Protected Health Information (PHI) and Personally Identifiable Information (PII) requirements. Support for this study was provided by Daniel K. Inouye Graduate School of Nursing, Uniformed Services University of the Health Sciences.

Disclaimer: The views expressed are those of the author/presenter and do not represent the official views or policy of the Department of Defense or its components.
COMPARISON OF TWO METHODS OF INDUCING TRAUMATIC CARDIAC ARREST IN SWINE

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Background:
Traumatic injury is the most common cause of death on the battlefield and for ages 1-44 in the USA. Many of these deaths are associated with catastrophic hemorrhage that eventually results in traumatic cardiac arrest (TCA). Unfortunately, the likelihood of survival using current techniques, including CPR, is very low. A large amount of research time and money is directed at stopping hemorrhage (REBOA, tourniquets, expanding foam, etc.) and investigations into better resuscitation fluids. However, studies examining effective methods of treating hemorrhage-induced TCA are minimal despite the great potential of increased survival. Here we examine two methods to achieve TCA in order to test novel methods of treatment.

Materials & Methods:
This study is a retrospective analysis of historical data performed in the last 12 months. In all procedures, adult human-sized (70-90 kg) Yorkshire-Landrace swine were anesthetized, instrumented, and their spleen removed. TCA was accomplished by either controlled hemorrhage alone or by a combination of laparoscopic liver injury and controlled hemorrhage. In either method, cardiac arrest was defined as having a systolic blood pressure under 10 mmHg for three minutes before intervention. Hemodynamic and blood gas values were compared between the controlled hemorrhage and the combination groups.

Results
A total of 28 animals were entered into the study with few differences between groups before injury. As expected, both methods saw statistically significant changes in most hemodynamic factors, lactate, potassium, pH, and glucose when comparing baseline to arrest measurements. Interestingly, the two methods resulted in significant differences at arrest including potassium, lactate, and cardiac output. Controlled hemorrhage alone was used successfully to show that CPR is more effective while an Abdominal Aortic and Junctional Tourniquet is applied, while the combination method was used successfully to show that selective aortic arch perfusion can revive an animal from TCA.

Conclusions
Both models are useful for answering scientific and physiologic questions regarding TCA. However, differences do exist between the two methods. Further experiments will need to be performed to fully elucidate the benefits in each model.

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INTRODUCTION

Trauma is a major cause of pediatric mortality and morbidity world-wide including combat zones. Imaging during combat operations presents unique challenges as moving equipment into the battlespace carries challenges not seen in developed countries. Moreover, military hospitals have a primary mission to serve the warfighters and are not primarily designed for the pediatric patient. Previous studies have described the unique injuries of the pediatric patient in this setting, there is a relative dearth of data on imaging practices.

METHODS

We queried the Department of Defense Trauma Registry (DODTR), a data repository for DoD trauma-related injuries, from 2007 to 2016 for all pediatric trauma subjects seen in the emergency department (ED) at fixed-facilities in Iraq and Afghanistan. We are seeking to describe the radiology utilization during those encounters. Subjects were divided into groups based on Centers for Disease Control groups: <1 year, 1-5 years, 5-9 years, 10-14 years, 15-17 years.

RESULTS

During the study period there were 3439 subjects with data available for search with a total of 12402 imaging studies performed from the ED. The most common age group was 10-14 years. The major were battle-related injuries resulting from explosives, shrapnel and gunshot wounds. The most common plain film performed was a chest x-ray. The most common computed tomography (CT) scans performed were non-angiogram studies of the head, chest and abdomen. The most common ultrasound performed was the focused assessment with sonography in trauma (FAST).

CONCLUSIONS

Pediatric imaging was a common procedure in the emergency department during the initial evaluation and resuscitation. Given the relatively common usage of CT and ultrasound studies mission planning should consider the needs for imaging of the pediatric trauma patient.
A COMPARISON OF SURGICAL AIRWAY TECHNIQUES IN A SYN-CADAVER: A RANDOMIZED CROSS-OVER STUDY

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DEREK BROWN, JESSIE RENEE FERNANDEZ AND STEVEN SCHAUER - US Army Institute of Surgical Research

Background

Cricothyrotomy is a lifesaving surgical airway procedure that must be rapidly performed before critical hypoxia occurs. In the fixed-facility setting it is often considered a last resort. Currently, Tactical Combat Casualty Care (TCCC) guidelines recommend its use as a primary airway to patients responding to basic airway maneuvers. Data from recent military conflicts reported cricothyrotomy in 5.8% of combat medic managed airways with a failure to cannulate rate as high as 33% and a 50% iatrogenic complication rate. Methods to improve the outcomes associated with this anxiety-provoking procedure are needed.

Methods

This IRB-approved study compared the QuickTrach-2™ versus the Cric-Key™ with the Cric-Knife™ versus the standard open cricothyrotomy in a randomized cross-over design. Volunteer army paramedic trainees performed each procedure on a synthetic cadaver necks (SynDaver™ Adult Cric Trainer). All trainees had prior experience with the standard open technique and were shown a standardized video demonstrating the procedure for each device. The primary outcome measure was time to cannulation of the airway and the secondary outcomes were number of attempts, and provider preference.

Results

Preliminary data, with on-going data collection, has been collected on 21 subjects. The average time to cricothyrotoomy insertion for the standard open technique was 49 seconds (median 39). The average time to insert the QuickTrach-2™ is 42 seconds (median 32). Lastly, the Cric-Key/Knife™’s average time to insertion was 55 seconds (median 50). Only two participants needed a second attempt to insert a surgical airway using the standard open technique, while 3 participants missed in both the QuickTrach-2™ and Cric-Key/Knife™ groups. Fifteen trainees preferred the QuickTrach-2™.

Conclusion

In this limited data set, the QuickTrach-2™ had a trend to shorter airway cannulation times and was most preferred by medics when compared to Cric-Key/Knife™ and standard open technique. First attempt success with similar for each group.
HYBRID SEQUENCING AND PHYLOGENOMIC ANALYSIS OF RARELY ISOLATED NON-SHIGATOXIGENIC ENTEROHEMORRHAGIC ESCHERICHIA COLI (EHEC) O157:H7

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Background: Human disease severity in enterohemorrhagic Escherichia coli (EHEC) infections is a direct result of Shiga toxin production, a major virulence hallmark of the O157:H7 serotype. However, atypical non-Stx producing O157:H7 strains have been rarely isolated, and the genetic basis of these Stx negative phenotypes remains unknown. For this study, we have assembled 13 stx-negative O157:H7 strains from North America, Europe and Asia. This unique collection provides an excellent opportunity to characterize the evolutionary basis of Stx negative phenotypes on a lineage- and genome-wide scale.

Methods: Strains were subjected to Whole Genome Sequencing and Typing (WGST) strategies to probe for genetic relationships with high phylogenetic accuracy and resolution. We sequenced and closed the genomes applying NGS short/long read hybrid technology. Reads were generated on the Illumina MiSeq, PacBioRS and MinION platforms, and assembled with either Spades or HGAP3 and annotated with Prokka. Custom developed bioinformatic pipelines were used to catalogue and annotate SNPs in the core genome. The carriage of accessory Stx prophage genomes or any remnants thereof was interrogated by genomic- (e.g. PHASTER) and PCR-based phage profiling strategies.

Results: Based on the core SNPs, we established a phylogenetic hypothesis and placed the stx-negative strains in the broader context of the O157:H7 step-wise evolutionary model. Sampled strains were classified into five different phylogenetic clades (3, 5, 7, 8 and 9) according to Manning et al., indicative of their independent evolutionary history. We further confirmed that the strains’ stx-negative status was either caused by the secondary excision of complete Stx prophage genomes or by partial loss of the stx locus, while remnants of the Stx prophage are still maintained.

Conclusion: Our comprehensive analyses of genomes and cultures allowed us to retrace the individual evolutionary pathways that resulted in the strains’ atypical Stx negative phenotypes. Understanding the genetic basis of O157:H7 strain-to-strain variability in Stx production is foundational to improve risk assessment, biosurveillance and the development of alternative Stx prevention strategies with translational application for other STEC pathovars.

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CHARACTERIZATION OF TRAUMA-RELATED UPPER EXTREMITY AMPUTEES AND THEIR OCCUPATIONAL THERAPY TREATMENT

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Background: Military combat operations result in the sustainment of traumatic injuries that require amputation and subsequent rehabilitation. This retrospective study characterizes the injuries, rehabilitation, and outcomes of patients with upper extremity (UE) amputation who received occupational therapy at the Center for the Intrepid (CFI). This study aims to 1) determine the overall treatment lengths and individual rehabilitation phases according to the level of UE amputation, and 2) examine outcome measure scores based on different amputation levels.

Methods: Chart review is ongoing of approximately 100 patient records from a CFI database. Data are gathered through outcome measures of the Disabilities of the Arm, Shoulder, and Hand (DASH), Box and Block Test (BBT), Southampton Hand Assessment Procedure (SHAP), Numeric Pain Rating Scale, and Assistance of Daily Living (ADL) levels. The study will also gather demographic factor information and occupational therapy treatment characteristics. Data will be analyzed using multiple comparisons tests, one-way and two-way ANOVAs, and Pierson correlations.

Results: Data collection is ongoing and results have not yet been determined.

Discussion: Following an amputation, an individual’s life and functional performance are impacted. Categorizing and statistically analyzing the data on injuries, rehabilitation, and outcomes can help plan or project future rehabilitation interventions.

Conclusion: This study will serve to increase the foundational knowledge for the occupational therapy treatment of UE amputees. Completion of the study is needed for full data analysis and implications.

Keywords: Upper Extremity, Amputation, Occupational Therapy, Rehabilitation

Track & Category: Inpatient and Outpatient Care, Poster presentation
MINIMALLY INVASIVE ECLS REDUCES MINUTE VENTILATION AND DELAYS DEVELOPMENT OF ARDS IN A MODEL OF EN-ROUTE CRITICAL CARE

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INTRODUCTION: Smoke inhalation and burns are common causes of lung failure in combat and led to acute respiratory distress syndrome (ARDS) in 30% of mechanically ventilated casualties admitted to our burn center. The mainstay therapy for ARDS patients is mechanical ventilation, which is by itself injurious and exacerbates lung injury; necessitating a search for novel lung sparing critical care solutions.

We proposed minimally invasive extracorporeal life support (miniECLS) as an adjunct to mechanical ventilation with the strategic aim of minimizing ventilator settings and reducing ventilator induced lung injury. In this study we used a model of ARDS due to severe smoke inhalation and 40% total body surface area burns. We investigated 2 miniECLS devices: Hemolung (Alung Inc. Pittsburg, PA, 15.5 Fr catheter) and NovaLung MiniLung (Xenios Inc., Heilbronn, Germany, 18 Fr catheter). We initiated support right after injury and evaluated efficacy in reducing ventilator settings. We hypothesized that miniECLS enables a significant reduction in minute ventilation and delays development of ARDS.

METHODS: Anesthetized female Yorkshire pigs (43.5±0.5 kg, n=30) underwent intubation, mechanical ventilation and sterile instrumentation. After baseline (BL) data collection animals received smoke inhalation injury followed by a 40% TBSA full thickness flame burn. Animals received continuous monitoring of physiologic parameters for 72-hours. Immediately post injury animals were randomized to 3 groups: animals either received the Hemolung (n=9); Novalung (n=8) or no device (Injured Control, n=10). MiniECLS was initiated immediately after injury in the veno-venous jugular configuration. After initiation of miniECLS, ventilator support was reduced using the ARDSNet algorithm to achieve 6–8 ml/kg tidal volume and lower respiratory rates.

RESULTS: Mean time to ARDS was: 16±3.37hrs for Injured Controls; 52±7.45hrs for Hemolung (p<0.05) and 53.7±8 in the Novalung group (p<0.05; Figure 1). Figure 2 shows PFR over time. In many cases, animals receiving miniECLS dipped under the PFR threshold and then recovered. Vt/Kg was lower in Novalung at 72 hours, in Hemolung at 24, 48 and 72 hours and in controls at 48 and 72 hours without between group differences. PFR was lower in Novalung at 72 hours and in Hemolung at 24, 48 and 72 hours without group differences. RR was higher in Injured Controls. MV was lower in both Novalung and Hemolung groups and significantly lower than controls. Both Hemolung and Novalung caused a reduction in VCO2 by about 50% compared to baseline. Mortality was 25% (2/8) in the Novalung group, 66% (6/9) in the Hemolung group and 50% (5/10) in the Injured Control group, no between-group differences.
**Conclusions:** Use of miniECLS reduced minute ventilation and delayed ARDS development in a model of ARDS due to smoke inhalation and burns. MiniECLS is a useful adjunct and mitigation intervention to mechanical ventilation in ARDS and may be an effective therapeutic intervention during extended evacuation times.

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UTILITY OF OPTICAL COHERENCE TOMOGRAPHY AND ULTRASOUND FOR DIAGNOSIS OF ARDS

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INTRODUCTION: Acute Respiratory Distress Syndrome (ARDS) is diagnosed using chest X-ray and invasive blood gas analysis. ARDS in mechanically ventilated patients is defined as \( \text{PaO}_2 \)-to-\( \text{FiO}_2 \) ratio (PFR) less than 300 with X-Ray findings of bilateral infiltrates, without cardiogenic pulmonary edema. Ultrasound (US)-derived assessment of lung edema is of diagnostic utility in our animal model of ARDS. We evaluated the utility of optical coherence tomography (OCT), an in-vivo laser-based imaging technique, for diagnosis of airway edema. We compared OCT and US with PFR, and histological diffuse alveolar damage (DAD) scores in a model of ARDS due to smoke inhalation and 40% total body surface area burns. We hypothesized that airway and lung edema quantified by OCT and US correlates with PFR and DAD and could be useful diagnostic tools in ARDS.

METHODS: Anesthetized female Yorkshire pigs (n=11) were selected from ongoing studies in our model of ARDS due to smoke inhalation and burns. US images were taken at the 6th and 8th intercostal space near the mid axillary line on both the left and right side. Higher US Lung Comet numbers indicate increased lung edema. OCT was performed using a device made by the Beckman Laser Institute, Irvine, CA. Mucosal thickness was measured on OCT images acquired at the carina and right main stem bronchus. PFR was calculated from arterial blood gases. US, OCT, and arterial blood gas measurements were performed at BL, 0, 24, 48 and 72 hours post injury. Histopathological assessment for diffuse alveolar damage (DAD) was performed on lung tissues. DAD scores are a product of alveolar fibrosis, interstitial fibrosis, protein aggregates and air spaces. Two-way ANOVA with repeated measure was conducted to look at group differences for PFR, OCT, and ULS. DAD differences between the ARDS and no ARDS group used a Wilcoxon two-sample test. Pairwise Spearman correlations were performed between OCT, ULC, PFR and DAD.

RESULTS: Of 11 animals, 5 developed ARDS. The remaining 6 did not develop ARDS. The groups split PFR trajectories at 24-hours; the ARDS group continued to have lower PFR. Spearman Correlations were conducted between OCT, PFR, and ULS. There was a significant, weak correlation between the variables when comparing all animals (OCT/PFR \( r=-0.38885 \) \( p=0.0063 \), OCT/ULS \( r=0.44607 \) \( p=0.0024 \), PFR/ULS \( r=-0.50045 \) \( p=0.0005 \)). Similar correlations were found in the ARDS group (OCT/PFR \( r=-0.51116 \) \( p=0.0150 \), OCT/ULS \( r=0.50947 \) \( p=0.0154 \), PFR/ULS \( r=-0.41768 \) \( p=0.0474 \)) and non-ARDS group (OCT/PFR \( r=-0.22097 \) \( p=0.2780 \), OCT/ULS \( r=0.31254 \) \( p=0.1556 \), PFR/ULS \( r=-0.60460 \) \( p=0.0029 \)). Lung damage DAD score correlated with PFR at 48 hours (\( r=-0.73193 \) \( p=0.0390 \)) and 72 hours (\( r=-0.82952 \) \( p=0.0109 \)).

CONCLUSIONS: OCT and ULS correlated with PFR; this correlation was stronger in the ARDS group. OCT and ULS are less invasive than blood draws, readily available at the bedside and show potential as diagnostic tools in ARDS. Further work in this area will be done to reconfirm these findings.
in larger datasets. We recommend that OCT and US become a part of the ICU toolbox used to detect early changes in patients at risk of ARDS.

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A Novel Bioresorbable/Biointegratable/Biocompatible Dressing for Negative Pressure Wound Therapy

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Background: Negative pressure wound therapy (NPWT) aims to improve healing by secondary intention of acute and/or chronic wounds by dynamic vacuum assisted removal of wound exudate, promoting granulation. The standard of care in NPWT uses a polyurethane sponge dressing (PUSD) applied to the wound as a filler to help facilitate vacuum suction. The PUSD is non-biodegradable and needs removal every 2-3 days, causing repetitive trauma during wound healing. We developed three novel bioresorbable/biointegratable/biocompatible sponge-dressing scaffolds (3B-SDS) and evaluated their feasibility and efficacy in optimizing wound healing and limiting need for dressing changes in a pre-clinical porcine NPWT wound model.

Material and Methods: Ten full thickness wounds were created on six swine. Four randomly chosen wounds served as controls undergoing wet-to-dry (WTD) dressing changes (two wounds) and PUSD NPWT (two wounds). The remaining six wounds underwent treatment with the novel 3B-SDSs. All wounds were assessed every 3 days until creation of a skin graftable area or until the project end date of 1 month. The primary outcome measure was time to skin graftable area. Wound planimetry and histology were secondary outcome metrics.

Results: Both control treated wounds developed a skin graftable area by POD9. The 3B-SDSs were completely incorporated into the wounds and developed a skin-graftable area by POD12-15 with a larger area of granulation tissue and less wound contraction compared to controls. Histological assessment of biopsies showed granulation tissue developing in all wounds with granulation tissue seen throughout the 3B-SDSs wounds indicating scaffold incorporation.

Conclusions: The use of 3B-SDSs provided a scaffold for cellular ingrowth minimizing wound contraction and were incorporated into the wounds without the need for dressing changes. These novel bioresorbable, biointegratable, and biocompatible sponges have the potential to revolutionize wound care. Future studies involve optimizing the formulation/structure of 3B-SDS, assessing an increased number of larger wounds, and performing immunohistochemical staining.

Acknowledgement: Jian Ling SWRI (Southwest Research Institute)
REACHING ACROSS STATE LINES: TELEHEALTH TRANSFORMS HEALTHCARE FOR TODDLER WITH NEWLY DIAGNOSED JUVENILE DERMATOMYOSITIS

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Juvenile Dermatomyositis (JDM) is a rare autoimmune systemic vasculopathy that predominantly affects the muscles and skin. It is defined by symmetrical proximal muscle weakness, elevated muscle enzymes, and a characteristic violaceous rash over the eyelids with erythematous papules on the extensor joint surfaces. With prompt diagnosis, and aggressive treatment, JDM patients exhibit much less morbidity and mortality. The following case demonstrates a toddler with an atypical presentation of JDM in which the use of RelayHealth patient-provider tool, digital pathology slides, and video teleconferencing facilitated diagnosis, enhanced patient tracking, and provided optimal care and collaboration with subspecialty providers across state lines.

A previously healthy 2 year 11-month-old female with an unremarkable birth history presented to a remote facility in her hometown with a 7-month history of bilateral knee pain and progressive muscular weakness. After evaluation and diagnosis of rhabdomyolysis, the decision was made to transport her to a larger medical institution with a dedicated pediatric inpatient unit and subspecialty capabilities for further assessment. As her disease course progressed she became non-ambulatory, exhibited voice changes, and had oromotor difficulties when swallowing. During her course of care, the patient required admission at numerous facilities for specialty procedures including swallow studies, electromyography, muscle biopsy, and Nissen fundoplication with g-tube insertion.

As multiple provider subspecialties were involved during this time including Genetics, Neurology, Pulmonary, Cardiology, Anesthesia, Surgery, and later Rheumatology it was important for all parties to stay up to date on new findings and test results. The digital record keeping system and patient-provider online system became a vital lifeline, providing a comprehensive timeline of events and data in combination with an expedited communication tool respectively. Digital pathology slides created following surgical muscle biopsy specifically provided remote subspecialist with a missing link to help seal our patient’s diagnosis.

Following diagnosis, our patient was evaluated by rheumatology. Now 11 months out from disease onset, she was found to have a newly developed heliotrope and malar rash, in conjunction with semi-firm pea sized nodules through both upper extremities. Treatment with steroids, methotrexate, folic acid, and vitamin D was initiated. To retain the patient within a single hospital system for both subspecialty and preventative care, a referral was made to a pediatric rheumatologist with a focus in autoimmune myopathies of childhood. After her diagnosis was again confirmed, she received an initial course of extended duration IVIG and her case was returned to her primary care manager (PCM). Once again, the electronic medical record served as a huge pipeline to gather and disperse documentation for a smooth transition from the inpatient to outpatient setting.

The care of this patient is currently ongoing. Geographic isolation has been overcome through the use of video teleconference. This technology has allowed her PCM to collaborate with her pediatric rheumatologist in order to discuss the patient’s case, and provide optimal assessment and care.
WHO IS DISTRESSED? APPLYING THE DIABETES–RELATED DISTRESS SCALE IN A DIABETES CLINIC

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Background:
The American Diabetes Association recently released a position statement on psychosocial care of patients with diabetes recommending assessment of diabetes-related distress (DRD) with validated scales such as the Diabetes-related Distress Scale (DDS). However, there are no published data to date describing the use of the DDS in a clinical setting.

Materials and Methods:
We measured DRD, using the DDS, in patients enrolled to our diabetes clinic with results reported as it pertains to diabetes type and medication regimen [Type 1 diabetes (T1DM), Type 2 diabetes with insulin use (T2DM-i), Type 2 diabetes without insulin use (T2DM)]. Chart review, of Diabetes Center of Excellence patients, identified 810 patients who completed a baseline DDS over a 1 year period. We categorized the DDS results as follows: < 2.0 = little or no DRD; 2.0–2.9 = moderate DRD; and ≥ 3.0 = high DRD. In addition, we evaluated four domains: Emotional Burden (EB); Physician-related Distress (PD); Regimen-related Distress (RD); and Interpersonal Distress (ID).

Results:
High total DDS was most prevalent in T2DM-i patients (8.8%); mean total DDS in T2DM-i (1.79) was significantly higher compared to T1DM patients (1.61; p = 0.02). High RD was more prevalent in T2DM-i and T2DM groups (19.1% and 18.2%, respectively), compared to patients with T1DM (11.1%) with significant differences in means between T1DM (1.84) and T2DM-i (2.12; p = 0.01). Although means were not statistically different, high EB was most prevalent in T1DM and T2DM-i groups (17.4%; mean = 1.88 and 19.7%; mean = 2.09, respectively), compared to T2DM (10.8%; mean = 1.89).

Conclusions:
This study is the initial step to identify DRD in a clinical setting; this will allow emphasis of psychosocial interventions in each diabetes group and routine reevaluation of psychosocial well-being using DDS, with the goal of improving diabetes-related outcomes. Further research is needed to assess other contributing factors related to DRD and identify interventions to reduce DRD.

Topic: Open category- psychosocial care

Submission Category: Poster

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Keywords:
Diabetes-Related Distress, Diabetes, Insulin

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Depression Trajectories and Risk-Taking Behaviors among Active Duty and Retired U.S. Military Personnel with HIV Infection

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Background and Significance: Previous studies have suggested linkages between psychological symptoms, such as depression and anxiety, and sexually risky behaviors or general sexual risk. Researchers have hypothesized that depression can lead to cognitive distortions, which in turn can negatively impact rational decision-making, thus resulting in emotional influences on behaviors. However, previous investigations have primarily focused on HIV positive civilians, whereas HIV positive military personnel has been largely overlooked. This study is designed to fill this research void by examining the multifaceted linkages between depression trajectories and risk-taking behaviors among active duty and retired U.S. military personnel with HIV infection.

Methods: This study utilized clinical data (n = 666) consisting of the medical history of military personnel over a period of 28 years (1988-2016), which was matched with the HIV Natural History Study Risk Behavior Survey conducted from 2015 to 2016, to explore the linkages between active duty and retired male military personnel’s depression trajectories and substance abuse, risky sexual behaviors and contraceptive use. Latent class analysis was employed to create three classes of depression trajectories over a period from 1988 to 2016, namely, low depression trajectories, recent onset depression trajectories, and high depression trajectories. The latent class was further dummy-coded with the low depression trajectory class serving as the reference.

Results: Regression models (n = 641) indicate that study participants with recent onset depression and high depression trajectories are 3.6 and 3.8 times more likely to have had sex with 5 or more new sexual partners in the last three months than those with low depression trajectories, respectively. Furthermore, study participants (n = 341) with high depression trajectories are 2.47 times more likely to have one or more anonymous sexual partners in the last three months than those with low depression trajectories. The regression analysis (n = 345) also shows that study participants with high depression trajectories are 2.36 times more likely to have one or more main/steady partners in the last three months than those with low depression trajectories. In regards to alcohol use, study participants (n = 651) with recent onset depression trajectories are 1.65 times more likely to have frequent alcohol use in the past year than those with low depression trajectories. Finally, it is found that study participants (n = 288) with recent onset depression and high depression trajectories are 45% and 54% more likely to report never/sometimes using condoms with new sexual partners in the past three months than those who report often/always using condoms.

Conclusion: Results suggest that consistent previous studies HIV positive military personnel with recent onset depression and/or high depression trajectories are more likely to engage in higher levels of substance abuse and risky sexual behaviors than those who have low depression trajectories.
THE IMPACT OF A NOVEL BIOBEHAVIORAL INTERVENTION ON PHYSIOLOGIC STATE, PERCEIVED STRESS AND AFFECT

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Background: Our nation is suffering from the consequences of the stresses associated with the past 16 years of war.1-3 US employers spend $300 billion a year for employee medical care and lost days from work due to stress.4 The search for innovative and cost effective means of mitigating the effects of stress is needed now more than ever and was the basis for this pilot investigation. Laughter yoga (LY) fosters positive emotions, engagement, relationships, meaning and accomplishment (PERMA), the active components of wellbeing that make up the evidence-based model of wellbeing developed within the field of Positive Psychology.5 Our study’s purpose was to explore the practice of the biobehavioral intervention, LY, as an intervention to mitigate the physiologic and psychological effects of stress for a military graduate student population.

Materials & Methods: Mixed method quasi-experimental pre-test post-test wait-listed group design. Participants included 41 military medical and allied health graduate students age 23-52 (M=31), randomly assigned to experimental and wait-listed control groups. The experimental group met for an hour LY session twice a week for first two weeks, while control continued with usual activities. Wait-listed control participated in LY during weeks three and four, while experimental group then returned to regular academic and life behaviors. Measures were collected at baseline, after two weeks and then again after four weeks. Physiologic measures and self-report measures were also collected before and after each laughter yoga session. Outcome measures included: heart rate variability, peak expiratory flow rate, Perceived Stress Scale, Positive Affect Negative Affect Scale, Patient Health Questionnaire 8, Standard Form 36, and Connor-Davidson Resilience Scale scores, as well as participant responses to open-ended questions. Data analysis conducted using SPSS (v.22) for parametric and nonparametric testing; thematic analysis of open ended responses to

Results: Subjects showed statistically significant decreases in measures of heart rate variability and increases in peak expiratory flow rate, positive affect, resilience and general health and mental health scores when compared to baseline. Participants reported improvements in mood, relationships and health behaviors in responses to open-ended questions.

Conclusions: This pilot study provides preliminary evidence that laughter yoga may improve peak expiratory flow rate, psychological health and lead to unexpected benefits in personal, social and professional relationships.

Key Words: Laughter Yoga, Heart Rate Variability, Peak Expiratory Flow Rate, Perceived Stress, Positive Affect, Resilience

Topics: Open: Work is related to protecting, maintaining, and improving health.
Caregivers: Family Caregivers and Medical Providers

Submission Categories: Research Papers and Poster Session
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DISCLAIMER: The views expressed are those of the author(s) presenter(s) and do not reflect the official views or policy of the Uniformed Services University of the Health Sciences, the Department of Defense, or its components. The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI40-402.

References

Objective: There is limited data that describes the effects of the type of prehospital airway intervention on morbidity and mortality. Our aim was to compare the survival and morbidity of patients receiving cricothyrotomy vs. other advanced airway interventions in the prehospital setting.

Background: In the combat setting, airway compromise is the second leading cause of preventable death. Cricothyrotomy, endotracheal intubation, and supraglottic airways are potentially lifesaving interventions performed in the prehospital setting. Successful performance of securing an advanced airway is variable and may be attributable to operator experience, availability of equipment, nature of injuries and/or suboptimal patient selection. The optimal prehospital airway intervention in the combat setting has not been well defined.

Methods: Our study is an IRB approved, retrospective record review including trauma patients from 2011 to 2014 who were air evacuated by MEDEVAC from their point of injury (POI). Trained data abstractors collected injury description, provider type, procedures performed, analgesics administered, survival, and 30-day outcomes. Subjects with airway interventions were grouped according to airway type: nasopharyngeal/oropharyngeal, supraglottic, endotracheal intubation, and cricothyrotomy. Chi-squared tests (or Fisher’s exact test when appropriate) were utilized for categorical data, and analyses of covariance (ANCOVAs) were used for continuous data to adjust for head/facial injuries and injury severity scores (ISS).

Results: Data were abstracted from 1,237 subjects, with 617 subjects receiving an airway. There were 568 nasal/oral airways, 22 supraglottic airways, 4 endotracheal intubations, and 23 cricothyrotomies. Medics preformed 422 nasal/oral airways, 14 supraglottic airways, 1 intubation, and 12 cricothyrotomies. Paramedics preformed 97 nasal/oral airways, 8 supraglottic airways, 3 endotracheal intubations, and 8 cricothyrotomies. Nurse/PA/MDs preformed 23 nasal/oral airways. Subjects with an airway intervention had significantly lower survival rates and vent-free, ICU-free, and hospital-free days. Subjects who had a supraglottic airway had less ICU-free and hospital-free days than subjects who had a cricothyrotomy. There was no significant difference in survival between supraglottic vs. cricothyrotomy patients.

Conclusions: After adjusting for head/facial injuries and ISS, we found no significant difference in survival between patients receiving a supraglottic airway vs cricothyrotomy. However, subjects with a supraglottic airway had more ICU and hospital days than subjects with a cricothyrotomy.

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INTRODUCTION:

Although studies have found an association of suicide related behavior (SRB) and antiepileptic drugs (AED), and the Food and Drug Administration has identified the entire class of AEDs as suicidogenic, no clear evidence of causal association or class effect established. Increasing use of AED’s in non-epileptic conditions such as psychiatric disorders and chronic pain complicate the understanding of the relationship between AED exposure and SRB. Similar to studies examining SRB and depression treatment, studies examining the temporal patterns of SRB and AED treatment find that the peak of SRB occurs BEFORE the initiation of AEDs. We compared the trends of SRB before and after initiation of AED therapy among AED users with epilepsy and without epilepsy to individuals without AED use controlling for sociodemographic characteristics and mental health comorbidity.

METHODS:

We obtained Veterans Health Administration (VA) health system data for a retrospective cohort study of Veterans deployed in support of Iraq and Afghanistan wars (IAV) who received VA care during fiscal years 2013 and 2014 and who did not receive AEDs prior to the study period. The index date for AED users was the date of first AED prescription and the first health care encounter for individuals without AED exposure. We identified SRB 12 months before and after the index date based on ICD-9 codes. We also identified indicators of mental health comorbidity (diagnoses of mental health chronic pain conditions (ICD-9 codes), antipsychotic and antidepressant medication use, and psychiatric hospitalization) 12 months prior to index date. We conducted generalized estimation equation (GEE) analyses to access the trend of SRB prevalence the year prior to and after the index date controlling for sociodemographic and indicators of mental health comorbidity. To further confirm the differential SRB trend between AED users with and without epilepsy, we conducted similar GEE analyses among AED users adjusting for inverse propensity scores weights of being diagnosed for epilepsy.

RESULTS:
The GEE analysis of the full cohort showed a significant curvilinear trend of SRB prevalence over the 24-month study period for AED users indicating that the probability of SRB diagnoses increased over time before the index month and then decreased after the index month. Similar curvilinear SRB probability trajectory was observed among non-AED users, but the likelihood for SRB was significantly lower (Odds Ratio: 0.16; 95% CI 0.14-0.19) throughout compared to AED users. GEE analysis among AED users adjusting for inverse propensity score weights for epilepsy status suggested that the SRB prevalence trajectory was similar between AED users with and without epilepsy (See Figure1).

CONCLUSIONS:

While individuals with AED exposure had higher likelihood of SRB, the trend started before the AED exposure and was not differentially associated with epilepsy status. Given the limited information available on depression severity in this administrative data it is possible that the significant effect for AED exposure is due to residual confounding of mental health comorbidity. Patients with risk factors for SRB, whether taking AED or not, should be carefully monitored for mental health symptoms and SRB.

Figure1: Likelihood of Suicide related behavior over time by AED exposure and epilepsy status.

Title: Host MicroRNAs in the Interplay of Immune Effector Cells involved in Anti-Chlamydial Immunity

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Institution: ¹ South Texas Center for Emerging Infectious Diseases and Center of Excellence in Infection Genomics, University of Texas at San Antonio, One UTSA Circle, San Antonio, TX-78249.

Background: Genital *Chlamydia trachomatis* may lead to reproductive sequelae including fibrosis and inflammation. While the role of molecular regulators namely microRNAs (miRs) is not well examined in
Ct, the contribution of downstream immune pathways/genes leading to genital tissue exacerbation and tissue remodeling is known.

**Objective:** Given the regulatory link between miRs and immunity, we determined the contribution of selected miRs in immunity and development of pathology in *Chlamydia muridarum* (Cm) infection.

**Methods:** C57BL/6 wild type (WT) were intravaginally infected with Cm and cellular infiltrates (flow cytometry), miRs and genes (real-time PCR) and genital pathology was analyzed. *In vivo/ ex vivo* experiments using miR agonist/antagonists for gain and loss of function respectively were performed. Down-selected miRs were validated (real-time PCR) in cohorts of Ct infected women.

**Results:** We observed significant upregulation of miR-155 in WT bone marrow derived dendritic cells (DC), and miR-182 in splenic Ag-specific CD4+ T-cells. Using mimics and inhibitors, we determined that miR-155 contributed to DC activation. Co-cultures of miR-155 over-expressed in DC and miR-182 over-expressed in Ag-specific CD4+ T-cells, or miR-155/- DC with miR-182 inhibitor treated Ag-specific CD4+ T-cells, resulted in IFN-γ production comparable to that of Ag-specific CD4+ T-cells isolated from Cm infected mice. MiR-182 was significantly up-regulated in intranasally vaccinated mice protected against Cm infection. *In vivo* depletion of miR-182 resulted in reduction in Ag-specific IFN-γ and genital pathology in Cm infected mice. Importantly, significant regulation of miRs in Ct D infected women was indicative of the translational relevance.

**Conclusion:** To the best of our knowledge, this is the first study to report an interaction of miR-155 and -182 resulting in Ag specific immune responses against an intracellular pathogen.

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PREDICTORS OF LONG-TERM OPIOID USE IN ACTIVE DUTY MILITARY: PSYCHOTROPICS, PROCEDURES, PAIN

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Background: In the United States, chronic pain is more prevalent among active duty (AD) military service members (44%) than civilians (26%). Assessing factors associated with acute versus 3 long-term opioid use patterns (episodic, long-term low dose [LTLD], long-term high dose [LTHD]) may facilitate opioid risk mitigation. We predicted differences in system-level, clinical and opioid characteristics among opioid use patterns.

Materials and Methods: Administrative de-identified data (2012-2013) from the TRICARE Pharmacy Data Transaction Service and M2 DataMart included prescription information and diagnosis codes. Inclusion criteria: AD enrolled in TRICARE for \( \geq 11 \) months who received \( \geq 1 \) opioid in a year. Opioid episodes defined as: Acute \(< 3 \) months) and episodes greater than 3 months: episodic \(<120 \) days supply/10 prescriptions), LTLD \(>120 \) days supply/10 prescriptions, average MME \(<20mg\), LTHD (same as LTLD except average MME \(>20mg\)).

Results: Multinomial logistic regression identified risk factors associated with episodes (acute episodes as comparator). Cohort included 242,578 AD (43.8% Army, 83.9% male and 62.2% 18-25 years old). Individuals co-prescribed benzodiazepines were significantly more likely to have LTLD \(4.36 \text{ CI}[3.90, 4.86]\) and LTHD \(5.18 \text{ CI}[4.45, 6.03]\). Similarly individuals co-prescribed antidepressants were significantly more likely to have LTLD \(13.63 \text{ CI}[12.09, 15.37]\) and LTHD \(19.60 \text{ CI}[16.60, 23.15]\). Similar patterns were found for AD Army (vs. Air Force and Navy), and individuals who had major inpatient procedures or back pain.

Conclusions: Results are similar to that observed in civilians. Factors exist that are unique to military context, e.g., service branch. Areas of concern and potential modifiable risk factors include co-prescribing.

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The views expressed are those of the author and do not reflect the official views or policy of the Department of Defense, Department of Veterans Affairs, or its Components.
Partial Purification and Characterization of an Acid Phosphatase

from *Acinetobacter baumannii*

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Abstract

Acid Phosphatases (EC 3.1.3.2) are a ubiquitous class of enzymes that catalyze hydrolysis of phosphomonoesters at an acidic pH, and have been implicated as virulence factors enhancing intracellular survival. The acid phosphatase of *A. baumannii* is an acidic protein that behaves as a 57 kDa dimer comprised of two monomers of 27 kDa and hydrolyzes 4-MUP maximally at pH 6.5, and exhibits no sensitivity to the classical inhibitor of Alkaline Phosphatase, Cysteamine Phosphate supporting the assignment as an acid phosphatase. The enzyme does not readily hydrolyze O-phosphorylated amino acid substrates, *i.e.*, Serine, Threonine, and Tyrosine. Hydrolysis of 4-MUP is stimulated by Co^{2+} and is inhibited by EDTA. It is relatively insensitive to the classic acid phosphatase inhibitors Sodium Tartrate and Sodium Fluoride (IC\textsubscript{50} = 20 and 50 mM, respectively). In contrast, hydrolysis of 4-MUP is very sensitive to Sodium Vanadate (IC\textsubscript{50} = 0.013 mM) as well as Cu^{2+}, Zn^{2+}, and Fe^{2+} divalent cations. Additionally, 4-MUP hydrolysis is inhibited by P\textsubscript{i} and PP\textsubscript{i} (IC\textsubscript{50} = 0.9 and 2.0 mM, respectively). Although PP\textsubscript{i} behaves as a competitive inhibitor, no transphosphorylation using PP\textsubscript{i} as donor and glucose as acceptor was detected. NMR analysis of the 57 kDa dimeric band is consistent with BLAST and substrate specificity/inhibitor analyses supporting the acid phosphatase of *A. baumannii* as being a member of the DDDD superfamily possessing HAD-like conserved motifs I and III, the physiological function of which remains to be elucidated.
DIFFERENCES IN PTSD SYMPTOMS AMONG POST-9/11 VETERANS WITH BLAST- AND NON-BLAST TBI

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An estimated 52% of deployment-related traumatic brain injury (TBI) cases are attributed to IEDs. Symptoms of posttraumatic stress disorder (PTSD) are reported approximately twice as often by service members who screen positive for mild TBI (mTBI) than those with no reported TBI (Yurgil et al., 2013). However, determining if TBI is a risk factor for PTSD has been difficult to establish, possibly in part due to the range of incidents that cause mTBI, which are typically collapsed across events during analysis. Importantly, being dazed or knocked unconscious during a blast-related mTBI (e.g., from IED’s, RPG’s) has the potential to expose individuals to extreme life-threatening situations, dismemberment, and/or death of fellow service members or noncombatants (Hoge and Castro, 2014). In the current study, we hypothesized that veterans with blast-related mTBI would report significantly greater scores of PTSD than those with non-blast related mTBI or no TBI after controlling for demographics and types of trauma.

This study is a secondary analysis of a sample of veterans who participated in a larger longitudinal study and had served in support of the post-9/11 wars in Iraq and Afghanistan. Of the 345 enrolled, 36 were excluded due to: not completing the baseline assessment; or diagnosis of schizophrenia or bipolar. The current analysis was further limited to those who endorsed no TBI or mTBI only (n = 218). Veterans were then categorized: no TBI (n = 68); non-blast related mTBI (n = 83); and blast-related mTBI (n = 67). A baseline assessment was conducted during which participants completed a diagnostic interview and self-report questionnaires. TBI was measured using a clinician-administered interview (Vasterling, 2008), which assesses the number, recency, type of injury, and clinical sequelae associated with TBI. PTSD symptoms were measured using the Clinician-Administered PTSD Scale (CAPS; Weathers et al., 1994).

A between-subjects analysis of covariance was performed with the three TBI groups. Covariates included demographics and lifetime trauma exposure. After square root transformation of the dependent variable (CAPS current severity) and adjustments with covariates, PTSD scores differed significantly by TBI group, F(2,210) = 6.97, p = .001, partial η2 = .06, medium effect. Planned contrasts revealed that PTSD symptoms among individuals with blast-related mTBI was significantly higher compared to both no TBI, p = .009, 95% CI [-2.4, -.34], and non-blast related mTBI, p < .001, 95% CI [-2.72, -1.83]. The adjusted marginal means indicated the smallest PTSD scores among non-blast TBI (M = 3.8, SE = .30), the largest among blast-related mTBI (M =5.5, SE = .36), and those with no TBI (M = 4.2, SE = .34) falling between the other two groups. These data suggest that the context under which mTBI occurs (blast vs. non-blast) may affect subsequent PTSD symptoms. Future studies should further examine other qualities associated with a wide range of mTBIs (e.g., loss of consciousness, single/repeated, complicated) to better understand the relationship between mTBI and PTSD.
Quantitative analysis of antibodies to Zika virus Envelop and NS1 proteins in vaccinated rabbits

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Abstract

Zika virus, a member of Flavivirus has been linked to both microcephaly and Guillain-Barre Syndrome (GBS). Currently, no vaccine nor drugs are available for treatment of Zika infection. Vaccines for Flavivirus have been developed using whole inactivated Yellow Fever virus (YFV) as well as YFV-vectored constructs expressing Dengue Envelop-PrM protein. Thus, Flavivirus proteins show promise as vaccine candidates. The aim of this work was to explore the use of purified recombinant Zika proteins (Envelop and NS1) in a rabbit model as potential vaccine candidates. Quantitative Envelop and NS1 antibody ELISAs were developed to monitor levels of IgG and IgM during the course of vaccination. Recombinant Envelop and NS1 proteins appeared highly immunogenic both giving rise to an IgG response 3-weeks post-immunization which increased out to approximately 110 days post-immunization and decreasing slightly thereafter. However, quantitation of the respective responses indicated a high titer of IgG elicited against the Envelop protein (~4,500 µg/ml serum) and a significantly lower titer for NS1 (~100 µgm/ml serum). In contrast to the IgG response, the elicited IgM response to both Envelop and NS1 proteins was ‘biphasic’ in nature. Quantitation of the Envelop protein response resulted in 2 peaks (~55.0 µg/ml serum) arising 20 and 110 days post-immunization. Although the NS1 raw response was also ‘biphasic’ with peak values occurring 50 and 110 days post-immunization, quantitation of the IgM response indicated a general increase in titer out to 110 days post-immunization albeit lower, i.e., ~20 µg/ml serum). Findings reported here indicate recombinant Envelop protein is very immunogenic, and thus may serve as a quick, safe, and more economical alternative prototype to pursue in lieu of whole virus or vectored vaccines. The availability of Zika Envelop and NS1 recombinant protein based antibody ELISA reagents for detection of IgG and IgM could be useful for development of diagnostic formats for the diagnosis of Zika infection.

Introduction

Zika virus was first discovered in the serum of a rhesus macaque monkey in the Ugandan Zika Forest in 1947¹, and subsequently observed in a human a few years later in Nigeria. Zika virus is a Flavivirus transmitted by the *Aedes Aegypti* mosquito² which is endemic to the Southern, Eastern, and Mid-Eastern parts of the United States. Due to the large area inhabited by the mosquito³, and the proximity to South America and the Caribbean where the current outbreak originated, it has recently become a major health concern in the United States⁴. Currently, 4,750 cases have been confirmed in the US with 433 pregnancy related cases⁵. The majority of cases observed have been travel-related with the first 14 cases arising by localized transmission occurring in Miami, Florida in July, 2016⁶. Due to the
localized nature of infection observed, the CDC has for the first time in its history issued a warning not to travel to an American neighborhood [6].

Zika viral infection does not initially give rise to severe symptoms with 80% of all cases nonsymptomatic, and the remaining 20% giving rise to minor flu-like symptoms [7]. Currently, the major concern for Zika viral infection is the increase in microcephaly observed in pregnant women in mosquito infected areas which the CDC has recently concluded Zika virus as the causative agent [8]. Microcephaly is a lifelong condition associated with much smaller head size giving rise to symptoms ranging from seizures, developmental delay, cognitive deficit with movement/balance, feeding, hearing, and vision problems, and in severe cases death [8]. Additionally, Guillain-Barré Syndrome (GBS) is a disorder increasingly observed in individuals in areas where Zika virus is prevalent. Guillain-Barré Syndrome is a disorder that causes the immune system to target parts of the peripheral nervous system resulting in myelin sheath degradation thus decreasing neuronal transmission leading to weakness, tingling sensations, and in severe cases paralysis. Although the greater majority of GBS individuals recover from the most severe cases, some individuals experience long-term symptoms [8].

Zika virus pathogenesis is still not understood. Currently, the mode of viral transmission includes blood, fluid exchange, and sexual intercourse [7]. Currently, no vaccine or anti-viral therapeutic agents exist for treatment of Zika infection [7]. Additionally, Zika infection is difficult to diagnose due to 1) co-infection or 2) prior infection with related viruses, e.g., Dengue, Chikingunya, Yellow Fever, and West Nile which are also endemic to areas where Zika virus is indigenous [10]. Thus, misdiagnosis can occur due to cross-reactivity of diagnostic reagents with proteins of other closely related viruses generating false positives for Zika infection [10]. Alpha Diagnostics International (ADI) has developed enzyme-linked immunosorbent assays (ELISA) for detection of antibodies elicited against Zika Envelop and NS1 recombinant viral proteins using a rabbit model. Data reported here demonstrate the detection of Zika elicited immunoglobulins, and contributes to understanding the immune response to Zika infection, and development of new diagnostic reagents and vaccine candidates.

Materials and Methods

Recombinant proteins: Zika Virus Envelop (Envelop/251 amino acids, Accession# AHL43464.1, MR 766 strain) and NS1 (354-amino acids, Accession# BAP47441) proteins were expressed in SF9 and E. coli, respectively, and purified >95%.

PAGE and sequencing analysis: Electrophoresis was carried out under denaturing conditions according to the method of Laemmli [11]. Recombinant Envelop and NS1 protein (1.6 and 1.4 μg, respectively) were heated for 5 minutes at 95 °C in the presence of SDS and β-mercaptoethanol, and applied to 10% BIS-Tris gels (Life Sciences Technology, Inc). Electrophoresis was carried out at constant voltage (80) for 1.5-2.0 hours at room temperature. Gels were stained with Coomassie Blue.
**Animals:** Adult, New Zealand White males (5-6 lbs) were used for antibody production in a USDA approved facility with applicable approved IACUC protocols.

**Immunization protocol:** Rabbits were immunized as shown below by subcutaneous injections (3-4 sites) of recombinant Zika protein antigens (ADI, San Antonio, TX): Envelop protein 50 uL (135 ug protein/mL) and NS1, 50 uL (130 ug protein/mL). Due to very low antibody titers following 5 injections, NS1 dosage was doubled, *i.e.*, 260 ug/50 uL for injections 6 and 7. A Pre-immune bleed was collected prior to immunization. Immunization was performed on Day 0, and subsequently at 2, 4, 6, 8, 10, and 12 weeks. Bleeds were carried out at 3, 7, 9, 11, 13, 15, 17, and 19 weeks, respectively. Sera were separated at room temperature by centrifugation (15 minutes at 3000 rpm), and stored at -20 °C until used.

**ELISA plate preparation:** ELISA plates were prepared by coating overnight at 4 °C. For Envelop protein IgG and IgM detection, antigen was coated at a concentration of 0.5 ug/mL in PBS. For NS1 IgG and IgM detection, NS1 antigen was coated at a concentrations of 0.1 and 0.5 μg/ml, respectively, in PBS. Plates were washed with 50X wash buffer 3 times. Stablecoat reagent (100 uL) was added to each well, incubated at room temperature for 1 hour after which time wells were aspirated using an ELISA wash machine, and subsequently dried at 30 °C for 3 hours.

**ELISA:** Assays were carried out as follows: Serum (100 uL) was added to each well at indicated dilutions, and incubated for 1 hour. Wells were washed 3X with wash buffer followed by addition of 100 uL horse radish peroxidase (HRS) immunoglobulin conjugates (Goat anti-rabbit IgG or Goat anti-rabbit IgM, ADI, San Antonio, TX), and incubated for 30 minutes at room temperature. Following washing 5 times with wash buffer, 100 uL 3,3′,5,5′-Tetramethylbenzidine (TMB) solution was added to each well, incubated for 15 minutes at room temperature, and reactions were terminated by addition of 100 ul Stop solution. Absorbance at 450 nm was monitored using an ELISA Plate reader (MPR-2100, Awareness Technologies).

**Generation of standard curve and quantitation of ELISA IgG/IgM:**

Generation of standard curve and quantitation of ELISA IgG/IgM was generated as follows: rabbit IgG and IgM (Equitech Bio) was coated at specific concentrations, *i.e.*, 3, 10, 30, and 100
HRP conjugate (100 uL Goat-anti Rabbit IgG or Goat-anti Rabbit IgM) was added to strips at appropriate dilutions (IgG, 1:200 or IgM, 1:100) for 30 minutes. Following washing (5 times), 100 ul TMB was added to each well, incubated for 15 minutes at room temperature, and absorbance at 450 nm determined following addition of stop solution. Absorbance for standards was linear from 3 to 100 ng. ELISA absorbance values were all quantitated within this linear range by appropriate dilution. Concentration was achieved by multiplication of respective extrapolated A_{450} values by the dilution necessary to achieve A_{450} values within the standard linear range.

Results

Shown in Figure 1 is an SDS PAGE analysis of expressed Envelop and NS1 recombinant proteins used in this study. Envelop recombinant protein migrates as a single electrophoretic band of approximately 35 kDa (Frame A); whereas, NS1 recombinant protein migrated as 2 electrophoretic bands resulting from cleavage during purification of approximately 40 and 45 kDa (Frame B). Immunization with recombinant Envelop and NS1 proteins elicited high raw absorbance values starting about day 21, increasing thereafter to approximately day 110, and decreasing slightly thereafter out to day 120 (Figure 2A). Shown in the inset (Figure 2A) is the IgG standard curve used to quantitate, i.e., titer the respective antigen response (Figure 2B) indicating increasing levels of Envelop protein elicited IgG from day 20 out to day 110. IgG response to NS1 recombinant protein also increased in similar fashion, but appears at background level due to scaling (Figure 2B), but was shown to increase steadily from day 20 out to approximately day 90 post immunization, i.e., ~100 ng/ml, cf. Figure 4B. In contrast to Zika recombinant antigen IgG response, raw absorbance values for IgM appear biphasic in nature with maxima for recombinant Envelop protein elicited at approximately day 20 and 110 post-immunization (Figure 3A); whereas, NS1 elicited IgM response indicated maxima values at approximately day 50 and 110 post-immunization (Figure 3B). Quantitation of the elicited IgM response was lower for NS1 (~10 and 20 µgm/mL at 50 and 110 days post-immunization, respectively) compared to that observed for Envelop recombinant protein (~55 µgm/mL at 20 and 110 days post-immunization). A summary comparison of IgG and IgM response for Envelop and NS1 recombinant proteins is shown in Figure 4A and B, respectively.

Discussion

Zika recombinant Envelop protein elicited a robust IgG response starting approximately 3 weeks post-immunization continuing out to 110 days post-immunization (~4500 µgm/ml) consistent with an expected ‘adaptive’ albeit continuous response following 5 subsequent injections, i.e., roughly 4 months after the initial injection. In contrast, IgG elicited to Zika recombinant NS1 protein albeit lower was significant (~100 ng/ml at day 90 post immunization). Both Envelop and NS1 recombinant protein elicited IgM levels were observed to be lower in comparison (2 maxima of approximately 50 µgm/ml 20 and 110 days, and 10-25 µgm/ml 50 and 110 days post-immunization, respectively) than that observed for IgG. One possibility explaining the much lower IgM titers is inhibition or cross-reactivity, i.e., competition of immune reagents elicited to similar/identical epitopes. Future experiments involving selective precipitation of serum IgG and subsequent IgM quantitation could shed further light on this issue. If IgG is indeed competitively blocking IgM binding to the target antigen, detectable IgM levels should increase.
in its absence. It is also worthy of note that the NS1 recombinant protein appears to have been proteolytically clipped which could also contribute to the lower elicited IgG and IgM responses.

Currently a number of vaccines are in development using recombinant proteins. Although recombinant protein vaccines can be more expensive to produce, not as immunogenic as natural pathogen proteins, and thus eliciting a less robust T\textsubscript{c} response, such an approach offers some advantage over live, attenuated or inactivated vaccines, e.g., stability, no need to use whole organisms, can be manipulated to increase immunogenicity, and no chance of mutation thus reversing attenuation as in live vaccines. Sanofi Pasteur (Lyon, France) is producing an attenuated recombinant yellow fever virus containing the Zika Envelop gene. Other biotechnology groups, e.g., Bharat Biotech (Hyderabad, India), and Protein Sciences Corporation (Meriden, Connecticut)\textsuperscript{[12]} are using viral surface antigen expression to induce immune responses. Although our data suggest that the Envelop protein appears to be the best vaccine candidate of the two antigens evaluated, the small but significant IgG response to NS1 could be very useful in discriminating previously vaccinated animals from those with active ongoing Zika infection which could be of significant diagnostic value.

As with all animal model derived data, there are serious limitations to human extrapolation, e.g., vaccination of rabbits was carried out using a mycobacterium adjuvant which is highly antigenic persisting much longer than other adjuvants\textsuperscript{[13]}. However, Mycobacterium adjuvants are banned for human use by the FDA due to toxicity, and can only be injected subcutaneously or intraperitoneally in animals due to complications that can arise via other routes. Alternatively, aluminum salt adjuvants are available for human vaccine development but could lead to lower antibody titers as they are not as persistent or antigenic. Additionally, in the rabbit model described here, booster immunizations were given every 2 weeks in contrast to the human in which booster immunizations are typically given several months to a year apart.

**Conclusion**

The Zika Envelop protein is a major viral surface protein involved in various steps of the viral life cycle. IgG titers produced in response to both Zika Envelop and NS1 recombinant proteins increased with each subsequent injection, i.e., 3 through 7; the peak NS1 IgG titer being roughly forty five-fold less than that observed for Envelop recombinant protein. IgM levels elicited by both Envelop and NS1 recombinant proteins were lower, i.e., at least 180-fold less than the IgG response to the Envelop recombinant protein. Early sequence and structural comparisons of the Zika Envelop protein with that of other flaviviruses suggest that overall the Zika Envelop protein is unique among flaviviruses, although parts of it resemble its homologs in West Nile, Japanese Encephalitis, and Dengue viruses\textsuperscript{[14, 15]}. Thus, additional evaluation must be carried out to 1) evaluate cross-reactivity of Envelop recombinant protein elicited antibody with other Flavivirus recombinant proteins, and 2) determine if the antibodies produced are effective at limiting Zika virus transmission. Data presented here support 1) the Zika Envelop protein's potential as a vaccine candidate\textsuperscript{[16, 17]} in a rabbit model and, 2) the usefulness of the NS1 IgG response in discriminating prior vaccine exposure from active viral infection as well as ELISA reagents.
Acknowledgements

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References


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Figure 1: SDS-PAGE analysis of Zika Envelop and NS1 recombinant proteins.

Figure 1: SDS-PAGE and sequencing analysis was carried out as previously described under 'Materials and Methods'.

Figure 2: Assessment of IgG elicited by recombinant Envelop and NS1 Zika Antigens.
**Figure 2**: NS1 and Envelop recombinant protein elicited IgG for different bleeds was determined as previously described under Materials and Methods. **Frame A**: Anti-serum raw absorbance values (closed squares = Envelop protein; closed triangles = NS1 protein). A Dilution factor of 1:60,000 and 1:1,500 for Envelop and NS1 recombinant protein was used, respectively. **Inset**: Rabbit IgG Standard Curve. A rabbit IgG titer strip was prepared as described under Materials and Methods and standard curve derived (y = 33.02x - 5.82). **Frame B**: Envelop and NS1 IgG titers as a function of post-vaccination time. The titer of elicited IgG was achieved by extrapolation to the standard curve (closed squares = Envelop titer, closed triangles = NS1 titer).
Figure 3: Assessment of IgM elicited by recombinant Envelop and NS1 Zika Antigens.

Frame A: Anti-serum raw absorbance values (closed squares = Envelop protein; closed triangles = NS1 protein). A Dilution factor of 1:600 and 1:300 for Envelop and NS1 recombinant protein was used, respectively. Inset: Rabbit IgM Standard Curve. A rabbit IgG titer strip was prepared as described under Materials and Methods and standard curve generated ($y = 33.03x - 1.35$).

Frame B: Envelop and NS1 IgM titers as a function of post-vaccination time. The titer of
elicited IgM was achieved by extrapolation to the standard curve (closed squares = Envelop titer, closed triangles = NS1 titer).

**Figure 4: Comparison of elicited IgG and IgM responses to Envelop and NS1 recombinant antigens.**

**Frame A:** Envelop protein elicited IgG (solid squares) vs. elicited IgM (closed triangles).

**Frame B:** NS1 protein elicited IgG (solid squares) vs. elicited IgM (closed triangles).

**Frame C:** Theoretical response

**Figure 4:** Comparison of observed to theoretical response. **Frame A:** Envelop protein elicited IgG (solid squares) vs. elicited IgM (closed triangles). **Frame B:** NS1 protein elicited IgG (solid squares) vs. elicited IgM (closed triangles). **Frame C:** Theoretical response.
Prevalence of Wolbachia Surface Protein (WSP) Antibodies in Humans and Animals

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Wolbachia is maternally inherited, intracellular bacterium found in ~40% of all insects, arthropods and all human filarial nematodes. In mosquitoes, the presence of Wolbachia causes conditional sterility and can inhibit the transmission of certain viruses, such as Zika, Dengue, Chikungunya, Yellow Fever, West Nile, as well as the infectivity of the malaria-causing protozoan, Plasmodium and filarial nematodes. Thus Wolbachia, a pandemic endosymbiont offers great potential for elimination of a wide-variety of devastating human diseases. The 26-kda Wolbachia surface protein (WSP26), is the most abundantly expressed antigenic protein of Wolbachia. To understand the role of Wolbachia in the etiology of parasitic disease and the potential modalities in flaviviruses vector control, it is necessary to develop tools to detect and measure WSP26 antibodies in animals and humans.

We have cloned, expressed and purified the WSP26 in E. Coli (>95% pure, ~26- Kda, His-tag). WSP26 was highly antigenic in rabbit and produced very high tittered antibodies. Recombinant WSP26 antigens and rabbit antibodies were used to develop a prototypic ELISA to detect antibodies in rabbit sera. The same method was adopted to detect basal levels of WSP26 antibodies in human and animal samples. Laboratory grown young mice (Balb/c, C57BL6, Swiss Webster) had negligible levels of WSP26 antibodies. Aged mice or retired breeder (>12-months) appears to have been exposed to some parasitic or insect containing Wolbachia as evident by elevated levels of WSP26 antibodies. A screening of limited samples of humans showed elevated levels of WSP26 antibodies in humans (~50%). The study also found variable prevalence (40-60%) of WSP26 in other animals (cats, dogs, chickens, bats, horse, bovine, pig, and camels). Availability of WSP26 antibody ELISA should help us understand the etiology and significance of WSP26 antibodies in the development and control of parasitic diseases.

Key Words: Wolbachia, Flavivirus, Parasitic disease.
**Chlamydia trachomatis** Pulmonary Infection Induces Inflammatory Pathology in MicroRNA Deficient Mice

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**Background**: *Chlamydia trachomatis* (Ct) causes pneumonia in both neonates by perinatal transmission and adults by person-to-person respiratory secretions. Anti-Ct host immunity strives to clear the infection but may result in collateral damage to tissue structure and function. Despite our knowledge of anti-Ct immunity in the lung model, there is very limited information on the role of microRNA (miR) regulation leading to tissue pathology following infection.

**Objectives**: The objective of this study was to determine the contribution of miRs in development of lung pathology.

**Methods**: Four to six week old male C57BL/6 wild type (WT) and miR-deficient mice were intranasally infected with *C. muridarum* (Cm- murine strain of Ct) and were monitored for disease progression (health monitoring). Histopathology was determined using hematoxylin and eosin (H&E) and microscopy based scoring techniques in infected lungs.

**Results**: Histo-pathological evidence suggested that Cm infection in miR-deficient mice resulted in significant alteration in lung architecture compared to WT mice by day 9 post challenge (2 way repeated measures ANOVA, P<0.05). Ag-specific immune cell trafficking was significantly regulated in miR-deficient mice compared to WT mice following Cm infection (ANOVA with Bonferroni correction, P<0.05).

**Conclusion**: These initial findings indicate a significant contribution of host miRs in regulating inflammatory pathology in Cm infected mice. Given the timings of these events, ongoing efforts in our laboratory involve correlating these findings with specific targets and pathways involved in miR-mediated pathogenesis.

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EXPERIENCE  AND  EFFECTIVENESS  OF  AN  OCCUPATIONAL  THERAPY  BASED  SLEEP  ENHANCEMENT  PROGRAM  ON  MILITARY  SERVICE  MEMBERS  AT  JOINT  BASE  SAN  ANTONIO

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Background: Since the onset of the Global War on Terror, a large number of active duty service-members (SM) have reported experiencing difficulties gaining adequate sleep or being dissatisfied with their sleep quality. Sleep difficulties experienced by this population may affect their ability to carry out the mission. For this reason, interventions, such as sleep hygiene, should be explored. To date, there are scarce studies evaluating the effectiveness of sleep hygiene on active duty service members, or studies exploring the barriers to adherence faced by service members, when attempting to establish new sleep behavior patterns. This study sets out to 1) determine how clinical sleep outcome variables (e.g., sleep environment, total sleep time, current sleep hygiene knowledge, etc.) are affected within a group receiving an occupational therapy (OT) based sleep hygiene intervention, 2) explore the relationship between sleep quality and perceived impact on occupational performance in military service members, and 3) identify the factors that challenge sleep hygiene adherence and impact sleep in military service members.

Methods: This mixed-methods study will recruit active duty SMs from Joint Base San Antonio (JBSA), Fort Sam Houston, that have a primary complaint of poor sleep quality or quantity. Study subjects will complete screening questionnaires at baseline to initially assess their key sleep characteristics, and their sleep behaviors will be monitored via a weekly sleep diary. All SMs will then receive two sessions of an OT based sleep hygiene program in a group setting. Each SM will be re-assessed at the conclusion at 3-weeks post-treatment. Approximately 20% of the SMs will be randomly selected to participate in a semi-structured qualitative interview to explore their perceptions of the relationship between sleep and their occupational performance.

Results: Data collection and recruitment into this study is ongoing.

Discussion: Adoption of new sleep behaviors and practices can be difficult when faced with high professional demands, limited control over one's daily schedule, and minimal ability to modify one's sleep environment. Understanding the unique factors associated with limited adherence will help therapists alter the method in which sleep hygiene interventions are delivered with this population, as well as assist in establishing realistic sleep modification goals.

Conclusion: The resulting product of this study may add to the greater body of knowledge, improve occupational therapy practice, and advance the implementation of the U.S. Army's Performance Triad initiative. Full completion of this study is needed for full data analysis and determination of specific factors for adherence.

Keywords: Sleep Hygiene, Occupational Performance, Military
Abstract: Neurocysticercosis (NCC) or cerebral infection by the larval stage of the pork tapeworm Taenia solium is the main cause of acquired-epilepsy in developing countries and an important neglected parasitic disease in the US. A mixed Th1/Th2 develops in the brain, contrasting the canonical Th2 pathway associated with peripheral helminthic infections. Notably, when comparing disease susceptibility of BALB/c and C57BL/6 mice, we found that disease progression was more severe in BALB/c mice, correlating with increased parasite burdens and enhanced macrophage infiltration. However, eosinophil infiltration was indifferent between the two strains. It is still enigmatic what the contribution of the macrophage population is during NCC. Our aim is to compare the innate and adaptive immune response in the absence of inflammatory macrophages, utilizing CCR2-deficient mice, and assess their role in brain pathology. Our results show that C57BL/6 mice lacking macrophages exhibited increased disease susceptibility. Therefore, we hypothesize that macrophages skew the immune response towards a Th1 pathway in BALB/c mice but contribute towards a protective Th2 pathway in C57BL/6 mice. To test our hypothesis, we will characterize the immune effector phenotype of the sorted macrophage population from infected brains. Furthermore, in efforts to eradicate the infection with minimal damage to nervous tissue we propose to test the effect of blocking infiltration of eosinophils to the brain prior to administration of anti-parasitic drugs. These studies will provide a clear understanding of the role of macrophages during murine NCC with potential translational applications for use of combination therapies for the management of NCC.
Abstract: Filoviruses are highly infectious, with no FDA-approved drugs available for their treatment. The last Ebola virus outbreak killed about 11,000 people and highlighted the lack of and a need for new anti-filoviral drugs and therapies. Most efforts to find such drugs have involved only a few strains of Ebola virus and testing relatively small drug libraries or compounds that have shown efficacy against other viruses or diseases. A requirement to handle these viruses at biosafety level 4 (BSL-4) is another bottleneck in these efforts. Here we report the first and largest high-throughput screening of 319,855 small molecules from the MLSMR library against Marburg virus and Ebola virus. We developed and used a quantitative, high throughput screening platform based on high resolution microscopy to determine the mechanism of action of entry inhibitors. Nine of the most potent, novel compounds that blocked infection by both viruses were analyzed in detail using this platform. The compounds inhibited known key steps in Ebola virus infection mechanism by blocking either cell surface attachment, macropinocytosis-mediated uptake or endosomal trafficking. Each inhibitor was active in primary human macrophages thereby demonstrating their potential to be developed as drugs.
VESTIBULAR DYSFUNCTION AND DIZZINESS IN POST-9/11 VETERANS: A CHRONIC EFFECTS OF NEUROTRAUMA CONSORTIUM STUDY

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Background

It is well established that the vestibular system is particularly sensitive to traumatic brain injury (TBI). Dizziness is one of the most commonly reported clinical symptoms, affecting 20-30\% of the general population, and the cause is often associated with vestibular (inner ear balance) dysfunction. A prominent complaint after TBI, it is difficult to disentangle vestibular problems caused by the TBI itself from those of direct sensory organ trauma without specialized vestibular assessment. Those that report chronic complaints of vertigo/dizziness report increased personal and health care burden and decreased quality of life. The purpose of this study was to describe the prevalence of vestibular dysfunction and dizziness and explore their associations with TBI and common associated comorbidities in a cohort of Post-9/11 Veterans.

Materials & Methods

This retrospective observational study used data from the national Veterans Health Administration (VA) data repository from fiscal years 2001 through 2014. Individuals with at least three years of VA care, with one or more years of care in 2007 or after, were included in the analysis. We
identified comorbidities that may be associated with vestibular dysfunction and/or dizziness in inpatient and outpatient data using diagnosis codes entered during VA care. We then completed two logistic regression analyses, one each for vestibular dysfunction and dizziness.

Results

Among all Post-9/11 Veterans who received VA care during the study period, 570,248 met inclusion criteria for this study. Of these, 0.45% were diagnosed with vestibular dysfunction and 2.57% with non-specific dizziness. Women and individuals over 27 were significantly more likely to have vestibular dysfunction or dizziness. An individual with vestibular dysfunction or dizziness was approximately 16 times more likely to have the other. Those with either vestibular dysfunction or dizziness were significantly more likely to have hearing loss, tinnitus, headache, balance problems, or cerebrovascular disease. Relative to those with no TBI, every severity of TBI was significantly more likely to have comorbid dizziness; conversely, only those with moderate/severe TBI were significantly more likely to have a vestibular dysfunction diagnosis. Lastly, those with dizziness, unlike those with vestibular dysfunction, were more likely to have post-traumatic stress disorder, depression, cognitive problems, or visual problems.

Conclusions

While there were many similarities among those with vestibular dysfunction and dizziness, there were also notable and clinically relevant differences. However, the two conditions differed in that those with vestibular conditions were more likely to have moderate/severe TBI while those with dizziness were more likely to have any severity of TBI, relative to those with no TBI. There is likely overlap in individuals with vestibular dysfunction and those with dizziness; that is, many patients with dizziness don’t undergo vestibular assessment, and thus, are not identified as having a vestibular condition. Although dizziness is a common clinical complaint, it is more likely to be associated with mental health problems, a broader array of common post-concussive complaints, and all severities of TBI than those with more specific vestibular dysfunction diagnoses. These findings underscore the need for more thorough vestibular testing among those with dizziness.

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Disclosure Statement

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BENZODIAZEPINE USE AMONG LOW BACK PAIN PATIENTS CONCURRENTLY PRESCRIBED OPIOIDS IN THE MILITARY HEALTH SYSTEM BETWEEN 2012 OR 2013

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Background: Dramatic increases in the amount of opioids prescribed for chronic non-cancer pain, particularly low back pain, exist among those served by the military health care system. The combination of opioids and benzodiazepines poses numerous safety risks for the patient including respiratory suppression, oversedation, and overdose. In a large national sample of veterans, risk of fatal overdoses increased when opioids and benzodiazepines were concurrently prescribed. Despite the justified concerns regarding the abuse liability and the long-term safety and efficacy of opioids for chronic pain, they continue to be commonly prescribed with benzodiazepines. For example, one study report that 18-38% of patients with an opioid prescription received a benzodiazepine. These high-risk prescribing patterns have contributed to the fatal overdose epidemic. There is scant evidence regarding opioid and benzodiazepine prescribing practices among active duty service members with low back pain. It is important to understand factors associated with benzodiazepine use in this population to identify those most vulnerable to safety issues. To this end, we investigated factors associate with concurrent opioid and benzodiazepine prescribing among active duty service members with non-malignant low back pain who started their first opioid episode in 2012 or 2013.

Materials and Methods: Study population included active duty service members: (1) not deployed at the time of care, (2) diagnosed with non-malignant low back pain and (3) received their first documented opioid prescription in the military health system in 2012 or 2013. Analyses were conducted on a de-identified dataset created by the Data Discovery, Analytics, and Research (DDAR) team within the Enterprise Intelligence Section (EI) within the Defense Health Agency (DHA) that was derived from the Military Health System Mart (M2). The dataset was approved by the institutional and Department of Defense regulatory agencies. A logistic regression analysis was conducted to examine the use of benzodiazepine with the following variables: sociodemographics, opioid characteristics, psychiatric and physical factors.

Results: The cohort was 42,253 active duty service members receiving opioids with a low back pain diagnosis. Overall, the sample was predominantly male (78.54%), and half were between the ages of 18-25 years olds (50.04%). The most common service branch was Army (51.72%). Results from logistic regression analysis indicated individuals prescribed a benzodiazepine were significantly more likely to be prescribed at least one long acting opioid: 1.71 CI[1.46, 1.99] versus short-acting, receive chronic opioid therapy (>90 days): 2.39 CI[2.24, 2.56], and also have been prescribed an antidepressant: 2.07 CI[1.89, 2.28]. Additionally, those prescribed a benzodiazepine were significantly more likely to be diagnosed with a substance use disorder: 1.29 CI[1.13, 1.47].

Conclusion: Our findings suggest that differences in patient characteristics across a variety of domains may raise safety concerns and quality of care issues. The results are consistent with previous
findings among both US veterans and civilian populations. To our knowledge, this is among the first to examine factors associated with benzodiazepine use in a low back pain population receiving opioids.

Keywords: opioids, benzodiazepine, and low back pain

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**In Vivo Regenerative Response Enhanced In Critical Size Bone Defects Using High Performance Micro Environments**

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Bone marrow mesenchymal stem cells (BM-MSCs) therapies are a common treatment of non-union fractures since they have been shown to promote tissue repair and regeneration due to their ability to immunomodulate the microenvironment, stimulate angiogenesis, and give rise to multiple cell types. To improve the functionality of recruited BM-MSCs in a wound-healing environment in vivo, a cell culture substratum referred to as High Performance Micro Environment (HPME) was generated using bone marrow stromal cells. **The objective of this study is to observe if the High Performance Micro Environment (HPME) is conducive to bone defect healing in a critically sized rat model defect as analyzed by µCT methods.**

**Methods:** *Animal model and critical sized defect:* A critical sized femoral segmental defect (6mm) was created in the right femur of skeletally mature Sprague Dawley rats (4mo/old). Experimental femurs were stabilized by a polydactyl plate (27x4x4mm) held together by six threaded Kirschner wires. Two different groups were analyzed: A) Defect filled with Medtronic™ Mastergraft® granules and B) Defect filled with Mastergraft® and HPME. Groups also had a Cytoplast® collagen wrap around the defect site. Animals healed for either 4 or 8 weeks (n=7). µCT analysis: Following the harvesting of the experimental femurs, they were scanned using microcomputed tomography SkyScan1076 scanner at a spatial resolution of 8.77µm. Bone Volume and Polar moment of inertia were obtained, all data was analyzed by a two-way ANOVA followed by Tukey's test for post hoc analysis of significance.

**Results:** All the samples maintained bone stability and showed continued healing within the animal model during radiographic observation (Fig 1). Functional regeneration was measured by the polar moment of inertia from µCT analysis, and it was found that both groups exhibited significant increases (p<0.01, Fig 2A). There was significant increase in bone regeneration from 4 to 8 weeks in the presence of HPME (p=0.017, Fig 2B).

**Discussion:**

- While there is regenerated bone volume increase in both groups, there is a
significant increase in the rate of bone regeneration from 4 to 8 weeks in the group containing HPME.

- Both groups exhibit a significantly more functional bone organization at 8 weeks than at 4 weeks as measured by PMI.
- Results suggest that continued regenerative activity is maintained in critical sized defects by the addition of HPME.

References

UTILITY OF THE SIMPLIFIED AUTOMATED VENTILATOR II AS A TRANSPORT VENTILATOR IN A COMBAT-RELEVANT MODEL OF LUNG INJURY

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Introduction: Mechanical ventilation (MV) is a life-saving intervention which has revolutionized critical care. A rarely discussed concept in mechanical ventilation is the belief that less sophisticated ventilators provide inferior care than more sophisticated machines. We undertook testing of a small, portable ventilator, the Simplified Automated Ventilator II (SAVeII, Automedx, Coppell, TX), during in vivo studies of combat-relevant trauma and en-route care, in conjunction with extracorporeal membrane oxygenation therapy (ECMO). The SAVeII is a compact, turbine-powered, battery operated ventilator, designed for field and pre-hospital use. We hypothesize that the SAVeII provides equivalent care to a state-of-the-art standard ICU ventilator during ground-level and high-altitude en-route care.

Methods: Female, non-pregnant, Yorkshire swine (n=7, 52.34±1.17 kg) underwent a model of combat-relevant trauma treated with ECMO. The study occurred over two consecutive days, in healthy state on day one, and in injured state on day two. Animals received time-cycled, volume-controlled, pressure-limited ventilation with a state-of-the-art ICU ventilator (Dräger V500, Dräger Medical, Lübeck, Germany). Animals then received ECMO via the Cardiohelp ECLS device (Maquet Gmbh, Rastatt, Germany), connected to a 23 Fr. dual lumen catheter (Avalon Elite, Maquet Gmbh, Rastatt, Germany) placed in the right jugular vein. Once ECMO was initiated, MV support was decreased to approximately 50% of baseline levels (8.00±0.28 Lpm vs. 3.58±0.50 Lpm minute ventilation before and after ECMO, respectively). Animals were then transferred to the SAVeII ventilator for the transport phase. Ventilator settings were matched to the V500 as closely as possible. Animals underwent a standardized flight profile: 30 minutes each at ground level, 5000ft., and 8000ft., 5 minutes 3000ft., 30 minutes 5000ft. After altitude exposure, animals were returned to the ICU overnight. The next morning, bilateral pulmonary contusions were inflicted, followed by chest tube placement. The travel and flight was repeated in injured state.

Results: There were no device complications or device errors noted. There was no degradation of support evident when comparing the ventilators, and PaO\textsubscript{2}:FiO\textsubscript{2} ratios were similar before and after application of the SAVeII. Analysis revealed no significant difference between measured and set ventilator values on the SAVeII when compared to the ICU ventilator. Differences were identified in heart rate (123±10 vs. 100±19 before vs. after SAVeII), mean blood pressure (87±4 vs. 81±3 after flight, SAVeII vs. ICU vent), and ETCO\textsubscript{2} (29±3 vs. 36±4, after flight, SAVeII vs. ICU vent), and only in animals in healthy state.

Conclusion: In this pilot study the SAVeII ventilator was found suitable for transport applications during ground and high-altitude evacuation. We did not encounter any issues with utility of this ventilator, and find it adequately equivalent to a reference ventilator. The uniqueness of this data is that it utilized the ventilator as an adjunct; the ECMO system provided significant off-loading of CO\textsubscript{2} and O\textsubscript{2} supplementation. The latter provided for large (circa 50%) reductions in ventilator settings and thus our
results and conclusions are pertinent to the utility of the SAVeII when ventilator settings are reduced. Future studies should involve additional data collection and equivalency testing for the SAVeII during critical illness and without concomitant use of ECMO.

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Host MicroRNAs Enhance Susceptibility to *Chlamydia trachomatis* Pulmonary Infection

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Background: *Chlamydia trachomatis* (Ct) is an obligate intracellular pathogen which infects mucosal surfaces including the eye, lung and genital tract. Primary and chronic infections in humans and animals are associated with immune responses, which aid in pathogen clearance.

Objectives: The objective of this study was to determine the role of miRs in bacterial colonization in lungs following intranasal infection with Ct.

Methods: Four to six week old C57BL/6 wild type (WT) and miR-deficient mice were intranasally infected with *C. muridarum* (Cm- murine strain of Ct) and were monitored daily for disease progression (percent body weight change). Mice were anesthetized and euthanized by cervical dislocation at day 9 post infection. The lungs were collected and homogenized in Dulbecco’s modified eagle medium (DMEM). Bacterial burdens in homogenates were quantified using immunofluorescence assays (cell cultures) and real time PCRs (DNA) targeted for detection of Cm.

Results: Pulmonary Cm infection in miR-deficient mice resulted in significant increase in bacterial burden compared to WT mice at day 9-post challenge (ANOVA with Bonferroni correction, P<0.05). Ag-specific IFN-γ immune response was significantly altered in miR-deficient mice compared to WT mice upon infection.

Conclusion: These findings indicate a contribution of host miRs in regulating bacterial clearance in Cm pulmonary challenged mice. Current ongoing investigations include determining the specific immune molecules involved in bacterial colonization in infected lungs.

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TRAJECTORIES OF COMORBIDITY IN IRAQ AND AFGHANISTAN WAR VETERANS: LONG-TERM HEALTH OUTCOMES ASSOCIATED WITH BRAIN INJURY SEVERITY

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Background

Prior studies examining traumatic brain injury (TBI) and associated comorbidities have been largely cross-sectional, with few evaluating the combined effects of TBI, PTSD, and chronic pain. Longitudinal assessment of TBI and functional recovery is critical given the often variable presentation and recovery patterns of post-concussion symptoms. In this study, we sought to determine how TBI severity is associated with self-reported symptoms of health and pain, somatization, and measures of mental health 5-7 years after entering Veterans Administration (VA) care.

Materials & Methods

A prospective longitudinal survey was conducted with individuals from a longitudinal cohort of Post-9/11 Veterans using a random sample stratified by comorbidity trajectories previously identified using latent class analysis (N = 9358). Surveys included measures of physical health status (recent overall health, pain ratings, and somatization) and mental health (post-traumatic stress disorder and depression symptomology). TBI severity was defined using an algorithm that incorporated data from the Department of Defense Trauma Registry, VA TBI screening and comprehensive evaluation, and VA health system data (resulting in categories of no TBI, Screen Positive Only (from the VA TBI screening), mild, moderate/severe, penetrating, and unclassified TBI). We first used bivariate models to examine outcomes among individuals by TBI severity. Then, we used generalized linear models (GLM) to assess the unique contribution of TBI severity to long-term outcomes among Post-9/11 Veterans controlling for demographic and military characteristics, deployment experiences, and comorbidity trajectory.
Results

Response rate for the survey was 23% (n = 2046). In bivariate analyses, individuals who had experienced No TBI or penetrating TBI reported significantly better overall health, pain ratings, somatization scores, PTSD symptomology, and depression scores than all other TBI severities. However, GLM analyses controlling for demographic and military characteristics, deployment experiences, and comorbidities found that many of these differences were no longer statistically significant. Among the physical health measures, the only significant differences that remained were those with moderate/severe TBI relative to those with no TBI on the somatization measure. On the post-traumatic stress disorder measure, the analysis revealed that those with unclassified TBI had significantly higher symptomology than those with no TBI.

Conclusions

This study provides insight into long-term physical and mental health outcomes associated with TBI in Post-9/11 veterans and suggests that TBI continues to have a negative impact on outcomes, even after controlling for comorbidity, deployment experiences, and sociodemographic characteristics. However, our data also suggest that those with moderate and unclassified TBI seem to fare significantly more poorly than those with no TBI once these covariates are considered. Additional research is required to fully explicate what appear to be complex interactions among TBI severity, physical and mental well-being, combat exposures, and socioeconomic resources in this population.

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**SPATIALLY CONTROLLED MECHANICAL PROPERTIES FOR MUSCULOSKELETAL ENTHESES**

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**Introduction:** The transition or enthesis between musculoskeletal tissues provides a unique challenge for researchers trying to create synthetic grafts that are viable alternatives to gold standard autografts. The importance of the substrate stiffness on cell response requires choosing materials that mimic the mechanical properties of the native tissue. The enthesis between bone and ligament requires a distinct transition between the compressive stiffness and tensile strength of the tissues respectively. Hydroxyapatite (HA) has been utilized for bone grafts because its compressive properties are adequate (1). However, HA does not possess the needed tensile strength for ligaments. Researchers have either sought to develop combinations of materials to create an enthesis, or have ignored the enthesis using one material with ligament properties and the addition of osteoconductive coatings. These often lead to failure at the junction between the materials or within the bone tunnel in vivo due to the lack of tissue integration. Another challenge of the native enthesis between bones and ligaments is that it occurs within less than one millimeter and has four distinct regions (2). The goal of this project is to mechanically tune the properties of one continuous graft, thereby creating a strong enthesis.

**Methods & Results:** Our chosen material, silk, has a tunable secondary protein structure. Silk fibroin is also known to be biocompatible, biodegradable and non-immunogenic (3). To treat the silk grafts, aqueous silk fibroin is aliquoted into a cylindrical mold, frozen and lyophilized (4). The cylindrical silk graft is then placed vertically in an acrylic model attached to a peristaltic flow loop. The model is filled with methanol to specific levels to treat the bone and ligament portions of the graft in accordance with previously determined timeframes for bone (Figure 1A) and ligament (Figure 1B) properties. The enthesis is formed by treating the section between the bone and ligament portions for timeframes at intervals between the bone and ligament treatments (Figure 2).

**Conclusion:** By eliminating the need for bonding or physically merging two separate materials to form an enthesis, this research decreases the complexity and failure rate of synthetic musculoskeletal grafts by having one material with properties mimicking the native enthesis.

**References:**

LOW DOSE rhBMP-2 DELIVERY FROM HYDROXYAPATITE-COLLAGEN SCAFFOLDS EFFICACIOUS FOR DELAYED RESTORATION OF CRITICAL Sized CALVARIAL MODEL

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Background: Craniomaxillofacial (CMF) injuries cause disfigurement and dysfunction, diminishing quality of life and contributing to social and economic burdens. In recent years there has been a growing interest on stimulating new bone formation using growth factors such as recombinant human bone morphogenetic protein 2 (rhBMP-2) in addition to already used osteoconduction techniques. Clinically available rhBMP-2 delivery devices are far from ideal because they employ burst release of supra-physiological doses of rhBMP-2 to achieve a robust osteogenic effect, introducing concerns related to the risk of ectopic bone formation, severe inflammation, safety and cost. Reconstruction of large segmental defects in the craniofacial skeleton has classically been challenging, especially in secondary reconstruction, where definitive bone reconstruction is attempted at a later time than that of defect creation. Consequently, controlled rhBMP-2 delivery mechanisms might be needed in chronic defects to yield the same clinical results as in acute defects. To evaluate the capability of a novel treatment of controlled delivery of rhBMP-2 and the clinical challenge in the delayed healing clinical setting, the objective of this study was to evaluate bone regeneration in a delayed healing rat calvarial critical size defect model. Using this model evaluated a drug delivery mechanism in which the location and time rhBMP-2 is controlled; therefore, controlling the location where bone is regenerated.

Materials and Methods: Poly(lactic acid) (PLA) microparticles encapsulating rhBMP-2 were synthesized using water-insolvent emulsion evaporation technique and then attached to hydroxyapatite-collagen scaffolds using gas plasma discharge and microparticles deposition. rhBMP-2 release profiles and bioactivity of the delivery platforms were evaluated in vitro. Moreover, osteogenic differentiation of human embryonic palatal mesenchymal (HEPM) cells in response to rhBMP-2 delivered were evaluated in vitro. Using different doses and rhBMP-2 locations, the delivery platforms were then evaluated in a critical size delayed healing model in the rat calvaria comparing them to clinical standards using µCT analysis.

Results: In vitro results indicated successful encapsulation of rhBMP-2 in the PLA microparticles, as well as platform stability and retention of activity of the encapsulated growth factor for 8 weeks. Regenerated bone volume of the treated rat calvarial defects was evaluated postmortem using µCT analysis to visualize high resolution detail of regenerated bone. For bone callus, clinical control group was significantly lower than all other groups at 4 and 8 weeks. Interestingly, we observed significant bone formation at weeks 4 and 8 using approximately 4% and 20% of the clinically recommended rhBMP-2.
dose. Location, quality and quantity of bone regenerated of low-dose rhBMP-2 groups were compared to clinical control, showing improved performance for the low-dose rhBMP-2 groups.

**Conclusions:** In this study we evaluated a novel treatment of controlled rhBMP-2 delivery in the clinically challenged delayed healing in rat calvarial model. Our results suggest that by increasing the local residence time of BMP-2 at the site of the injury it is possible to reduce the therapeutic dose, bringing down not just the cost of the therapy but also potentially increasing its therapeutic efficacy. Other strategies including multiple growth factors should be considered in the future.
BONE HISTOMORPHOMETRIC ASSESSMENT OF DISTANT BONES IN A RAT MODEL FOLLOWING A CREATED NON-UNION DEFECT

Alejandro L Morales Betancourt, Sergio Montelongo, Teja Guda, Mark Appleford.

In the United States 65.8 million of musculoskeletal injuries occur annually, this represents treatment costs of $176.1 billion. In average, US population will suffer two bone fractures during their life term. Initial fractures could potentially lead to secondary fractures due to loss of bone density that may alter bone properties. Yet, the causal mechanism relating it to the healing process is unclear. The present study evaluates the osteocyte lacunar and Haversian distribution in different sites along the skeleton to find a correlation between bone density loss and lacunar canaliculi network (LCN) reorganization to preserve skeletal homeostasis. A critical sized (6mm), non-union defect was created in the right femur of 42 rats. Each animal received one of three implants treated to different mineral concentrations. The rats were evaluated after 2 and 4 weeks. Left femur, right and left arms, iliac crest, calvaria and vertebrae bones were harvested from each animal to investigate remote effects during the healing process. Preliminary assessments using microCT scanning revealed that bone loss occurred primary in long bones. The samples were treated with histological techniques followed by software evaluation (BioQuant Osteo, Nashville, TN) of thickness, volume, Haversian canal area, and distribution of Osteons and osteocytes in the cortical architecture of long bones, as well as volume and strut analysis of trabecular architecture on flat bones. It has been discovered that long bones show a reduction in bone density, and the cellular activity behind is unrevealed. This investigation will provide the opportunity of predicting mineral deficit at certain remote skeletal sites as a result of fracture healing, and the potential ability to reduce remote secondary fracture risks through supplemental treatments that target those sites. Partially funded by NIH GM007717.
RANDOMIZED CROSSOVER STUDY OF TRAINING BENEFITS OF LOW-FIDELITY ECMO SIMULATION VERSUS ANIMAL MODEL - AN INTERIM REPORT

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Background: Extra-Corporeal Membrane Oxygenation (ECMO) is a classic low-volume, high-risk procedure that allows for long-term heart-lung bypass. As advanced pulmonary and cardiovascular support measures evolve, fewer patients are requiring ECMO, limiting a provider’s exposure to ECMO initiation and management of life-threatening emergencies. Historically, animal models have been the gold-standard for ECMO training due to their ability to replicate complex physiology and anatomic variation. Recently ECMO simulation models have become more sophisticated and are increasingly incorporated into routine training, however no study has directly compared which modality is best suited for optimal emergency ECMO skills proficiency, safety and teamwork training. We hypothesize that the animal model will be superior for advanced providers in a subset of complex tasks while simulation may be superior for junior providers in mastering basic emergency maneuvers.

Materials and Methods: 64 trainees representing 4 clinical disciplines will complete a pre-lab didactic session. The trainees will be randomly assigned to Track A (animal lab 1st; simulation 2nd) or Track B (simulation lab 1st; animal 2nd). Our ECMO simulator is a state-of-the-art cannulation task trainer embedded into a low-fidelity mannequin, which is connected to our standard ECMO circuit. Fogg simulator transducers and Laerdal® display software will be utilized to provide real-time vital sign and pressure measurements. 7 unique ECMO scenarios will be timed for task completion and performance will be objectively evaluated using a standardized assessment tool. The results will be analyzed and stratified by discipline using software designed to compile results and control for inter-rater reliability. Participants will also complete a pre/post lab self-assessment survey and pre-lab cognitive questionnaire regarding ECMO management principles that were covered in the pre-lab didactics.

Results: To date, all performance checklists and training aids have been developed for each of the 7 scenarios. A didactic package incorporating power-point and video files has been developed. Video of each scenario was recorded to establish inter-rater reliability among observers. A realistic SynDaver™ vascular access pad ECMO Cannulation Model has been developed and refined to provide anatomically and functionally accurate cannulation opportunities for the low-fidelity simulation arm. To date, we have enrolled 29 participants in the study with 13 participants completing both the simulation and live-tissue labs.

Conclusion: Data collected is periodically reviewed with the intent of conducting an interim analysis after 50% of participants have been enrolled, randomized, and participated in their first study arm. We anticipate this study will help determine if animal or simulation ECMO training is best suited for optimal emergency ECMO skills proficiency, safety and teamwork training. Furthermore, the data may
further reduce the need for ECMO animal training by identifying its greatest strengths so that its scope may be narrowed to more targeted provider experience levels and specific physiologically complex scenarios in an evidence-based fashion.

Acknowledgements: The views expressed herein are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army or the Department of Defense or the U.S. Government. This study was reviewed and approved by the Brooke Army Medical Center Institutional review board and determined to be exempt research. This study has been conducted in compliance with the Animal Welfare Act and the principles of the Guide for the Care and Use of Laboratory Animals. The authors acknowledge the simulation center at Brooke Army Military Center for their dedication.

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**Regulation of Host MicroRNAs in *Chlamydia muridarum* Infected McCoy Cells**

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**Background:** The hallmark of genital chlamydial infection is the development of upper genital tract pathology in the form of hydrosalpinx and oviduct and/or tubal dilatation. Although molecular events leading to genital tissue exacerbation and cellular architectural remodeling are unclear, establishment of a robust infection early on and the induction and/or dampening of host molecules and pathways are critical for establishment of long term effects of infection. A better understanding of these processes are crucial for designing better strategies to abrogate chlamydial infection.

**Objectives:** In our initial reports, we established the contribution of *Chlamydia muridarum* (Cm) associated microRNAs (miRs) in bacterial colonization, pathogenesis and anti-Cm immunity at early stages of infection (day 6 post intravaginal Cm challenge in C57BL/6 mice). The objective of our current study was to determine the cell-specific regulation of selected cohorts of miRs found to be regulated in Cm infected genital tissues.

**Methods:** McCoy cells (ATCC® CRL-1696™) were infected with Cm EBs and by 24 hrs post infection collected for RNA extraction. Using miR specific PCRs assays, we determined the effect of Cm on regulation of downselected miRs in infected McCoy cells compared to mock infection.

**Results:** We observed distinct cohorts of miRs regulated compared to mock infection. Amongst these, miR-9, -16, and -29 previously reported by us and others, were found to be altered upon infection. While not much is known about the specific role of these miRs in chlamydial colonization *in vitro*, our ongoing studies include determining the direct effect of these miRs on targets that contribute to chlamydial infectivity.

**Conclusion:** This study provides evidence for regulation of specific miRs in cells which are highly conducive to Cm infectivity and may aid chlamydial colonization.

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OPTIMIZATION OF SILK HYDROGELS FOR CELL DRIVEN EXTRACELLULAR MATRICES
Mubeen Sultana, Joseph J. Pearson, Paul E. Dowell, and Teja Guda

Introduction: Expenditure for both type I and II diabetes was estimated around $245 billion in 2013. Type I, autoimmune-induced diabetes requires frequent insulin injections and has no long-term cure. Complications related with Type I diabetes include HHNS (hyperosmolar hyperglycemic non-ketotic syndrome), stroke, DKA and ketones, neuropathy, nephropathy high blood pressure, blindness and gastroparesis. There is currently no solution available for this pathology, but researchers are trying to find a cure by “resetting” the destruction caused to the pancreatic islets in Type I diabetes through transplantation. However, the efficiency of allograft transplantations is very low because of low transplantation viability and acute immune responses resulting in low survival and therapeutic efficacy. Here we propose to examine the efficacy of a natural polymeric silk-based hydrogel to encapsulate host stem cells and potentially create a protective layer for pancreatic islet transplants.

Methods & Results: Silk is known for desirable biocompatible properties and high mechanical integrity. Silk hydrogels in particular are biocompatible, can be chemically modified, and designed to have a slow degradation rate. In this study, we optimized different concentrations of silk solutions to evaluate the mechanical properties of the resulting silk hydrogels and to determine the effect of silk concentration on cell response. Silk cocoons were processed by boiling in sodium carbonate and then dissolved in lithium bromide. The dissolved solution was dialyzed with water resulting in a silk and water solution. The solution was then frozen, lyophilized and rehydrated twice before forming hydrogels. The water and silk solution was able to form a hydrogel through sonication, vortex treatment and electrical stimulus. However, we tried to decrease the gelation time by using different combinations of the polymerization stimulus. It was determined that two minutes of sonication, followed by five minutes of vortex treatment resulted in repeatable, consistent hydrogel formation. The hydrogels were characterized using scanning electron microscopy, Fourier transform infrared spectroscopy and rheology for morphological, relative beta-sheet proportion and mechanical properties respectively (Figure 1).

Conclusion: These results displayed consistent properties throughout the various groups tested. Future in vitro studies will determine the effect of the silk concentration on mesenchymal stem cell response and the suitability of silk as a protective material for islet transplantation.

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VALIDITY OF DEMENTIA AND COGNITIVE DISORDER DIAGNOSES IN A SAMPLE OF IRAQ AND AFGHANISTAN VETERANS AS DETERMINED THROUGH REVIEW OF MEDICAL CHART EVIDENCE

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Background
The prevalence of dementia and cognitive disorder diagnoses among Iraq and Afghanistan Veterans (IAV) has steadily increased over the past decade. The purpose of this study was to determine the validity of these diagnoses in electronic medical records and describe the prevalence of mental health (MH) and Traumatic Brain Injury (TBI) service connected disability among the IAV who have received them.

Materials and Methods
We obtained data from the national Veterans Health Administration (VA) data repository to identify a cohort of IAV who received a dementia or cognitive disorder diagnostic code two or more distinct times (at least one week apart) during fiscal years 2001-2014. Under the guidance of three board-certified neuropsychologists, we built a chart abstraction tool to collect data from medical records necessary for determining the validity of dementia/cognitive disorder diagnoses. Chart abstractors and neuropsychologists reviewed data for evidence supporting a diagnosis, such as neuropsychological testing, or an injury/condition prohibiting or negating the need for cognitive testing such as severe TBI or Huntington’s disease. We also looked for brain imaging, origin of diagnosis, MH and TBI service connected disability (SCD), and, in cases that included a neuropsychological assessment, team neuropsychologists reviewed the associated medical note to determine if the diagnosis was supported by the results summarized in the author’s report of that assessment.

Results
Of the 400 Veterans in our cohort, we determined 36% (n=143) had a valid diagnosis based on evidence in their medical records. Neuropsychological assessment supporting the diagnosis was found in 80% of those validated cases. The cases determined to have non-validated (61%) or questionable (3%) diagnoses either contained no evidence of formal neuropsychological/cognitive testing, test results were invalid due to failures on objective performance validity measures, or the results of a comprehensive neuropsychological assessment contradicted the diagnosis after its origination with another clinician or visit. Of the overall cohort, 77% had SCD for MH conditions and 30% had SCD for TBI. Of the non-validated cases, 82% were service connected (SC) for MH and 28% were SC for TBI. Of the valid cases, 66% were SC for MH and 34% SC for TBI, respectively.

Conclusions
We found 64% of this cohort did not have a cognitive disorder or dementia diagnosis that could be validated. In-depth chart abstraction highlighted factors associated with cognitive diagnoses in need of closer investigation including MH, medications, TBI, and diagnostic practices. The prevalence of MH SCD among this sample signifies MH as a common modifiable factor in treating cognitive complaints in
this cohort. Many non-validated cognitive disorder or dementia diagnoses appeared to be based upon patient self-report of cognitive complaints rather than objective medical evidence and formal neuropsychological testing. Importantly, the perceived prevalence of cognitive impairment and dementia among IAV is distorted by incorrect diagnoses. Of consequence at an individual level, attachment of an inaccurate diagnosis of cognitive disorder or dementia may obstruct a patient’s course of appropriate treatment and/or potential for improved cognitive functioning.

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Disclosure Statement

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PHENOTYPE AND TRANSCRIPTOME ANALYSIS OF CENTRAL NEURONAL AND GLIAL POPULATIONS IN MULTIPLE SCLEROSIS

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BACKGROUND: Investigation of the cellular and molecular mechanisms of neurodegenerative diseases is hindered by the simple fact that central nervous system (CNS) tissue is difficult to obtain from patients without risk of disability. Strategies have traditionally utilized animal models or human post-mortem or CNS biopsy tissue. However, human induced pluripotent stem cells (iPSCs) can be derived from multiple tissue sources, including skin or blood (reviewed in Lewandowski et al., 2016). From such minimally invasive processes, a disease of interest can be modeled in vitro, allowing cells derived from patients with the disease to be compared to those derived from healthy controls.

Multiple sclerosis (MS) is the quintessential autoimmune demyelinating disorder of the CNS. Autoimmune relevance is congruent with animal models, genomic studies, and the mechanisms of action of effective therapeutic agents. However, a unifying understanding of the etiology of MS is lacking (Rae-Grant et al., 2013). What is clear is that over time, MS leads to areas of degeneration in both white and grey matter of the CNS, which correlate with disability. These lesions allow an avenue for regenerative cell-based therapies in MS. Here, we test the hypothesis that intrinsic differences in the biology of resident CNS cell populations allow development of an inappropriate inflammatory process leading to MS.

MATERIALS & METHODS: The study protocol has been approved by the Institutional Review Board of the 59th Medical Wing, Lackland Air Force Base, TX. Subjects with a confirmed diagnosis of MS are being recruited from the San Antonio Military Medical Center Neurology clinic, with a goal of study groups of 8 individuals. Once the MS group has been established, age and gender matched controls will be recruited. Consenting subjects will undergo skin punch biopsy of the inner upper arm. Once fibroblast cultures are obtained, the cells will be reprogrammed via forced expression of a defined cocktail of genes (OCT4, SOX2, KLF4, MYC/NANOG, and LIN28) which promotes pluripotency (Takahashi et al., 2007). iPSCs will then be differentiated to oligodendrocytes, astrocytes and neurons via exposure to defined trophic factors as previously reported (Jiang et al., 2016; Thiruvalluvan et al., 2016; Pamies et al., 2016). We will then compare lineage-specific differentiation efficiency and proliferation as well as cell-cell interaction, and migration of these various cell types. Additionally, transcriptome analysis will be conducted on cell subpopulations derived from each study group to query for candidate processes leading to such differences.

RESULTS: The study is currently enrolling subjects; preliminary data are expected to be obtained in spring of 2017.

CONCLUSIONS: Our study is the first to explore intrinsic abnormalities in CNS cell populations derived from patients with MS, which if targeted therapeutically, may empower new therapies including autologous cell based treatment to repair demyelination and/ or re-establish neurodegenerative losses.

ACKNOWLEDGEMENTS AND FUNDING SUPPORT: This study is funded by the Clinical Research Division, 59MDW, Lackland Air Force Base, TX.
Chemoprophylaxis will play a key role in the campaign to eradicate malaria, and the rationale for using drugs targeting the *Plasmodium* liver stage is clear: prevent both human disease and parasite transmission back to the vector. Liver stage screens to date have defined compound activity as a significant reduction in parasite size and/or abundance. This hit definition assumes that parasite maturity and size are tightly correlated throughout liver stage development, which we show is not necessarily true during the late liver stage in *Plasmodium berghei*. Further, compounds that kill the parasite only late in development, would be missed entirely in canonical screens. In order to identify compounds that can arrest the parasite at any point in liver stage development, we have implemented a multimodal screening workflow assessing parasite growth, abundance, and maturation, based on a vital luminescence assay, followed by high content imaging of infected HepG2 monolayers after the completion of liver stage development. This allows us to identify all potential liver stage active antimalarial compounds, most importantly, the high value class that lead to parasite killing during the late liver stage. A proof-of-concept screen of the Malaria Box identified compounds that do not substantially alter parasite size or abundance during the liver stage, but do block maturation, preventing formation of infectious merozoites. We now have miniaturized our assay to 384 well plate format, and adopted a reseeding procedure to further increase throughput for screening larger compound libraries.
REGULATION OF INTERLEUKIN-1 SECRETION BY MICROGLIA IN EXPERIMENTAL MODELS OF MULTIPLE SCLEROSIS

Charles A. Garcia, Sandra M. Cardona, Andrew S. Mendiola, Kaira Church and Astrid E. Cardona

Multiple Sclerosis (MS) is an inflammatory demyelinating disease for which an exact cause is unknown. MS affects 2.5 million people worldwide, with about 200 new cases diagnosed each week in the U.S. The combined actions of environmental factors in genetically susceptible individuals trigger a cascade of events that cause central nervous system (CNS) inflammation, myelin loss and neuronal damage. Destruction of myelin and damage to nerve fibers (axon damage) translate into unpredictable signs and symptoms, culminating often in motor impairment, visual disturbances and cognitive decline. Microglia are the resident macrophages of the CNS (brain, spinal cord and eyes) and display a unique steady motility of long arms that extend and retract from the cell membrane, allowing close interactions will all nearby cells of the CNS. Microglia are traditionally perceived as brain immune cells that govern mostly detrimental responses, because of their efficacy in releasing inflammatory molecules. However, recent discoveries have shed light into new roles of microglial in fine tuning neuronal circuitries and shaping neuronal communication. Of relevance is the presence of the fractalkine receptor (CX3CR1) on the surface of microglia, whose expression correlates with decreased release of interleukin 1-beta (IL-1β) in the brain. Preliminary studies in the Cardona lab showed that absence of CX3CR1 correlates with increased levels of IL-1β, increased neuronal damage and enhanced inflammation in models of multiple sclerosis. IL-1β is a soluble protein that upon release to the extracellular space exerts potent detrimental effects to neurons, inducing cell death. Moreover, IL-1β acts on blood vessels increasing vascular permeability, and promotes macrophage activation. However, the mechanisms by which fractalkine and its receptor on microglia, CX3CR1 inhibits the production and release of IL-1β is unknown. Using our experimental models of MS and in vitro grown microglia, we will test the hypothesis that fractalkine by interacting with its receptor CX3CR1 on microglia, induces a downregulation of pattern recognition receptors (Toll and NOD-like receptors) that are needed to initiate the cascade that leads to IL-1β production.

To test the hypothesis first we compared the expression of Toll-Like receptors (TLRs) and NOD-Like receptors in brain tissues from wild type and CX3CR1-deficient mice under naïve (non-disease) and diseased states. For this we used the experimental autoimmune encephalomyelitis (EAE) model that resembles aspects of the pathology of MS. Normal and EAE tissues were subjected to RNA extraction and transcripts of TLR and NOD-like receptors were assessed by real time quantitative RT-PCR. Preliminary results indicate that in comparison to naïve, EAE wiltype mice had increased expression of TLR2, whereas IL-1β expression remained constant. To further validate the hypothesis we will compare the expression of TLR and NOD-Like receptors in microglia grown in culture in the presence or absence of exogenous fractalkine. Using a BV2 microglial cell line, and upon activation with fractalkine for 24 hrs, TLR and NOD receptors will be evaluated in mRNA samples. Validation of selected genes will be performed by immunohistochemistry of by flow cytometry. This study will be instrumental to use fractalkine as an anti-inflammatory treatment in models of MS.
The protective role of CXCL11 against pulmonary cryptococcosis


Department of Biology, and The South Texas Center for Emerging Infectious Diseases

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Cryptococcus neoformans is an opportunistic fungal pathogen that causes cryptococcal pneumonia and life-threatening meningoencephalitis in immunocompromised and immunocompetent individuals. We previously have shown that protection against experimental pulmonary infection with a genetically modified strain of H99 that produces murine IFN-γ, H99γ, is mediated through IFN-γ/STAT-1 signaling pathway. Activation of STAT-1 signaling leads to the production of CXCL9, CXCL10 and CXCL11 chemokines, each which are CXCR3 receptor ligands, and pulmonary leukocyte recruitment. C57BL/6 (B6) mice produce a non-functional CXCL11 protein and thus we hypothesize that B6 mice will be susceptible to experimental pulmonary infection with H99γ. B6 mice were observed to have a 40% survival rate, compared to 100% survival of BALB/c mice and an 80% survival rate of F1 mice (first generation of BALB/c x B6) at day 60-post inoculation. After 60 days post-inoculation F1 mice infected with H99γ had a significant decrease in CFUs compared to B6 mice. We observed significantly increased production of CXCL11 in F1 and BALB/c mice compared to B6 mice following pulmonary infection with H99γ. These data suggest that the production of CXCL11 chemokine is necessary for optimal protection against pulmonary C. neoformans infection.
**Candida-Streptococcus** Biofilms on Titanium Dental Implant Material and its Consequences for Antimicrobial Drug Resistance

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The University of Texas at San Antonio.

**Background:** The oral cavity serves as a nutrient-rich haven for over 600 species of microorganisms. Although many are essential to maintain the oral microbiome, some microorganisms have a higher probability of spreading oral infection such as caries, periodontis, endodontic and mucositis. This condition is further exacerbated in immunocompromised patients with dental implants, leading to resilient deep-seated infections. The microbial colonization in such infections are mixed-species in nature and adapt to biofilm mode of growth. We have developed an in vitro model to screen for antimicrobials against *Candida-Streptococcus* mixed-species biofilm infections pertinent to peri-implant diseases.

**Methods:** This study involved growing biofilms with *S. gordonii* wild-type strain DL1.1(Challis) and *C. albicans* wild-type strain SC5314 in a 48-well microtiter plate containing sterile titanium discs. The alloy used is Ti-6Al-4V, which is commonly used in dental implants. Sterilization of titanium discs was performed by a series of washings with acetone and ethanol solutions, distilled water and 2% v/v detergent solution. Biofilms were grown in each well of the plate using 300μl of mixed *C. albicans/S. gordonii* microbial culture and incubated for 24 h inside a CO₂ incubator at 37°C. To mimic physiological conditions, the cultures were grown in BMM synthetic saliva. For control studies, the biofilms were grown in a common laboratory media for mixed cultures [1:1 (v/v) RPMI 1640/Todd Hewitt Broth + 0.02% (w/v) yeast extract]. Final concentration for *S. gordonii* bacterial cells was 1x10⁷ cell/ml whereas for *C. albicans* concentration was 1x10⁶ cell/ml in either media used. Scanning Electron Microscopy (SEM) and fluorescent microscopy studies were conducted to examine the overall structure of the resulting biofilms. Antimicrobial susceptibility testing was performed by adding equal volume of drugs at desired concentrations to wells containing preformed biofilms and incubating for an additional 24 h at 37°C. The viability of cells after treatment was estimated with Presto Blue® reagent.

**Results:** The formation of single and mixed *C. albicans/S.gordonii* biofilms on titanium discs was characterized based on morphology, 3D architecture (SEM) and exopolymERIC matrix production (fluorescent microscopy). Overall, mixed biofilms formed on titanium discs showed increased resistance to both monotherapy and combination therapy of antibacterial (Clindamycin) and antifungals (Amphotericin B and Fluconazole) to single species biofilms.

**Conclusions:** This method allows testing commonly used biomaterials to support microbial biofilm formation in the buccal environment. Furthermore, our results highlight the need for antimicrobial agents and strategies that target both single and mixed species biofilms.
PREVALENCE OF HUMAN PAPILLOMAVIRUS GENOTYPES AMONG WOMEN WITH ABNORMAL PAP SMEARS IN THE MILITARY HEALTH SYSTEM

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Human Papillomavirus (HPV) infection is present in the majority of cervical cancer cases and represents the most common sexually transmitted infection among United States Military service members. Immunization for HPV is not currently considered to be mandatory at inception of military service. The primary objective of this study was to examine the prevalence of vaccine preventable cervical disease among women enrolled in the Military Health System.

This is a retrospective cross-sectional study of Pap smear results and HPV genotyping data among active duty (AD), dependents and retired females, ages 25-65, who were enrolled in the United States Military Healthcare System (TRICARE) and assigned to primary care clinics in the San Antonio Military Medical Center (SAMMC) catchment area from June to December 2014. Demographic data, Pap smear results and HPV genotyping data were characterized and stratified by age, military service branch, military rank and beneficiary category. Laboratory testing for HPV on Pap smear samples includes high-risk genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68. HPV genotyping was conducted based on physician order and not directed by specific laboratory algorithms or published clinical practice guidelines. A subgroup analysis focused on the quadrivalent HPV vaccine-eligible group, namely women aged 34 and younger at the time of data collection. SPSS version 22.0 was used to conduct all statistical analyses.

There were a total of 43,098 women enrolled to local clinics and 7,819 Pap smears obtained between June and December 2014. The number of abnormal Pap smears was 2,120 and there were 3,745 high-risk genotypes among all samples. Younger age categories and senior enlisted rank were more likely to have high-grade lesions on Pap smear (p<0.001). The overall sample prevalence of high-risk HPV in this population was 10.6%. HPV positivity rates differed by age with 18.4% positive among 25-34 year-olds, 9.3% positive among 35-44 year-olds, 7% among 45-55 year-olds and 7.7% positive among 55-65 year-olds. Similar to the trend among high-grade cervical lesions, the prevalence of high-risk HPV types was more common among younger age groups. Participants who were eligible for the quadrivalent HPV vaccine during childhood and adolescence had the highest HPV positive rates among this study population. The mean age among individuals positive for a high-risk HPV genotype was 39 years old vs. 44 years for HPV negative subjects (P<0.001, CI 3.2-5.4). A regression model confirmed a statistically significant difference in age among HPV positive versus negative patients, and the odds of acquiring a high-risk HPV infection decreased with age. Additionally, the odds of acquiring a high-risk HPV infection was lower for non-active duty women, and there was a significant difference between AD personnel and dependents of AD. Subgroup analysis on vaccine-eligible individuals included 42 cases and 42 matched controls. HPV-negative individuals were more likely to initiate (p<0.001) and complete
(p<0.001) the quadrivalent HPV vaccine before Pap testing, as compared with HPV-positive subjects. This analysis strongly supports a role for routine vaccination among Active Duty and Dependent females within the Military Health System.

1. This analysis is part of an approved Defense Health Agency Protocol, entitled Human Papilloma Virus (HPV) Vaccination Rates Among Active Duty Air Force Recruits
2. Funding Source: Immunization Healthcare Branch (IHB), Defense Health Agency (DHA) Grant: Project Number IHBG-16-08.
3. Conflicts of interest: There are no conflicts of interest.
DISSECTING THE ROLE OF THE FRACTALKINE RECEPTOR DURING EAE: NEW APPROACH UTILIZING A HUMANIZED ANIMAL MODEL

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Multiple Sclerosis (MS), an inflammatory demyelinating disease of the central nervous system (CNS) is the leading cause of nontraumatic neurological disability in young adults in the North America and Europe, affecting more than two million people worldwide. While immune mediated destruction of the CNS myelin and oligodendrocytes are considered the primary pathology of MS, it is well established that progressive axonal loss is the major cause of neurological disability.

Resident microglia can play detrimental and protective roles during CNS inflammation, but the regulation of their effector functions remains unclear. Previous data from our laboratory showed that Fractalkine/CX3CR1 signaling regulates microglia neurotoxicity in selected models of neurodegeneration.

Fractalkine is a transmembrane chemokine expressed by neurons and peripheral endothelial cells, which acts both as an adhesion molecule and as a soluble chemotaxtractant upon proteolytic cleavage. In the CNS, fractalkine functions by signaling through its unique receptor, CX3CR1 expressed by microglia. During experimental autoimmune encephalomyelitis (EAE), an inflammatory demyelinating disease used experimentally in rodents as a model for multiple sclerosis, CX3CR1 deficiency confers exacerbated disease characterized by severe inflammation and neuropathology. Among the CX3CR1 human polymorphisms, the CX3CR1I249/M280 variant is present in ~20% of the population and exhibits reduced adhesion for fractalkine conferring defective signaling. However, the role of CX3CR1, microglia function and its effect on neuronal damage during multiple sclerosis remains unsolved.

The aim of this study is to assess the effect of weaker signaling through the human CX3CR1I249/M280 receptor on EAE disease, axonal damage and expression of ciliary neurotrophic factor (CNTF). We hypothesize that dysregulated microglial responses in absence of CX3CR1 signaling enhance neuronal/axonal damage via downregulation of CNTF, a key survival factor for neurons and oligodendrocytes.

To test our hypothesis, we have generated by insertion, an animal model that expresses the CX3CR1I249/M280 human variant into the mouse CX3CR1 locus. Active EAE was induced in humanized mice via MOG(35-55) peptide immunization.

Our results show an exacerbated EAE phenotype in mice expressing the human CX3CR1I249/M280 receptor, characterized by accelerated disease onset and higher maximum EAE score in comparison to WT mice. These results correlated with severe CNS inflammation and increased neuronal loss in the cerebellum, a similar phenotype observed in mice lacking the mouse Cx3cr1 gene. Expression of the human variant correlated with diminished levels of soluble fractalkine in the CNS of diseased mice. In addition, the induction of EAE led to downregulation of cntf transcript levels in mice bearing the CX3CR1I249/M280 receptor in comparison to WT mice. Interestingly, flow cytometry data showed slight downregulation of MHC-II and CD68 activation markers in humanized mice, suggesting an alteration in microglia function induced by defective CX3CR1 signaling. Our results provide instrumental validation of defective function of the CX3CR1I249/M280 human variant and the foundation to broaden the understanding of microglia dysfunction during neuroinflammation.
This work was supported by The National Institutes of Health (SC1GM095426 to AEC) and National Institute on Minority Health and Health Disparities (G12MD007591).
The Association of Epilepsy Specialty Care with Patient Reported Outcomes and Satisfaction

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San Antonio, TX

OBJECTIVE: Epilepsy is a complex disorder that requires specialized knowledge for accurate diagnosis, classification, and treatment. Neurologists/epileptologists tend to provide care to patients with severe epilepsy with therapeutic challenges while most other patients with epilepsy tend to receive care within the context of primary care. This study examined the association of patient reported outcomes related to seizures, medication side effects, mental health symptoms, and satisfaction with care for individuals who received the majority of their care by neurology/epilepsy specialists, and hypothesized that a) those receiving epilepsy/neurology care would have more problems reported on seizure severity, medication side effects and mental health symptoms and b) higher levels of satisfaction than those who received the majority of their care in primary care or the emergency department.

METHODS: From the population of Veterans who received VA care 2012-2014, we identified individuals that met criteria for epilepsy based on diagnosis (ICD-9-CM codes 345 [epilepsy] and 780.39 [convulsion]) and concomitant seizure medication. We then identified 2000 individuals stratified by age and sex, validated epilepsy diagnosis using medical chart abstraction, and mailed surveys to approximately 1600 individuals in the fall of 2015. Surveys included the personal impact of epilepsy scales (PIES), questions on satisfaction with care, the source of the majority of epilepsy care, and average monthly seizure frequency. We calculated the seizure, medication side effects, and comorbidity (mental health symptoms) subscales using the PIES scoring algorithm. The satisfaction item rated satisfaction with care meeting needs as 1-5. We classified the primary source of care the prior year as Neuro/Epilepsy (NE) vs Primary care/Others (PO). Because the impact of epilepsy has been found to vary by demographic characteristics and mental health comorbidity we also included demographic and mental health comorbidity identified in VA medical records (ICD-9-CM codes 2001-2014). Bivariate statistics compared demographic characteristics, seizure frequency, mental health comorbidity (chi-square), PIES subscales, and satisfaction (t-test) by primary epilepsy care source. Regression analyses determined if there were significant differences on PIES subscales and satisfaction after controlling for demographic, seizure frequency, and mental health characteristics.
RESULTS: 535 individuals responded to the survey (35% response rate) and 429 patients (80% of responders; 28% of those surveyed) completed over half of the survey. Of these 82% were males, 68% were white and 188 (44%) received the majority of NE care. There were no significant differences by sex or gender; elderly patients (> 65yrs) received majority of care by PO. Patients with NE care reported more problems with seizures and mental health symptoms. (P= 0.018 and P= 0.02); there was no difference on medication side effects or if care met needs. After controlling for mental health comorbidity, demographic characteristics and seizure frequency there were no differences between NE and PO groups on any measures.

CONCLUSION: Neurology/Epilepsy group tend to provide care for patients with more severe epilepsy which can be associated with higher mental health symptoms. No difference is noted in epilepsy care between the NE and PO groups if epilepsy is fairly well controlled.
Using CellProfiler and automated confocal feedback microscopy to quantify Plasmodium liver stage phenotypes and antimalarial compound activity.

Charleston West, Javier Mota, Andreu Garcia Vilanova, and Kirsten Hanson

Malaria, a significant global health burden, is caused by Plasmodium parasites transmitted via the bite of an infected anopheline mosquito. Disease is exclusively cause by blood stage parasites that replicate cyclically in erythrocytes, and the transmission forms of the lifecycle are also found only in erythrocytes. Before any blood stage development or disease can occur, Plasmodium parasites first undergo an obligatory development and replication phase in the liver. The liver stage is thus a key target for antimalarial prophylaxis, as killing the parasite in the liver would prevent both transmission and disease. The liver stage is initiated when a motile sporozoite invades a hepatocyte via formation of a parasitophorous vacuole. The liver stage parasite develops as a syncytium, rapidly increasing in size and DNA content, until a cellularization process is triggered, resulting in the formation of thousands of single celled progeny called merozoites, which will go on to infect erythrocytes. The general time course of liver stage development and several developmental milestones are known for the rodent model parasite Plasmodium berghei, but the amount of developmental heterogeneity seen within populations over the course of one developmental cycle, as well as the effects of known antimalarial compounds on parasite phenotypic diversity have not been characterized.

For such an analysis to be meaningful, a reasonably large sample of high-resolution parasite images is required. We have implemented an automated confocal feedback microscopy workflow for imaging terminal P. berghei liver stages, interfacing online parasite identification in CellProfiler with Leica Matrix Scanner software for automated imaging via a TCP/IP communication protocol. This allows us to continuously acquire high magnification, high resolution parasite images without investigator intervention. Quantifying and categorizing Plasmodium development through the liver stage can be a powerful tool when investigating parasite growth and the effectiveness of antimalarial compounds. Utilizing the image analysis software CellProfiler, and the automated feedback microscopy technique, we can accurately and confidently measure phenotypes in large sample sets.

Automated feedback fluorescence microscopy is a process which allows us to quantitatively analyze substantially large image sets without the sacrifice of time due to manual input. While initiating this technique, the microscope automatically scans the sample taking low resolution images which are sent to the analysis software CellProfiler (Carpenter 2006). CellProfiler is used as a filter where preset parameters are applied to each image. If the software detects an object of interest, the coordinates are fed back to the microscope software where high resolution images of varying channels are acquired. This process repeats itself for the entirety of the sample. After completion, CellProfiler is utilized again
for image quantification. Using this software, we can designate a multitude of parameters to measure based on size, intensity, and location, among others.

When investigating Plasmodium heterogeneity, CellProfiler can be used not only to measure various attributes, but as a predictor of these same parameters as well. Plated HepG2 cells were infected with GFP expressing Plasmodium berghei sporozoites. These cells were fixed every 3 hours between 48 and 66 hours post infection creating a timecourse. These samples were acquired using automated feedback microscopy and quantified with CellProfiler. Our resulting data accurately demonstrates the variability from parasite to parasite. Further, due to the size of our measured sample set, we can visualize and demonstrate variability within entire populations even within a single timepoint. The accuracy obtained using CellProfiler allows us to analyze data sets of thousands of images without the strenuous need for confirmation of its validity. Further, the ability to accurately categorize and describe parasites within large image sets can allow the acquisition of substantial statistics with which to quantify parasitic phenotypes.


THE PERSONAL IMPACT OF EPILEPSY (PIES) ON VETERANS

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Background: The impact of epilepsy on patient lives is increasingly recognized as being multifaceted with challenges specific to epilepsy. In addition to the disorder itself, patients with epilepsy (PWE) face the added burden of medication side effects and comorbidities associated with epilepsy. Side effects of anti-epileptic medications commonly include sedation, and PWE are at increased risk of specific comorbidities such as depression. Researchers have developed The Personal Impact of Epilepsy Scale (PIES) to better describe how epilepsy influences patient lives. The PIES is a patient reported outcome that consists of three domains: seizure severity, medication side effects, and comorbidities. Previous studies have looked at the impact of epilepsy using generic health assessments or epilepsy specific assessments lacking one of the domains addressed by the PIES. To our knowledge, this is the first study to describe the impact of epilepsy using the PIES.

Materials & Methods: A postal questionnaire was used to examine patient reported outcomes among 1,500 veterans with epilepsy (VWE) nationwide who were treated at the Veterans Health Administration between 2012-2014. Survey items included the PIES and demographic characteristics. Subscale scores for each domain and an overall score were calculated using the PIES scoring algorithm. Subscale scores range from 0-100 and the overall score ranges from 0-300 with higher scores indicating better outcomes. Because age and gender have been shown to affect the quality of life, we examined variation of epilepsy impact by age and gender.

Results: Surveys were returned by 537 VWE. PWE age 65+ reported less impact of seizure, fewer medication side effects, and fewer comorbidity impairments compared to PWE age 18-44 and PWE age 45-64. Similarly, men with epilepsy reported less impact of seizure, fewer medication side effects, and fewer comorbidity impairments compared to women with epilepsy.

Table 1: PIES scores by age cohorts

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean Subscale A -- Seizure Severity (SD)</th>
<th>Mean Subscale B -- Medication (SD)</th>
<th>Mean Subscale C -- Comorbidity (SD)</th>
<th>Total PIES Score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-44</td>
<td>79.88 (27.87)</td>
<td>69.74 (23.57)</td>
<td>64.70 (22.21)</td>
<td>198.73 (62.81)</td>
</tr>
<tr>
<td>45-64</td>
<td>78.00 (27.11)</td>
<td>72.27 (23.76)</td>
<td>63.77 (26.29)</td>
<td>198.43 (69.01)</td>
</tr>
<tr>
<td>65+</td>
<td>86.26 (24.44)</td>
<td>79.82 (20.31)</td>
<td>74.16 (23.01)</td>
<td>222.24 (66.17)</td>
</tr>
</tbody>
</table>
Table 2: PIES scores by gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean Subscale A -- Seizure Severity (SD)</th>
<th>Mean Subscale B -- Medication (SD)</th>
<th>Mean Subscale C -- Comorbidity (SD)</th>
<th>Total PIES Score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>73.99 (28.60)</td>
<td>69.68 (26.42)</td>
<td>63.60 (26.77)</td>
<td>192.88 (72.07)</td>
</tr>
<tr>
<td>Male</td>
<td>82.74 (25.83)</td>
<td>75.60 (21.91)</td>
<td>68.39 (24.61)</td>
<td>209.90 (66.73)</td>
</tr>
</tbody>
</table>

**Conclusions:** Older patients and men perceive fewer problems associated with epilepsy compared to younger patients and women. This is consistent with prior research in VWE using a generic health measure. However, it is not clear if the observed differences are a direct reflection of age/gender, or proxies for other factors, such as the type of specialty care, patient-physician relationship, or socioeconomics that may affect the patient reported outcome. Furthermore, it is not clear what a 10-point scale difference in PIES score means. In order to use this measure to inform clinical care, research is needed to identify the minimal clinically important difference.
Using 3D Hydroxyapatite-Collagen Composite Scaffolds and Spatial Temporal Variation to Promote Vascularized Bone Tissue Regeneration

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Introduction: Bone fractures are quite common and while most heal naturally, severe bone injuries such as those caused by trauma often do not heal on their own and require a tissue graft for repair. Many of these grafts fail due to a compromised blood supply. These failures suggest the rate and extent of vessel in-growth are crucial and needed for successful bone regeneration.¹,² Other studies have also indicated that biomimetic extracellular matrix components such as hydroxyapatite (HA) and collagen are ideal as they are biocompatible and occur naturally in bone³. As such, spatial-temporal seeding variations of co-culture cells in 3D HA collagen composite scaffolds were evaluated in this study for enhancement of osteogenesis and angiogenesis.

Materials & Methods: Composite scaffolds were prepared by casting 4 mg/ml collagen hydrogels within a porous 3D HA scaffold. Using a previously described template coating process⁴, HA scaffolds were prepared with an average porosity of 80%. Initial experiments demonstrated an increase in VEGF production on day 7 when bone mesenchymal stem cells were seeded alone on composite scaffolds. In this study, optimized concentrations of human embryonic palatal mesenchymal cells (HEPMs) and human umbilical vein endothelial cells (HUVECs) were seeded with spatial-temporal variation (Fig. 1): Group 1 having HEPMs seeded 7 days before HUVECs seeding, Groups 2 having HEPMs seeded 6 hours before HUVECs seeding, and Group 3 having HEPMs and HUVECs cast in the composite scaffolds. Production of vascular markers (VEGF, Ang-1, and angiogenin) and alkaline phosphatase (ALP), an early osteogenic marker, were measured at regular intervals using ELISA. Groups were compared using 2-way ANOVA across time and Tukey’s test (at p<0.05).

Results & Discussion: Groups 1 and 3 showed similar trends in ALP and vascular markers throughout the duration of the experiment (Fig 2a and b). Group 1 and 3 had an initial peak of ALP, which is indicative of osteoblast differentiation since ALP is an early osteogenic marker (Fig 2a). However, Group 2 had reduced and fairly consistent ALP production when compared to Groups 1 and 3 throughout the experiment, suggesting delayed HEPM attachment on the HA scaffold and hydrogel. All Groups showed an initial early increase in vascular markers Ang-1 (essential for organization, integrity, and
maturation of neo-vascularulture\textsuperscript{5}) and angiogenin (potent inducer of neovascularization \textit{in vitro}\textsuperscript{6}) (Fig 2c and d). However, vascular marker maturation levels were observed to decrease over time, suggesting the entrapment of vascular proteins in newly formed ECM. Hence, results imply both bone and vascularization are occurring.

\textbf{Conclusions:} Osteogenic and angiogenic differentiation are indicated for all scaffolds, suggesting the occurrence of bone and vascular activities. However, spatio-temporal differences in cell seeding resulted in profound differences early at day 7 which might impact tissue organization and maturation.

\textbf{Figures:}

\textbf{Acknowledgements:} Funding from NIH/NIGMS MARC U*STAR GM007717 and UTSA College of Engineering.

\textbf{References:}


Type 2 Diabetic Muscle: Characterization and Tissue Engineering

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Type 2 diabetes, a chronic disorder caused by insulin resistance, is the 7th leading cause of death in the United States with approximately 1.4 million new Americans being diagnosed with the disease each year. Until recently it was seen as a disease of middle-aged and elderly people, but it is now increasingly seen in adolescence and childhood with its prevalence increasing yearly worldwide. It is among one of the most dangerous disorders due to its ability to eventually affect every body part and cause numerous complications and co-morbid conditions, such as poor circulation leading to diabetic ulcer formation and non-traumatic lower-limb amputation.

It is understood that in the pathogenesis of type 2 diabetes the beta-cells in the pancreas, in charge of storing and releasing insulin, are unable to release enough insulin to keep blood glucose at normal levels. However, research has shown that skeletal muscle insulin resistance is considered to be the initiating or primary defect evident decades before beta-cell failure and evident hyperglycemia develops. Furthermore, among some of the top risk factors associated with type 2 diabetes is physical inactivity. Living an active lifestyle helps counteract the onset of type 2 diabetes due to exercise increasing insulin sensitivity, allowing cells to better use any available insulin to take up glucose during and after activity. Additionally, when muscles contract during activity, it stimulates another mechanism that is completely separate of insulin, this mechanism allows cells to take up glucose and use it for energy whether insulin is available or not.

With this foundation in mind, it is evident that a better understanding of the differences between non-diabetic and type 2-diabetic muscle is necessary. To accomplish this, first our lab will be doing an in-depth cellular characterization comparing healthy non-diabetic and type 2-diabetic skeletal muscle cells. In this comparison common cellular characteristics will be analyzed including cell proliferation rate, cell differentiation rate, cell morphology, and apoptotic markers, alongside with diabetic specific tests such as insulin stimulated glucose uptake, presence, abundancy, and location of glucose transporter type 4 (GLUT4) protein alongside other common proteins involved in glucose transport into muscle. Following cellular characterization, an in vitro model of tissue engineered non-diabetic and type 2-diabetic muscle constructs will be compared in both static and dynamic conditions (stimulating physical activity) using a similar methodology used in cellular characterization.

Ultimately, what we aim to find is similarities and differences among healthy non-diabetic and type 2-diabetic skeletal muscle cells and engineer an in vitro model for studying type 2 diabetes in muscle. Both goals which can contribute to the understanding and prevention of type 2 diabetes.

Sources:


EXAMINING THE RELATIONSHIP BETWEEN TBI AND MOVEMENT DISORDERS IN VETERANS

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Background: Approximately 15.2 - 22.8% of those deployed to Iraq or Afghanistan report experiencing a Traumatic Brain Injury (TBI) (McKee & Robinson, 2014), making it a significant military and public health issue. It has been suggested that the cascade of neurological consequences of a TBI could trigger neurodegenerative disorders (Chauhan, 2014). Some studies indicate that TBI could be a risk factor for Alzheimer’s disease and the direct cause of Chronic Traumatic Encephalopathy but, theoretically, TBI could be a risk factor for many neurodegenerative disorders (Faden & Loane, 2015), including movement disorders. The relationship between TBI and movement disorders has not been studied thoroughly and available research is typically limited by small sample size or poorly defined variables.

Materials & Methods: This study involved an analysis of existing data using medical records from the Veterans Health Administration. The relationships between TBI severity and diagnosis of three neurodegenerative disorders: Parkinson’s Disease (PD), Multiple Sclerosis (MS), Amyotrophic Lateral Sclerosis (ALS) were examined. Participants included Veterans who deployed during the Iraq or Afghanistan conflicts and later sought VA care. The sample was restricted to those who were seen at least once per year for three years and were seen for at least one visit after fiscal year 2008 and yielded 606,828 medical charts. TBI severity (mild, moderate, severe, penetrating) was categorized using the DoD criteria (O’Niel, 2013). An “unclassified TBI” category was created for ICD9 codes that did not clearly indicate TBI severity, according to DoD criteria. It was hypothesized that there would be a significant relationship between all three movement disorders examined and all three severity categories of deployment-related TBI.

Results: Odds ratios were calculated, adjusting for gender, race, branch of service, and education. A significant relationship was found between the diagnosis of PD and previous deployment-related TBI across all three levels examined; an increased risk of PD was found for moderate/severe/penetrating TBI (OR 3.61; 95% CI 2.28-5.70) mild TBI (OR 1.52; 95% CI 1.09-2.12) and unclassified TBI (OR 2.63; 95% CI 1.57-4.38). Additionally, only unclassified TBI was found to be a significant risk for diagnosis of MS (OR 1.68; 95% CI 1.25-2.25). TBI was not significantly related to ALS.

Conclusion: Support was found for the relationship between TBI and later diagnosis of some, but not all, neurodegenerative disorders. Future analysis should be conducted to further understand these relationships, including modality of TBI (whether blast or non-blast) and total number of TBIs incurred (single, recurrent). Furthermore, the relationship between TBI and Parkinson Plus disorders (e.g., progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration) merits additional investigation.
Long-term impact of the Columbine High School shooting on survivors.

Jillian Bailie, PsyM, MA; Cheryl Meyer, JD, PhD

Purpose
The purpose of this study was to investigate the long-term functioning of the students of Columbine High School (CHS) in attendance at the time of the shooting of April 1999. Specifically, the research question was: What is the long-term impact of the CHS shooting on the students who survived? The research focused on mental health, social, and emotional functioning.

Conceptual Foundation
While there is research available regarding survivors of traumatic events, there appears to be a lack of robust research regarding long-term implications for survivors of rampage school shootings and particularly a lack of research on the CHS shooting survivors. Considering the enduring influence the Columbine shooting has had on society, understanding the long-term implications is important. Because of the time elapsed from the event, the true long-term ramifications for survivors can be more fully ascertained. It is expected that for a large portion of the shooting survivors, there has been a long-lasting psychological impact from the trauma.

Methodology/Findings
Participants in this study were recruited from the students who were enrolled at CHS on the day of the shootings, April 20, 1999. Inclusion criteria was any student enrolled at the time of the shooting. Participants were asked to complete an online survey regarding demographic variables at the time of the shooting and questions on mental health, emotional, and social functioning both following the shooting and currently and the Impact of Events Scale- Revised (IES-R; Weiss & Marmer, 1997). The questionnaire included both qualitative and quantitative aspects. Initially, intrusion symptoms appeared to be the most common type of symptom for survivors, hyperarousal symptoms were the next most common, followed by avoidance symptoms. Currently, avoidant symptoms are the most common, followed closely by hyperarousal symptoms. Intrusion symptoms are the least common. The most common emotional response associated with experiences on the day of the shooting was avoidance, followed by hyperarousal, then intrusion.

Implications
The results of this study could help future survivors understand their experiences. Many respondents reported feeling isolated in their healing and like they were wrong or abnormal to have certain feelings or experiences in connection to the shooting. This study indicates that there are many lasting impacts of such a trauma and they are expressed in a variety of ways. Since many survivors have reported feeling isolated from others who have not experienced similar things, other communities might feel the same way. Many survivors reported making connections and spending time with their community was healing, therefore having a broader sense of community and understanding may help others experience healing in the future. Finally, having knowledge about other survivors’ experiences could give hope to future survivors and help them build models with which to cope. The results of this study can also inform treatment providers regarding presenting problems and long-term implications for survivors of rampage shootings.
DEPLOYMENT PREPARATION, PTSD, AND FAMILY FUNCTIONING IN RETURNING VETERANS

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Background: Returning veterans experience lengthy deployments away from their families and are at high risk for developing mental health disorders, including posttraumatic stress disorder (PTSD). Approximately 23% of returning Veterans are diagnosed with PTSD (Fulton et al., 2015). Those diagnosed with PTSD report higher rates of family functioning problems and difficulties with interpersonal relationships (Sayers et al., 2009). Evidence suggests that training and deployment preparation can serve as a protective factor against PTSD and reduces the negative impact of combat exposure on PTSD treatment response (Renshaw, 2011; Price et al., 2013). The current study examined the inter-relationships among training and deployment preparation, family functioning, and PTSD. Two mediational models were tested to determine whether: 1) PTSD mediated the relationship between deployment preparation and family functioning and 2) family functioning mediated the relationship between deployment preparation and PTSD symptoms. Given evidence that the relationship between PTSD and family functioning is bidirectional, it was hypothesized that both mediational models would be supported.

Materials & Methods: Participants were 139 veterans who served in support of the post-9/11 wars in Iraq and Afghanistan (N= 139; M_age= 37.5, SD=10.6; 15.2% female). Veterans completed assessments as part of longitudinal study on functional recovery following warzone deployment. During the baseline assessment, participants completed diagnostic interviews and self-report measures on training and deployment preparation (DRRI, King et al., 2006), PTSD symptoms (CAPS, Blake et al., 1995; PCL-M, Weathers et al., 1993), and family functional impairment (FAD, et al., 1983).

Results: Age, gender, education level, and combat experience were controlled for in all analyses. Between-subjects ANCOVA revealed Veterans who had been diagnosed with PTSD in the past month reported significantly higher family functional impairment than those who were not diagnosed with PTSD, F(1, 124)= 15.30, p< .001. Mediation analyses indicated that deployment preparation had a significant negative indirect effect on PTSD symptom severity (as measured by the CAPS) through family functional impairment, b= -.22(.07), 95% CI= -.40, -.11. Reciprocally, deployment preparation had a significant negative indirect effect on family functioning through PTSD symptom severity, b= -.03 (.02), 95% CI=- .08, -.004. PTSD symptom severity and family functioning were significantly associated in both models, b = .96(.34), p<.05, and b= .07(.02), p<.05. Similar results were found when the PCL-M scores were used as indicators of PTSD symptom severity.

Conclusion: Veterans who indicated that they were better trained and prepared for deployment had significantly lower PTSD symptoms and family functional impairment. These results emphasize the need for adequate training and preparation within military personnel. The significant associations between PTSD and family functioning also suggest treatments targeting PTSD may also improve family functioning, and vice versa.
A SILK-ALGINATE COMPOSITE FOR THE TREATMENT OF CRANIOFACIAL DEFECTS FOR THE MASQUELET TECHNIQUE

Paul Dowell, Joseph Pearson, Paul Gutierrez, Joo Ong, Teja Guda – The University of Texas at San Antonio

The treatment of skeletal defects resulting from disease, trauma, and congenital conditions presents a vast challenge for orthopedic surgeons. Traditional autograft and allograft treatments pose high financial costs, donor site morbidity, and disease transmission risks to patients with the ever-present potential for immunological rejection. Continual instrumentation, illumination, and magnification innovations have granted the necessary precision, flexibility, and control for the feasible orchestration of minimally invasive techniques. Ideally, scaffolding renders defect stability, impedes tissue closure, and bolsters intrinsic regeneration processes. Alginate has been regarded as a viable means for facilitating tissue regrowth which is attributed to its compositional similarity to the native extracellular microenvironment, adequate biocompatibility, minimal toxicity, biodegradability, and tailorability. The confinement of alginate within porous silk fibroin scaffolding will secure a temporary corridor, in which will define the three-dimensional geometry, as well as permit in situ gelation. The investigation will concentrate on the silk envelope by optimizing the fabrication parameters to maximize the structural and mechanical characteristics to the extent in which will tolerate physiologically-relevant forces and endure the establishment of alginate hydrogels.
PATTERNS OF ZOLPIDEM USE AMONG ACTIVE DUTY SERVICE MEMBERS: A RETROSPECTIVE COHORT ANALYSIS

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Background: The use of zolpidem to treat insomnia has increased dramatically in the last decade. Although concern exists regarding the adverse effects and rate of zolpidem use, there is little information on patterns of zolpidem use in active duty service members (ADSM). We sought to examine the prevalence and correlates of zolpidem use and long-term exposure in ADSMs.

Methods: The cohort included individuals who were ADSMs between FY2012-2013 and went on to use Veterans Health Administration (VA) services. Our retrospective cohort included ADSMs with at least one zolpidem prescription in FY13. Using inpatient, outpatient, and pharmacy data from the Military Health System (MHS) we identified individuals with zolpidem use in FY13; baseline characteristics (demographics, diagnoses) for these individuals were identified in FY12. The Pharmacy Data Transaction Service (PDTS) data were used to determine the prevalence of long-term (>30 days) zolpidem, psychotropic, and opioid prescriptions received in FY13. Bivariate and multivariable analyses were used to analyze the demographic and clinical correlates of zolpidem use.

Results: Of the 42,983 ADSMs who received care, 11.4% (N=4889) were prescribed zolpidem in FY13. The use of zolpidem was associated with age above 40 years, Hispanic ethnicity, diagnoses of anxiety, pain, insomnia, and psychotropic and opioid prescriptions; individuals with TBI had lower odds of receiving zolpidem. Of the ADSMs who received zolpidem, 66.2% (n=3237) had long-term use. In multivariable analyses, older individuals and individuals with PTSD, insomnia, and prescriptions of psychotropic and opioid medications had higher odds of long-term zolpidem exposure while African Americans had lower odds.

Conclusions: The current practices of insomnia pharmacotherapy in ADSMs fall short of the clinical guidelines and may reflect high-risk zolpidem prescribing practices that put ADSMs at risk for adverse effects and poor health outcomes.

Keywords: zolpidem; Hypnotics and Sedatives; Drug Utilization; Pharmacovigilance; Pharmacoepidemiology/trends; Military Personnel; United States Department of Defense

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**Disclaimer:** The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of the VA or the US government.
Protection Against Cryptococcosis is Enhanced Following Engagement of Mincle Receptor


The University of Texas at San Antonio, South Texas Center of Infectious Diseases

Cryptococcus neoformans, the etiological agent of cryptococcosis, is an encapsulated fungal pathogen responsible for approximately one million cases of meningitis worldwide; particularly among immunocompromised individuals. Protection against cryptococcosis relies on phagocytosis of the pathogen by pulmonary macrophages (MΦ) and dendritic cells (DCs). However, it is not well understood how these phagocytes recognize and induce protection against Cryptococcus. We hypothesized that recognition of Cryptococcus ligands by the pattern recognition receptor (PRR), Mincle, expressed on phagocytes and other cell types result in the induction of protective immune responses against C. neoformans. Mincle recognizes polysaccharide mannans and glycolipids, readily found in fungal pathogens. Consequently, the studies herein determined the role of Mincle in the recognition and subsequent protective immune response against C. neoformans. We observed an increase in ligands recognized by Mincle on the surface of a hyphae-forming Cryptococcus mutant, LW10, compared to the parental control Cryptococcus strain. Studies demonstrated that Mincle deficient mice immunized with LW10 and then challenged with WT H99 were significantly more susceptible to experimental pulmonary cryptococcal infection compared to WT mice. Current studies are focused on identifying the ligand(s) present in the cell wall of LW10 that are recognized by Mincle. Altogether, these studies suggest activation of Mincle signaling pathways within innate immune cells during C. neoformans infection augments protection against cryptococcosis.
AN ATYPICAL PRESENTATION OF INSULINOMA

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The presentation of an insulinoma can be insidious, leading to delays in diagnosis that can last years. A seizure is a severe manifestation of hypoglycemia, but focusing on the neurological evaluation can overlook an insulinoma as the primary etiology. Consequently, there are several reports of insulinomas initially misdiagnosed as epilepsy. Contrary to these reports, we present a case of new onset seizure that immediately led to the diagnosis and treatment of an insulinoma.

A 53-year-old obese male without history of seizures, altered mentation, or neuroglycopenic symptoms presented to an emergency department (ED) due to a new development of aggressive behavior followed by whole body convulsions. Initial workup was unremarkable and the patient was discharged to home. The following day, family members reported a recurrence of altered mentation for which he returned to the ED. His blood glucose was <40 mg/dL with otherwise normal electrolytes, complete blood count, hepatic and renal function. Drug screen and alcohol screens were negative. Brain MRI and electroencephalogram were normal. He received a 10% dextrose drip IV and eventually required octreotide 150 micrograms three times daily to maintain euglycemia. He started a supervised 72 hour fast, which was terminated within 1 hour due to a low blood glucose of 36 mg/dL with associated neuroglycopenic symptoms. Insulin antibody was not detected and the sulfonylurea screen was negative. Other studies revealed inappropriately elevated C-peptide, insulin, and proinsulin levels, with low β-hydroxybutyrate, overall suggesting the presence of an insulinoma. Abdominal MRI demonstrated a 4.4 cm enhancing pancreatic tail lesion. He underwent a distal pancreatectomy, revealing a 2.5 cm well-differentiated insulinoma. Genetic analysis was negative for MEN1. After surgery, hypoglycemia completely resolved and he had no seizure recurrence.

An insulinoma is an uncommon but treatable condition. Failure to associate the effects of an insulinoma with seizures can lead to a delay in diagnosis. An insulinoma should remain in the differential diagnosis of new onset seizures.
Assessing the Impact of Dronabinol on Patient Weight in a Chronic Pain Population

Robert Kennedy, JBSA-San Antonio Military Medical Center

Objectives:
Dronabinol, or synthetic delta-9-tetrahydrocannabinol, is an orally active cannabinoid and naturally occurring component of Cannabis sativa L. (marijuana). Dronabinol has an FDA labeled indication for appetite stimulation in patients with AIDS. Studies have demonstrated patients with HIV and AIDS experience increased appetite and may gain as much as 3.2kg but could also lose as much as 2kg while taking dronabinol. This weight gain is contrary to a epidemiological study that found the prevalence of obesity in regular cannabis users to be lower than obesity rates in non-cannabis users. Another study demonstrated that cannabis use was associated with a higher caloric intake but not associated with a higher BMI. As evidence is building that dronabinol may have a place in chronic pain management it would be beneficial for providers to know if dronabinol may cause weight gain in a population where obesity may agitate their pain condition. This study will evaluate the impact dronabinol may have on weight in a chronic pain population.

Methods:
This will be a retrospective cohort study of Joint Base San Antonio military medical records database going back roughly two years to identify patients prescribed dronabinol for off label use in pain management. Patients who meet inclusion criteria will be reviewed to determine the initial date of dronabinol therapy and starting weight. Starting weight will be compared to weight three, six, nine, and twelve months later to determine any weight change. Dronabinol patients will be matched with pain management patients who did not receive dronabinol to serve as controls. Case-controls will be compared to determine any significant change in weight.

Results:
Results pending, research will be complete by April 2017

Implications/Conclusions:
Pending, conclusion will be completed by April 2017

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Air Force, the Department of the Army, or the Department of Defense or the U.S. Government.
Background:
Pediatric cardiopulmonary arrests that occur outside the ICU are associated with increased mortality. Rapid response teams (RRT) are effective in preventing codes and improving mortality in pediatric patients. Our institution previously established a pediatric RRT system modeled after the adult RRT system that was triggered by one abnormal vital sign (VS) parameter. This system resulted in many triggered RRTs due to pediatric physiology that easily prompts vital sign changes in the setting of anxiety, fever, or medication delivery. The Pediatric Early Warning Score (PEWS) system is an evidence-based tool that evaluates 3 domains: behavior, cardiovascular, and respiratory and utilizes a flowchart to guide RRT activation (Table 2, Figure 1).

Materials and Methods:
The PEWS system was implemented on June 20, 2016. Data were collected on age, RRT activations, code blues, patient acuity, interventions performed, potential missed opportunities, patient care days, mean monthly discharges, and transfers to the ICU (Table 1, Figures 2 and 3). Patient acuity was estimated using a daily nursing workload tracker. Pre- and post-intervention Likert scale surveys were administered to all pediatric ward and ICU staff regarding perceptions and confidence in the pediatric RRT system. Categorical data were analyzed using Fisher’s exact and Chi-square statistical methods; p-values <0.05 were considered statistically significant.

Results:
Fifty-eight pediatric RRTs and 2 code blue events were activated during the study period. The post-intervention RRT rate decreased from 20.2 to 15.5 RRTs/1000 patient care days, despite no change in patient acuity. After implementing the PEWS system, there was an increase in clinically significant interventions (p=0.04), respiratory support (p=0.001), and ICU transfers (p=0.01). Sixty-seven (58%) pre-surveys and 73 (62%) post-surveys were returned. Physicians reported that PEWS improved nursing communication (p=0.02) and more accurately identified deteriorating patients (p=0.13). Compared to the PEWS system, physicians found that the VS based system neglected signs and symptoms important to identify deteriorating patients (p=0.0006). Pediatric ward staff reported the PEWS system improved management and prioritization of ill patients (p=0.02), and emphasized clinical autonomy for nursing (p=0.07).

Conclusions:
PEWS implementation has been an efficient and effective means of identifying deteriorating pediatric patients on the pediatric ward. Following implementation, there was a decrease in the rate of pediatric RRTs activated, despite no change in clinical acuity and increased ward census. Utilization of the PEWS has led to a more appropriate identification of deteriorating ward patients, as evidenced by the increase in clinically significant RRT interventions. Pediatric staff reported increased confidence in managing deteriorating patients and improved clinical autonomy for nursing staff.

Key words: pediatric, rapid response team, quality improvement, outcomes, medical emergency team

Table 1: Pediatric Rapid Response Team (PRRT) Demographics

<table>
<thead>
<tr>
<th></th>
<th>VS System (Oct 15-Jun16)</th>
<th>PEWS (Jul16-Dec16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median [IQR] Patient Age (years)*</td>
<td>5 [2, 7.25]</td>
<td>2 [1, 12]</td>
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<tr>
<td>Table 2: Pediatric Early Warning Score Criteria</td>
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<tr>
<td><strong>Behavior</strong></td>
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<td>• Playing</td>
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<td>• Alert</td>
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<tr>
<td>• Appropriate at Baseline</td>
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<tr>
<td>• Sleep</td>
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<td>• Fussy but consolable</td>
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<tr>
<td>• Irritable/inconsolable</td>
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<td>• Lethargic</td>
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<td>• Confused</td>
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<td>• Reduced response to pain</td>
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<td><strong>Cardiovascular</strong></td>
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<td>• Pink</td>
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<td>• Capillary Refill 1-2 seconds</td>
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<td>• Pale</td>
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<tr>
<td>• Capillary refill 3 seconds</td>
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<tr>
<td>• Grey or cyanotic</td>
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<tr>
<td>• Capillary refill 4 seconds</td>
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<td>• Tachycardia of 20 above normal rate</td>
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<td>• Grey or cyanotic</td>
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<td>• Mottled</td>
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<td>• Capillary refill 5 seconds or above</td>
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<td>• Tachycardia of 30 above normal rate or bradycardia</td>
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<td><strong>Respiratory</strong></td>
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<td>• Within normal parameters</td>
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<td>• No retractions</td>
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<td>• Greater than 10 above normal parameters</td>
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<td>• Use of accessory muscles</td>
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<tr>
<td>• 30% FIO2</td>
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<td>• 3+ Liters/minute</td>
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<td>• Greater than 20 above respiratory parameters</td>
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<tr>
<td>• 40% FIO2</td>
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<td>• 6+ Liters/minutes</td>
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<td>• Trach &amp; ventilator Dependent</td>
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<td>• ≥ 5 below normal parameters with retractions</td>
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<tr>
<td>• Grunting</td>
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<tr>
<td>• 50% FIO2</td>
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<tr>
<td>• 8+ Liters/minute</td>
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</table>

* Interquartile range
** PEWS was estimated in the pre-intervention group based on electronic chart review
*** Defined as patients meeting RRT criteria that did not have an RRT activated
**** Workload Management Score for Nursing Internet measured patient acuity

Figure 1: Pediatric Early Warning Score Flowchart
Figure 2: Pediatric RRT Interventions (Vital Sign System vs. PEWS)

- **PEWS Score 0-2**: Reassess and rescore at next routine assessment.
- **PEWS Score 3**: Notify Resident/intern and Charge RN of clinical change.
- **Individual PEWS Score 4 in any category**: Plan and collaborate with entire health care team.
- **PEWS Score 4**: Document and determine time of next assessment and resoring.
- **PEWS Score 5**: Notify Charge RN, resident/intern, supervising resident.
- **Page PRRT**.

*Families often know their child best. Please remember to listen to their concerns and advocate for them.

Figure 3: Pediatric RRT Tracking Data

- Vital sign-based
- PEWS

$p = 0.001$

$p = 0.04$

$p = 0.01$
The influence of race/ethnicity on the relationships among forms of distress, alcohol use, and alcohol related problems in a Veteran sample

Authors: Perrotte, J. K., Meyer, E., DeBeer, B., Kimbrel, N., Gulliver, S. B., & Morissette, S. B.

Introduction: Research suggests individuals use alcohol in response to distress. Few studies address the potential influence of race/ethnicity in this relationship. A study of Veterans indicated racial/ethnic differences in the relationship between post-traumatic stress disorder (PTSD) and alcohol use, (i.e., positive relationship between PTSD and alcohol use for non-Hispanic whites but not Hispanics). Research examining other forms of distress among Veterans (i.e., general stress, anxiety, and depressed mood) as related to alcohol use and alcohol related consequences is lacking. The present study addressed these research gaps within an exploratory framework.

Method: We performed a secondary analysis of baseline data from a VA-funded longitudinal study called Project SERVE, a study examining predictors of functional impairment and recovery among Veterans who served in support of the wars in Iraq and Afghanistan. The sample consisted of Veterans who identified as non-Hispanic white (n = 104; dummy-coded reference group), non-Hispanic black (n = 78), and Hispanic (n = 47). Participants were interviewed using a battery of validated psychological instruments and demographic items. Forms of distress (i.e., depressed mood, anxiety, and stress) were measured using subscales from the Depression, Anxiety, Stress Scales – 21 (DASS-21). The Rutgers Alcohol Problem Index (RAPI) assessed alcohol related problems. The Revised Daily Drinking Questionnaire (DDQ-R) assessed frequency and quantity of alcohol consumption. Control measures included age, gender, income, and PTSD symptoms (PTSD Checklist – military version, PCL-M).

Results: We employed a negative binomial regression strategy to account for the distribution of the alcohol variables. Primary analyses are organized by alcohol related outcome:

**Drinking frequency:** Stress was positively related to drinking frequency. There was an interaction between stress and race/ethnicity on drinking frequency. Non-Hispanic black Veterans experiencing higher stress and non-Hispanic white Veterans experiencing lower stress engaged in similar rates of drinking frequency. Also, when compared only to Hispanic Veterans, non-Hispanic whites experiencing lower levels of stress reported greater drinking frequency than Hispanic Veterans. Testing the interaction between anxiety and race/ethnicity on drinking frequency yielded similar patterns.

**Drinking quantity:** Stress was the only form of distress to exhibit a strong, positive association with drinking quantity, however a cross-over interaction emerged between anxiety and race/ethnicity as related to drinking quantity. Specifically, anxiety was positively related to drinking quantity for non-Hispanic blacks, but negatively related for non-Hispanic whites.

**Alcohol related problems:** Non-Hispanic black Veterans reported significantly more alcohol-related problems than non-Hispanic white Veterans. Depressed mood and stress were both positively related to alcohol-related problems. A cross-over interaction between anxiety and race/ethnicity on alcohol-related problems indicated that, when experiencing high levels of anxiety, non-Hispanic whites are much more likely than Hispanics to endorse alcohol-related problems. A similar pattern was found when accounting for the interaction between stress and race/ethnicity on alcohol related problems.
Conclusions: Our study implies empirical merit in assessing forms of distress separately as related to alcohol use in this sample. Findings from this study support the clinical utility of accounting for race/ethnicity when considering the likelihood of Veterans engaging in alcohol use or experiencing alcohol related problems while encountering various forms of distress.
The Association of Teaching Institutions and Complications Due to Overdose or Incorrect Anesthesia Medication in the United States

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School of Medicine, University of Texas Health at San Antonio

Introduction: Although anesthesia is routine during most surgical procedures, fear of complications during anesthesia due to improper administration remains. However, limited information exists in the literature regarding rates of complications due to anesthesia medication errors. The purpose of this study is to determine the impact of teaching institutions on complications from overdose or incorrect anesthesia medications using a robust database.

Methods: Data was collected from the Healthcare Cost and Utilization Project (HCUP) database for complications due to anesthesia overdose or incorrect anesthesia medications (ICD-9 code 968.4) in the United States between 2007 and 2014. The cohort was dichotomized into teaching versus non-teaching hospitals and the data was analyzed using Z-Test.

Results: Between 2007 and 2014, there was a total of 2778 complications from overdose or incorrect anesthesia. Of the total cases, 66.8% were male and 76.3% were between 18 to 44 years of age. Among these, 1622 (58.3%) took place in teaching institutions showing a significant 200% increase from 2007 to 2014 (p < 0.001). (Fig. 1). Conversely, the complication rates in non-teaching institutions have demonstrated a steady decline since 2009. The discrepancy between both hospital types was the highest in 2014 in which the 255 incidents from teaching institutions made up 73.4% of the total anesthesia-related complications (p < 0.001).

Conclusion: In recent years, there have been significantly higher incidences of adverse effects related to anesthesia overdose or incorrect anesthesia medication administration in teaching institutions compared to non-teaching. Incidences gradually decreased in non-teaching hospitals during this 8-year study. This discrepancy might be due to the use of more in-training personnel such as anesthesia technicians, nurse anesthetics, and residents. Additionally, teaching hospitals treat a sicker patient population, which likely predisposes them to surgical complications and thus complex anesthesia administration. Perhaps improved anesthesia protocols and supervision in teaching hospitals can lower these incidents. Furthermore, prospective research is warranted to ascertain the causes for anesthesia administration errors.

Figure 1: Teaching vs. Non-Teaching Hospital Incidences of Complications Related to Overdose or Incorrect Anesthesia Medication in the United States During 2007-2014
Teaching Vs. Non-Teaching Hospital Discharges of Pois-Gen Anesth Nec/Nos (968.4)

![Graph showing teaching vs. non-teaching hospital discharges from 2006 to 2015.](image)

- **Teaching**
  - Equation: $y = 13.619x - 27178$

- **Non-Teaching**
  - Equation: $y = -12.214x + 24701$

- **Total**
  - Equation: $y = 1.4048x - 2477$

Discharges are plotted against Years from 2006 to 2015.
Poster #115

Detection of Mixed Bacterial Populations by Surface Enhanced Raman Spectroscopy (SERS)
Luis A. Martinez, PhD, Thomas E. Bird, BS, and Jonathan M. Stahl, CAPT, USN, DDS, MPH, PhD, John W. Simecek, DDS, MPH
Naval Medical Research Unit San Antonio

Background: The incidence of bacterial infections in warfighters has increased during the combat operations in Iraq and Afghanistan. The majority of the infections were caused by members of the ESKAPE (Enterococcus, Staphylococcus, Klebsiella, Acinetobacter, Pseudomonas, and Escherichia) group of pathogens. The rapid detection and diagnosis of microorganisms in the blood can improve the outcome of the infections, lessening the occurrence of morbidity and mortality. Current diagnostic techniques require plating, are tedious and time consuming, taking up to 48 hours for growth and examination of the bacterial colonies. The gold standard for diagnosis is the use of polymerase chain reaction (PCR) analysis. The drawback of PCR is the need for specific probes and the inability to multiplex the assay. The objective of this research is to evaluate the ability of SERS to detect bacteria in mixed populations.

Methods: An oblique deposition silver nanorod substrate was utilized to obtain spectra using a DXR™ tabletop Raman microscope. A total of four bacterial strains including, the Gram-positive Staphylococcus aureus, and Gram-negatives Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumonia at concentrations ranging from $10^7$ to $10^8$ colony forming units (CFUs) were tested. Mixture samples of S. aureus/E. coli, and P. aeruginosa/K. pneumonia were compared to pure bacterial scans for each of the bacteria tested. Bacteria mixture samples were prepared by mixing bacteria to create ratios in 10µl increments until reaching equilibrium at 50µl/50µl. The samples were scanned using the 10X, 50X, and 100X objective, and the resulting spectra were analyzed using principal component analysis (PCA) on MATLAB software. Samples were scanned five times at random locations on the well, and all experiments were repeated three times.

Results: Signature peaks were observed in the spectra of the pure bacterial cultures scanned with the 10X, 50X, and 100X DXR™ Raman microscope objectives. The spectra collected with the 10X objective demonstrates the sensitivity of SERS technology to distinguish the signature peaks in pure bacterial samples, as well as the mixed population bacterial samples. Analyses by PCA showed a segregation of the spectra toward the pure bacterial samples based on the predominant bacterial species in the mixture. The spectra collected with the 50X and 100X objectives were more dynamic, however, and followed the same trend observed with the 10X objective spectra. Although higher variability was observed in the spectra collected with the 50X and 100X microscope objectives, the PCA analysis showed a distribution that followed the same trend as the 10X objective.

Conclusions: The results of this study demonstrate the ability of SERS technology to distinguish between two different bacteria in mixed populations. The ability of SERS technology to differentiate between two bacteria establishes SERS as a potential rapid and effective diagnostic platform.
Effectiveness of Antimicrobial Peptide LL-37 and its Homologous Peptides Against ESKAPE Group of Pathogens

Luis A. Martinez, PhD, and Jonathan M. Stahl, CAPT, USN, DDS, MPH, PhD
Naval Medical Research Unit San Antonio

Background: The overuse and misuse of antibiotics in recent decades has led to an increase in bacteria that are multidrug resistant (MDR). The rise of MDR bacteria complicates the antibiotic therapies which in the past were used to control bacterial infections. The combat operations in Iraq and Afghanistan have seen an increase in the incidence of bacterial infections caused by members of the ESKAPE (Enterococcus, Staphylococcus, Klebsiella, Acinetobacter, Pseudomonas, Escherichia). As the number of antibiotic resistant bacteria rises, the development of new classes of antibiotics is falling behind. Antimicrobial peptides (AMPs) are amphipathic cationic peptides that have demonstrated broad spectrum antimicrobial activity against drug-resistant strains including methicillin-resistant Staphylococcus aureus with minimal toxicity to host cells. The objective of this project is to determine the antimicrobial activity of AMP LL-37 and its homologues against members of the ESKAPE group of pathogens.

Methods: A total of six bacterial strains including S. aureus (ST19, ST22), P. aeruginosa (ST14, ST16), and K. pneumonia (ST8, ST9) were treated with LL-37 and two homologues LL-37a and LL-37b. The homologues were identified and selected using the linked antimicrobial peptide (LAMP) database feature, basic local alignment search tool (BLAST). The AMPs were re-suspended in ultrapure water at a concentration of 5.5mg/ml. Bacteria at a concentration of 5X10^5 were subjected to concentrations ranging from 500µg/ml to 0.244µg/ml of AMPs LL-37 and its homologues in Mueller Hinton II media in 96 well plates. The plates were incubated in a BioTek plate reader at 37°C, and the OD600 was collected every hour for 19 hours.

Results: The data indicate LL-37 and LL-37a were ineffective against S. aureus ST19 and 22. S. aureus ST19 and 22 treated with LL-37b were completely eliminated at a concentration of 62.5µg/ml. Against P. aeruginosa ST14 and ST16, LL-37 eliminated the bacteria completely at a concentration of 125µg/ml. Homologue LL-37a had activity against ST14 and ST16 at 250µg/ml and 125µg/ml, respectively. Strains ST14 and ST16 treated with LL-37b showed complete elimination at 62.5µg/ml and 31.25µg/ml, correspondingly. K. pneumonia strains ST8 and ST9 treated with LL-37 were eliminated at a concentration of 500µg/ml. Strains ST8 and ST9 were eliminated at concentrations of 250µg/ml and 125µg/ml of LL-37a. Homologue LL-37b eliminated strains ST8 and ST9 at a concentration of 62.5µg/ml.

Conclusions: The results of this study indicate the higher activity of homologue LL-37b against Gram-positive and Gram-negative bacteria strains including S. aureus, K. pneumonia, and P. aeruginosa. The data suggest the importance of the peptide conformation to its interaction with the bacterial cell wall. Future work will focus on the continued efforts to identify peptides with high activity against MDR pathogens, as well as the immunomodulatory effects of the active homologues identified.
Background: Dental amalgam is a safe, low-cost, and durable restorative material. However, the amalgam must be removed from dental wastewater to comply with the US Environmental Protection Agency (EPA) guidelines. The EPA has issued a new mandate as of December 2016 which requires the use of dental amalgam separators with ≥95% efficiency in all dental practices that place or remove amalgam. The purpose of this study is to develop and test new chairside separator technologies, and to determine if commercially available chairside separator (DD2011P, Duel & Associates) comply with the EPA proposed rule.

Materials and Methods: Efficiencies of two activated carbon-block separator prototypes (AC-150 and AC-280), developed by Naval Medical Research Unit San Antonio (NAMRU-SA), were tested in a laboratory setting following the International Organization for Standard (ISO) 11143 protocol. In addition, DD2011P, paired with a flow monitoring system, was clinically evaluated to assess its compliance with the EPA proposed rule and to predict its lifecycle. Data associated with flow resistance, filter performance, and patient turnover were collected and post-proceed.

Results: AC-150, AC-280 and DD2011P separators performed above the 95% removal efficiency specified in the ISO standard, yielding 99.89%, 99.83% and 97.5%, respectively. Initial clinical tests showed the service-life of the DD2011P was approximately 300 days, and the clog defining pressure drop was 9.36 inHg. Clinical assessment of the activated carbon-block separators is currently underway.

Conclusions: The amalgam separators evaluated in this study demonstrated the ability to meet and surpass the EPA proposed rule. NAMRU-SA is currently developing improvements including smaller, more effective filtration materials, and a system that continuously monitors and reports filter performance, resulting in an effective and efficient “smart filter.”
ATTITUDES ABOUT WEARING SCRUBS IN PUBLIC: HEALTHCARE VERSUS NON-HEALTHCARE

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Introduction

The growing trend of wearing scrubs outside the clinical setting has sparked debate, particularly when the individual wearing scrubs is a healthcare professional. Scrubs are increasingly worn for non-professional purposes, and this poses risk of devaluing the professional meaning of scrubs. In the wake of this, we ask: should healthcare professionals wear scrubs outside clinical settings? We hypothesized that people who are not affiliated with healthcare would have differing viewpoints compared to healthcare people when it comes to seeing healthcare professionals wear scrubs in public.

Materials and Methods

We prepared a survey to assess the subjects’ opinion about wearing scrubs in public. The survey was sent by e-mail to healthcare students and employees at The University of Texas Health San Antonio and to non-healthcare students and employees at The University of Texas at San Antonio. The survey was also shared through social media. The 11 survey questions were divided into favorable and unfavorable statements and scored from 1 to 5 for each question with a total score ranging between 11-55. The total scores were analyzed and compared using a sample T-Test.

Results

2730 people responded to the survey. 68.8% of the responses came from females, 45.46% from healthcare subjects, and 34.5% from people with a bachelor’s degree. Responses from healthcare affiliates came from people who were significantly older (p<0.05). The mean healthcare related group responses scored 33.96 ± 7.65, while the non-healthcare group scored 34.47 ± 8.08, (p=0.096). The responses by gender also showed no significance between male and female participants, 34.3 ± 8.3 and 34.2 ± 7.7 respectively, (p= 0.673).

Healthcare subjects and non-healthcare subjects significantly agreed on the following: “Scrubs should only be worn by medical professionals” (p<0.05), “Scrubs should only be worn in a clinical or hospital setting where they are required” (p<0.05), and “Other professions that are not part of the medical field should not wear scrubs” (p<0.05).
613 subjects provided comments at the end of the survey. Most comments emphasized that wearing scrubs is acceptable from home to work and vice versa and that surgical scrubs should be removed before leaving the hospital. Majority expressed concerns for professionalism and for scrubs cleanliness, which remains uncertain.

**Conclusions**

This study found no significant difference in attitudes about wearing scrubs in public when healthcare and non-healthcare people were compared. Both groups agree with wearing scrubs in the clinical settings only. Healthcare professionals did not endorse the need to change their scrubs after work; non-healthcare subjects believed changing one’s scrubs before leaving clinical settings was proper. The authors believe healthcare institutions should emphasize wearing scrubs only in professional circumstances, differentiate between uniform scrubs and surgical scrubs, provide clean surgical scrubs to employees, and designate locker rooms to encourage staff to change prior to the end of the work period.

**References**


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Usage of Vasopressors In United States during a Decade

Shaadi Abughazaleh, Ali Seifi MD, FACP

Introduction: Vasopressors are a class of drugs that are widely use to cause vasoconstriction and increase Mean Arterial Pressure. Due to their strong effect on the circulatory system, they have become staple medications in hypotensive individuals, most notably with patients in shock and sepsis. The purpose of this study is to determine the usage of Vasopressors in the United States during a decade with a focus on Teaching institutions.

Methods: Data from the Agency for Healthcare Research and Quality’s Nationwide Inpatient Sample (NIS) was queried from 2004-2014 for inpatient admissions of patients who received an Infusion of Vasopressor anytime during their hospital course. Total number of patients who received this procedure (ICD-9 code 00.17) were adjusted by hospital characteristics and the cohort was dichotomized into two groups of Teaching and non-teaching institutions. Z-tests were performed using statistical analysis to assess for significant differences.

Results: During the study period we reviewed 106,881 patients who admitted primarily for hypotensive shock and required vasopressors. Among these population there was 50.65% Male, aged mostly between 65—84 y.o There was 22-30% mortality which initially decreased from 2004-2012 (p value 0.074) although not enough to prove significant with 95% confidence. Since 2012, the mortality rate has increased significantly (p value 0.00079). The LOS ranged from 6.3 to 7.1, with no significant change overall throughout the decade remaining around 7 days (P value >0.05).

Generally, the incidence of usage of vasopressors significantly increased from 2004 to 2014 (P value < 0.0000). When dividing the cohort into two groups, both T and NT group had significant increase of incidence during the cohort (P value < 0.00000). However, the usage was significantly higher in teaching institutions, especially during the recent years 2012-2014 (P values < 0.0000).

Conclusions: Our data shows that Vasopressor Infusion is being more common in the United States, as the use of this procedure has steadily increased since initial data was recorded in 2004. However, in teaching hospitals, the use has increased at a faster rate and there is now a significantly greater number of uses when compared to non-teaching hospitals, most notably in recent years. This increase in the trends, may be explained by “Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock” that outlined the importance of Vasopressor use. Since this, and many other studies that followed were published, Vasopressors have become a common practice in the treatment of these patients; this may explain the increase usage of these medications in both hospital categories. When assessing the increase in usage in teaching hospitals compared to non-teaching hospitals, there are many possible explanations. One hypothesis is based on the fact that teaching hospitals often treat patients that require more invasive and critical levels of care resulting in an increased usage of vasopressors. Another hypothesis is that teaching hospitals are more likely to be involved in research trials which compare outcomes based on novel treatment methods which can encompass the vasopressor class of medications in patients that would otherwise not receive them. One such study, The Surviving Sepsis Campaign which first launched in 2004 stated a number of goals aimed at
increasing the survival rate of sepsis diagnosed patients. In 2008, an initial update was created based on the data collected through 2007. Hospitals were then tasked with creating manuscripts that would be updated through 2011 and early 2012. With this new information in hand, hospitals, especially teaching hospitals more involved with research, began to use vasopressors to treat sepsis more liberally. Further studies are needed to determine the factors that explain the significant differences in vasopressor usage between teaching and non-teaching hospitals.

Figure 1: Number of Infusions of Vasopressors by Year in Teaching vs Non-Teaching Hospitals

References:


ANALYZING THE TRENDS IN HOSPITAL DISCHARGES AND NATIONAL HEALTH EXPENDITURES USING HCUP NATIONAL INPATIENT SAMPLE DATABASE

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Background: The National Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP) includes estimates of hospital discharges in the United States from 1993 through 2014. In 1997 the total number of hospital discharges was 33,230,554. By 2005, that number rose to 37,843,039, resulting in a 13.88% increase over that eight-year period. In 1990 and 2005 the national health expenditures were $721 billion and $2,024 billion, respectively, reflecting a 180% increase. The authors sought to study the trends in hospital discharges and national health expenditures from 2006 to 2014.

Methods & Materials: NIS estimates many different important data points, including hospital discharge, to evaluate important trends in healthcare. The total number of discharges reported in the NIS from 2006 through 2014 were compared to the total healthcare expenditures of the United States for the same years. The total discharges of privately insured patients and uninsured patients during this time period were also evaluated. The healthcare expenditure figures were obtained from the Centers for Medicaid and Medicare Services Report on National Healthcare Expenditure Accounts.

Results: Discharges peaked in 2008 at 38,210,889. After 2008 annual hospital discharges decreased to a nadir of 35,358,818 in 2014. The last time discharges were in that range was in 2000. Private insurance hospital discharges ranged between 13.5 million in 2008 to 10.8 million in 2014. Uninsured hospital discharges ranged from 2.3 million to 1.6 million. The only statistically significant change in discharges was in 2014 for the decrease in uninsured total discharges (p<.001). In 2006 and 2014 there were $2.1 trillion and $3.0 trillion, respectively, spent on healthcare. There is an inversely proportional relationship when comparing the discharges to the National Health Expenditures from 2006 to 2014. See Figure 1.

Conclusions: The trend in declining hospital discharges began in 2008, two years before the passage of the Affordable Care Act, five years prior to the introduction of health insurance exchanges and subsidies, and six years before Medicaid expansion. Factors such as the recession that began in 2008, preventive medicine, clinical evaluation techniques and interventions, and other contributing factors need be evaluated to better understand the decreasing trend in hospital discharges.
MEASURING PHYSICIAN COORDINATION OF CARE USING SOCIAL NETWORK ANALYSIS AND RELATIONAL COORDINATION

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BACKGROUND
Physician coordination of care has been examined using social network analysis (SNA) of connections between physicians based on shared patients in administrative data. While previous researchers found that patient sharing predicts existence of informal advice seeking, little is known how well SNA characterizes physician coordination. We examine SNA’s strengths for characterizing physician coordination using Relational Coordination (RC), a measure of task-related communicating and relating.

METHODS
Participants include primary and specialty care physicians in the Veterans Administration (VA). VA administrative data was used to identify, map relationships of physicians who shared ≥ 1 patient(s). SNA metrics include node degree (ND; number of shared patients by 2 physicians) and adjusted node degree (AND; sum of ND per facility/number of neurologists per facility). RC surveys asked 750 health professionals to rate 4 dimensions of communication (frequency, accuracy, timeliness, and problem-solving vs. blaming) and 3 dimensions of relationship quality (shared knowledge, shared goals, mutual respect) of medical professionals at their own facility and a referral facility on a scale 1-5 (least to most favorable). RC measures were included for analysis if they were from sites/physicians sampled for SNA. SNA and RC metrics were analyzed using Spearman’s rho and deemed significant where a = .05.

RESULTS
We used Fuchterman Reigngold layout in Gephi 0.9 to visualize physician networks at 66 facilities. Fig. 1 shows several case examples of networks with (a) evenly shared patients among primary and specialist physicians, (b) neurologists who coordinate care with other specialties, (c) one neurologist coordinating care among physicians, (d) internists and neurologists coordinating care more than primary physicians, (e) psychiatrists coordinating specialty care, as well as other patterns of coordination. RC measures were calculated on 57 of 165 respondents. Across the VA, patient sharing (ND) was significantly correlated with coordination (RC), rs (40) = 0.356, p = .022. Patient sharing among neurologists (AND) was significantly correlated with coordination (RC) at the national level, rs (40) = 0.337, p = .03. Patient sharing between neurologists within their own facilities (AND) was significantly correlated with accurate communication, rs (38) = 0.317, p = .049, and mutual respect, rs (36) = 0.396, p = .015. Shared patients between neurologists at referring facilities (AND) and accurate communication was also significantly correlated, rs (13) = 0.661, p = .014.

CONCLUSIONS
SNA as a measure of care coordination was supported by patterns of associations between SNA metrics and RC. Physician coordination occurs primarily through the VA’s electronic health record system, which provides access to progress notes, consultations, and discharge summaries. Accurate communication is required for patient coordination but there is little need for frequent communication. SNA may be mapped and its dynamics tracked over time thus making it a useful tool when designing interventions to improve care.
Evaluation of a Nitric Oxide Formulation against Multi-Drug Resistant Bacterial Biofilms

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Background: Multi-drug resistant (MDR) bacteria comprise 46-51% of all bacterial isolates and are one of the most common causes of clinical infections in civilian and military populations. MDR infections often form biofilms which protect bacteria from clearance by immune cells and reduce antibiotic efficacy by limiting the ability of antibiotics to reach bacteria within the biofilm’s core. Fortunately, nitric oxide (NO) is a small diatomic molecule that can potentially penetrate biofilms and exhibits broad-spectrum antibacterial properties. Ultimately, a stable NO formulation with sustained-release capabilities, activity against a broad spectrum of MDR bacteria, and minimal adverse effects on host tissue is needed for developing a field-deployable technology for treating MDR infections. Here, we evaluate the efficacy of an extended release NO formulation against biofilms of MDR bacteria as a potential new therapy for treating infections.

Materials & Methods: MDR isolates of Acinetobacter baumannii, Pseudomonas aeruginosa, and Klebsiella pneumoniae were selected from an inventory of isolates collected from combat-injured US military personnel. The NO release profile of an extended release formulation (NVN 4000; Novan, Inc., Durham, NC) was characterized over 24 hours using a Griess assay. Minimum biofilm eradication concentration (MBEC) assays were performed on biofilms cultured for 24 hours on 96-well Innovotech MBEC™ plates. Biofilms were challenged with 1-32 mg/mL of the NO-releasing formulation for 4 or 24 hours, and viable bacteria remaining in the biofilms were enumerated by colony forming unit (CFU) assays.

Results: The NVN 4000 formulation delivered an NO payload of approximately 1.6 μmols NO/mg formulation over 24 hours, with 73% of the NO released over the first 4 hours. Treatment of biofilms with NO for 4 or 24 hours resulted in a maximum reduction in recovered CFUs of 3- to 5-logs relative to untreated biofilms. The efficacy of NVN 4000 was dose-dependent with the greatest reduction in biofilm CFUs at 8-32 mg/mL. Overall, NVN 4000 showed activity against all bacterial isolates tested at 4 and 24 hours, but the extent of anti-biofilm efficacy was strain dependent.

Conclusions: The NVN 4000 extended release NO formulation demonstrated significant activity against biofilms of MDR bacteria. These results demonstrate the potential for an extended release NO formulation to be utilized as an alternative to antibiotics for treating MDR bacterial biofilms.
Targeted Gold Nanoparticle-assisted Laser Therapy for the Disruption of Methicillin-resistant Staphylococcus aureus Biofilms

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**Background:** Multi-drug resistant (MDR) pathogens are becoming the most common cause of infectious disease-related deaths around the world, killing more Americans every year than colon and breast cancer combined. Furthermore, infections caused by MDR bacterial strains, which comprise ~ 50% of all bacterial isolates, complicate the treatment and recovery of combat-injured US military personnel and adversely impact battlefield readiness. MDR pathogens commonly exhibit increased tolerance to antibiotics due to formation of biofilms (comprised of extracellular matrix and cells) that serve as a protective barrier against the immune system and antibiotic treatment. There is an urgent need to discover alternative strategies that are less prone to drug resistance and can improve the efficacy of mainstay antibiotic regimens. Here, we evaluated the use of targeted laser therapy as a potential alternative approach to destroy and disperse bacterial biofilms using an in vitro methicillin-resistant Staphylococcus aureus (MRSA) infection model.

**Methods:** Overnight cultures of MRSA were suspended at 107 CFU/mL in tryptic soy broth supplemented with 10% human plasma and grown in fibrinogen-coated glass-bottom 96-well microplates at 37°C under static conditions for 24 h. The resulting biofilms were pre-treated with anti-Staphylococcus aureus conjugated gold nanoparticles (GNPs, 65 µg/mL) or with non-targeted GNPs for 2 h and then exposed to pulsed laser irradiation (532 nm, 8 ns, 1 Hz). Biofilms treated with laser alone, non-targeted GNPs alone, or vehicle only were also included as controls. Confocal microscopy was used to visually assess the extent of biofilm damage, while colony forming unit assays were used to evaluate cell viability.

**Results:** Treatment of MRSA biofilms with a combination of anti-S. aureus conjugated GNPs followed by laser irradiation led to the most significant bacterial cell killing, with an 89±3% (mean±SD; n=3) reduction in viability relative to vehicle controls. The treatment also led to 96±2% (mean±SD; n=3) dispersion of biofilms as evidenced by confocal microscopy. In contrast, biofilms in the vehicle control group remained robust and viable. Likewise, biofilms treated with laser alone or GNPs alone remained unaffected. These results demonstrate the use of targeted GNP-assisted laser therapy as a potential strategy to physically and selectively destroy and debride biofilms (including matrix and cells) from a wound site, and thus eradicate an obstructive barrier to healing.

**Conclusion:** Targeted GNP-assisted laser therapy may improve delivery of antibiotics to biofilm-associated bacterial cells and enhance therapeutic efficacy of mainstay treatment regimens.
DELAYED ONSET OF METHEMOGLOBINEMIA IN A PATIENT WITH BURN AND INHALATION INJURY

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BACKGROUND / OBJECTIVE

Hydroxocobalamin (vitamin B12) is used in the treatment of cyanide poisoning because it is efficacious while avoiding the side effects associated with nitrite use. While erythema, hypertension with reflexive bradycardia, and chromaturia are commonly reported side effects of hydroxocobalamin, methemoglobinemia has not been reported. Methemoglobinemia is a relatively rare problem, which may cause intracellular hypoxia, cardiovascular collapse, and ultimately death if not appropriately treated. Despite reports of co-oximetry assay interference in animal studies, the effect on the actual hemoglobin fractions by hydroxocobalamin use has yet to be comprehensively studied and reported in humans. The purpose of this report is twofold: (1) to describe our recent, unusual experience of a burn patient who developed progressive methemoglobinemia within an hour of administration of hydroxocobalamin for the presumptive treatment of cyanide poisoning, and (2) to raise awareness of this potential adverse effect and encourage reporting of recognized cases in the literature as well as to the Federal Drug Administration.

METHODS

The patient’s electronic medical record was reviewed and literature review was conducted via PubMed.

RESULTS

A 47-year old man presented with 61% total body surface area thermal burns sustained during a tugboat engine explosion. Bronchoscopy revealed grade 1 inhalation injury. Noteworthy admission labs included lactate 9.24 ml/dL, methemoglobin 1%, carboxyhemoglobin 0.2%, blood urea nitrogen 23.3mg/dL and creatinine 1.49mg/dL. Despite largevolume resuscitation, serial arterial blood gases showed a persistently elevated lactate (7-8 mg/dL). A single dose of 5 grams intravenous hydroxocobalamin was given for presumed cyanide toxicity. Immediately thereafter, he became hypertensive and bradycardic, with an associated decrease in lactate to 5.51mg/dL, rise in methemoglobin to 4.10%, and oxygen desaturation by pulse oximetry to 76-80% on 100% FiO2 for the next 48 hours despite arterial oxygen saturations >95%. The methemoglobin level peaked to 13.40% within 14 hours. Methylene blue was not administered. He did not have genetic deficiencies or abnormal variants of hemoglobin.

CONCLUSIONS / SIGNIFICANCE

The delayed onset of methemoglobinemia in our patient is temporally associated with hydroxocobalamin use in the presence of persistent lactic acidosis and normal admission levels of carboxyhemoglobin and methemoglobin. Our patient was without pre-existing cardiovascular disease, anemia or genetic enzyme deficiencies. He did not receive any nitrate-containing compounds within the first 48 hours. Furthermore, the patient’s burn resuscitation included the use of vitamin C (ascorbic acid) infusion, which reduces levels of MetHb and is an alternative to methylene blue, particularly in those with G6PD deficiency or when
methylene blue is unavailable. The patient was diagnosed with primaxin-resistant Proteus mirabilis bacteremia 6 days post-burn. This would argue against development of methemoglobinemia as Proteus is a urease-producing bacteria, leading to a favorable alkaline environment. There was a significant 20-hour delay between time of burn and development of methemoglobinemia, making the possibility of absorption of toxin through burned skin via retained clothing less likely. Lastly, majority of burned areas were dressed in 5% mafenide acetate solution, which can induce methemoglobinemia within 10-30 minutes. However, the time of application to development of methemoglobinemia in our patient was over 10 hours.
Introduction: Acute respiratory distress syndrome (ARDS) is characterized by acute onset of hypoxemia, bilateral radiographic pulmonary infiltrates, pulmonary edema, and leads to multi-organ failure. ARDS may result from trauma, inhalation injury, burns, massive fluid resuscitation and transfusions. Extracorporeal Life Support (ECLS) may be used to support ARDS patients during transport, including during aeromedical evacuation. High mobility group protein box 1 (HMGB1) is an important indicator of damage-associated molecular patterns (DAMPs) expression and disease progression in ARDS. HMGB1 has been identified as a mediator of ARDS and is expressed in blood following activation of damaged cells. The effect of altitude change on HMGB1 expression during air transportation is unknown. We hypothesize that HMGB1 expression will be affected by changes in altitude to a greater extent in injured animals supported by ECLS versus healthy animals on ECLS undergoing the same altitude exposure.

Methods: Female Yorkshire pigs (52.34 ± 1.17 kg, n=7) were anesthetized and received arterial and venous catheters, followed by tracheostomy. Following baseline measurements, animals were cannulated and veno-venous ECMO was initiated (CardioHelp, Maquet Gmbh, Getttinge Group, Rastatt, Germany), via an Avalon 23 Fr. catheter inserted into the right jugular vein. Animals were transported to an adjacent building housing hypobaric chamber for experiment. Animals underwent a standardized flight profile: 30 minutes each at ground level, 5000ft., and 8000ft., 5 minutes 30000ft., 30 minutes 50000ft. After altitude exposure, animals were returned to the ICU overnight. The next morning, bilateral pulmonary contusions were carried out as previously described, followed by chest tube placement. The travel and flight was repeated in injured state. Samples were collected after ECMO initiation, before and after transports to the altitude chamber, after injury, and every 15 minutes during the flight profile. HMGB1 ELISA (IBL international, ST51011, NC, US) was utilized to analyze the level of HMGB1 in the blood at each time-point.
Results: This study involved 350 hours of ICU and en-route care. There were no changes in systemic levels of HMGB1 on day 1 throughout altitude exposure. HMGB1 was significantly elevated on day 2 following chest contusion (n=7 base line vs each time point *p<0.05, base line; 3.81±2.29, 24 hours’ post ECMO; 12.79±4.08, post injury; *33.55±6.38). No statistical difference was found for changes in HMGB1 expression during flight in uninjured state on day 1 or during injured state on day 2. Additionally, PaO₂-to-FiO₂ ratio (PFR) was significantly decreased on day 1 at both 5000 ft. and 8000 ft., as well as after injury on day 2, when compared to baseline PFR. Both PFR and HGMB1 level were correlated (Figure 1, *p<0.05, y = -7.2086x + 336.54, R² = 0.55). This study is currently ongoing, with additional sampling and data analysis in progress.

Conclusions: High altitude does not alter HMGB1 expression in uninjured state on ECLS. Pulmonary contusion causes a transient increase in HMGB1 levels. We conjecture that bedside assessment of damage associated molecular patterns confirms injury and may provide a useful monitoring capability during en-route care at ground level and altitude.

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**BENCHMARKING CO2 REMOVAL EFFICIENCY DURING ECCO2R**

**BY HEMOLUNG AND NOVALUNG**

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**INTRODUCTION:** Extracorporeal carbon dioxide removal (ECCO2R) is a form of minimally-invasive extracorporeal life support (ECLS) that combats hypercarbia, permitting reductions in ventilator settings, and reduces the risk of ventilator-induced lung injury. This study assessed CO2 removal efficiency by 2 ECCO2R devices: Hemolung (Alung Technologies, Pittsburgh, PA) and Novalung (Xenios, Heilbronn, Germany). The Hemolung uses a 15.5-Fr cannula, capable of blood flows up to 550 mL/min utilizing a centrifugal blood pump. The Novalung uses variable membrane and catheter sizes to achieve a range of blood flows, from ultra-low flow ECLS up to full ECMO. In this study we utilized an 18-Fr dual-lumen catheter (NovoPort, Xenios, Heilbronn, Germany) and iLA Activve MiniLung membrane for the Novalung. We present CO2 removal efficiency data on these devices from an ongoing study investigating the utility of ECCO2R in a model of ARDS due to smoke inhalation and burns. We hypothesized that both devices will provide significant (at least 30%) reductions in pre-membrane CO2 levels in the setting of lung injury.

**METHODS:** Female Yorkshire pigs received cooled wood-bark smoke inhalation and 40% TBSA flame burn. After injury animals were placed on either the Hemolung (n=8) or Novalung (n=7) via a dual-lumen catheter inserted into the right internal jugular vein. After initiation of ECCO2R ventilator settings were reduced according to ARDSNet. The rate of blood flow and sweep gas rate were recorded from each machine’s monitor. The amount of CO2 removed by the ECCO2R devices was calculated as the difference between the pre- and post-membrane partial pressures of CO2 (mmHg). The amount of CO2 removed per flow rate (mmHg/mL/min) through the membrane was calculated by taking the pre- and post-membrane CO2 difference, divided by the measured blood flow rate (mL/min). Data presented as means ± SEM.

**RESULTS:** On average, Hemolung reduced CO2 entering the membrane by 20.9 ± 0.65 mmHg of, while the Novalung – by 16.9 ± 0.58 mmHg of CO2. The Hemolung removed 6.9% more CO2 than the Novalung (total CO2 removed 44.4% ± 0.99% for Hemolung vs. 37.5% ± 0.93% for Novalung [Figure 1]).
The sweep gas rate of the Hemolung was recorded at 10 ± 0.0 L/min, while the Novalung sweep gas was recorded at 14.3 ± 0.41 L/min. Hemolung blood flow was 508.9 ± 2.89 mL/min, Novalung blood flow 673.6 ± 13.46 mL/min. The Hemolung removed 0.041 ± 0.0013 mmHg/mL/min, while the Novalung removed 0.027 ± 0.00116 mmHg/mL/min CO₂.

**CONCLUSION:** At similar pre-membrane CO₂ levels, with lower sweep gas and blood flow rates, the Hemolung removed a higher percentage of CO2 pointing to a higher efficiency of this device. However, both devices permit clinically significant CO2 removal levels. The Hemolung has the relative advantage of higher trans-membrane efficiency whereas the Novalung permits for modularity and continuity of ECLS and switching to a higher capacity membrane to include full ECMO, should the patients’ condition require escalation of therapy.

**Figure 1** – Hemolung (n=8) vs. Novalung (n=7) % CO₂ removed from blood.

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