TEXAS TECH UNIVERSITY
HEALTH SCIENCES CENTER

Jerry H. Hodge School *of* Pharmacy

Office of Sciences

Virtual

Eighteenth Annual

RESEARCH DAYS

June 10-11, 2021

Connecting Through Research

A Special Thanks

TEXAS TECH UNIVERSITY
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Office of Research

Schedule of Events

THURSDAY, JUNE 10, 2021

9:00-9:15 am: OPENING REMARKS..... **ULRICH BICKEL, M.D.**
Associate Dean, Office of Sciences
Professor, Department of Pharmaceutical Sciences
Texas Tech University Health Sciences Center | Amarillo, TX

9:15-9:30 am: DISTINGUISHED SPEAKER..... **LORI RICE-SPEARMAN, PH.D.**
President | *Texas Tech University Health Sciences Center | Lubbock, TX*

9:30-10:00 am: INTRODUCTION OF SPEAKER..... **QUENTIN R. SMITH, PH.D.**
Dean, School of Pharmacy
Texas Tech University Health Sciences Center | Amarillo, TX

10:00-11:00 am: KEYNOTE SPEAKER..... **DAVID S. BURGESS, PHARM.D.**
Professor and Chair, Department of Pharmacy Practice and Sciences
University of Kentucky, College of Pharmacy | Lexington, KY
" Precision Medicine for Gram-negative Infections"

11:00-11:30 am: BREAKOUT ROOMS..... **DISCUSSION WITH DAVID S. BURGESS, PHARM.D**
COLLABORATION BREAKOUT ROOMS

11:30-12:00 pm: BREAK FOR LUNCH.....

12:00-12:15 pm: AFTERNOON SESSION CHAIR..... **TREY PUTNAM, PH.D.**
Professor, Department of Pharmacy Practice & Department of Pharmaceutical Sciences
Texas Tech University Health Sciences Center | Dallas, TX

12:15-12:45 pm: DISTINGUISHED SPEAKER..... **TEDD L. MITCHELL, M.D.**
Chancellor | *Texas Tech University System | Lubbock, TX*

12:45-1:00 pm: PODIUM PRESENTATIONS – INTRODUCTIONS..... **DEVIN LOWE, PH.D.**
Assistant Professor, Department of Immunotherapeutics and Biotechnology
Texas Tech University Health Sciences Center | Abilene, TX

1:00-1:15 pm: JUNIOR GRADUATE PRESENTATION..... **MD. RAKIBUL ISLAM, MPHARM**
Junior Graduate Student
"Combination of Immune Checkpoint Inhibitor and Alendronate for the Treatment of Melanoma"

1:15-1:30 pm: RESIDENT PRESENTATION..... **EDWARD BERGMAN, PHARM.D.**
Resident PGY2
" Effect of an Educational Video Mini-Series on Interprofessional Preceptor Development"

1:30-2:00 pm: SEED GRANT AWARDEE PRESENTATION..... **ABRAHAM AL-AHMAD, PH.D.**
Assistant Professor, Department of Pharmaceutical Sciences
Texas Tech University Health Sciences Center | Amarillo, TX

2:00-2:30 pm: INVITED SPEAKER..... **KLEMENTINA FON TACER, DVM, PH.D.**
Assistant Professor, Department of Reproductive Biology and Oncology
Texas Tech University, School of Veterinary Medicine | Amarillo, Texas
"From Physiology to Pathology and Therapy: MAGE Proteins in Germ Cells and Cancer"

2:30-3:00 pm: BREAK AND POSTER JUDGES' MEETING.....

3:00-4:00 pm: LIVE POSTER PRESENTATIONS #1 AND JUDGING.....

FRIDAY, JUNE 11, 2021

8:30-9:30 am: LIVE POSTER PRESENTATIONS #2 AND JUDGING

9:30-9:45 am: INTRODUCTION OF SPEAKER....**THOMAS ABBRUSCATO, PH.D.**
Professor & Chair, Department of Pharmaceutical Sciences
Texas Tech University Health Sciences Center | Amarillo, TX

9:45-10:45 am: KEYNOTE SPEAKER..**THOMAS P. DAVIS, PH.D.**
Professor, Department of Medical Pharmacology
University of Arizona, College of Medicine | Tucson, AZ
"Leaky Barriers, Efflux Motion, and Drug Interaction at the BBB: Past Successes and the Road Ahead."

10:45-11:15 am: BREAKOUT ROOMS..**DISCUSSION WITH THOMAS P. DAVIS, PH.D.**
COLLABORATION BREAKOUT ROOMS

11:15-11:30 am: PODIUM PRESENTATIONS – INTRODUCTIONS..**HIRANMOY DAS, PH.D.**
Professor, Department of Pharmaceutical Sciences
Texas Tech University Health Sciences Center | Amarillo, TX

11:30-11:45 am: SENIOR GRADUATE STUDENT PRESENTATION..**DEREK BARTHELS**
Senior Graduate Student
"Protective Effects of Dental Pulp-Derived Stem Cells on Murine Astrocytes in an In Vitro Model of Astrogliosis"

11:45-12:00 pm: JUNIOR GRADUATE PRESENTATION ....**SADISNA SHAHI**
Junior Grad Student
"Urea-Based Analogs as Therapeutic Option for Brain Metastasized Triple Negative Breast Cancer"

12:00-12:15 pm: POST-DOCTORAL PRESENTATION..... **RIPON SARKAR, PH.D.**
Research Associate
" Kruppel Like Factor 2 (Klf2) Reduces Osteoclast Differentiation by Regulating Mitochondria, its Function, and Mitophagy"

12:15-1:00 pm: BREAK FOR LUNCH

1:00-1:15 pm: AFTERNOON SESSION CHAIR..**NADEZHDA GERMAN, PH.D.**
Assistant Professor, Department of Pharmaceutical Sciences
Research Advisory Committee Chair
Texas Tech University Health Sciences Center | Amarillo, TX

1:15-1:45 pm: DISTINGUISHED SPEAKER..**GUY LONERAGAN, PH.D.**
Professor and Dean, School of Veterinary Medicine
Texas Tech University | Amarillo, TX

1:45-2:15 pm: PRESENTATION BY GRADUATE SCHOOL..... **MICHAEL BLANTON, PH.D.**
Associate Vice President for Research
University Distinguished Professor and Senior Associate Dean, Graduate School of Biomedical Sciences
Texas Tech University Health Sciences Center | Lubbock, TX
"Promoting Quality and Diversity in Graduate School Admissions and other Initiatives"

2:15-2:30 pm: AWARDS CEREMONY

Keynote Speaker

Thomas P. Davis, Ph.D

Professor, Department of Medical Pharmacology
University of Arizona, College of Medicine
Tucson, AZ

Dr. Thomas P. Davis is Professor of Medical Pharmacology in the College of Medicine and Professor of Pharmacology and Toxicology in the College of Pharmacy, at the University of Arizona. He received his bachelor's degree in biology from Loyola University (1973), his M.Sc. in physiology from the University of Nevada (1975) and his Ph.D. in physiology/biochemistry from the University of Missouri (1978), with honors. He carried out award winning, postdoctoral training at Abbott Pharmaceutical Company as a development chemist in the therapy monitoring venture group (TDx) before joining the UA faculty in late 1980. Dr. Davis' research interests include studies of the molecular, biochemical and pathophysiological mechanisms associated with maintenance and disruption of the blood-brain barrier / endothelial cell tight junction and neurovascular unit. He has extensively studied the challenges of drug delivery across the blood-brain barrier while being continuously funded by the N.I.H. since 1981. He has published more than 240 peer-reviewed research articles with a H index of 65 and a i10 index of 184, has served as a chartered member on four N.I.H., brain disorders clinical neurosciences (BDCN) study sections, including N.S.F. and V.A. study sections. Dr. Davis also directed the synthesis of the new stroke drug, 3K3A activated protein C, while continuing to serve on the scientific advisory board of ZZ-Biotech LLC (2006-present). 3K3A-APC recently completed a successful Phase 2 "Rhapsody" Clinical Trial in 2018. Dr. Davis was awarded a special citation from the Chair of the Faculty for his extraordinary and expert service to the University of Arizona in 2001, a special award citation from Loyola-Marymount University College of Science and Engineering for inclusion on the Alumni Wall of Fame in 2003, and The Founders Day Award from The University of Arizona in 2011. Dr. Davis continues as a P.I. of a newly awarded NIH RO1 grant for 2020 to 2025 while also teaching two upper division Pharmacology and Toxicology classes and one graduate course in medical pharmacology in the Colleges of Medicine and Pharmacy at the University of Arizona, where he is in his 40th year. Web site: http://www.davislab.med.arizona.edu/

Keynote Speaker

David S. Burgess, Pharm.D., FCCP, FIDP

Professor anad Chair, Department of
Pharmacy Practice and Sciences
University of Kentucky, College of Pharmacy
Lexington, KY

Dr. David S. Burgess is Professor and Chair of the Department of Pharmacy Practice and Science at the University of Kentucky College of Pharmacy. He earned a BS in biology and chemistry from Murray State University, a BS in Pharmacy from the University of Kentucky and his Pharm.D. from the Medical University of South Carolina. He completed a residency in Critical Care/Surgery and an Infectious Diseases Pharmacotherapy Fellowship at the Medical University of South Carolina. Prior to joining the University of Kentucky in September 2012, Dr. Burgess was at the University of Texas at Austin College of Pharmacy and University of Texas Health Science Center at San Antonio for 18 years. In 2008, he was named Head of the Pharmacotherapy Division at the University of Texas College of Pharmacy and the Director of the Pharmacotherapy Research and Education Center in the School of Medicine at the University of Texas Health Science Center at San Antonio. Dr. Burgess is a member of several professional organizations including the American Society of Health-System Pharmacists (ASHP), American Colleges of Clinical Pharmacy (ACCP), and American Association of Colleges of Pharmacy (AACP). Furthermore, he has served on the Board of Directors as well as President for the Society of Infectious Diseases Pharmacists and on the Board and Chair of the ACCP Foundation (formerly known as Research Institute). He is a Fellow of the American College of Clinical Pharmacy (FCCP), Fellow of the Society of Infectious Diseases Pharmacists (FIDP) and Fellow of the American Association of Colleges of Pharmacy Academic Leadership Program. Dr. Burgess interests lie in the area of infectious disease and academic leadership. His infectious disease research focuses on understanding the mechanisms of bacterial resistance, pharmacokinetics, pharmacodynamics, outcomes and antimicrobial stewardship. He has provided a vast number of presentations and authored numerous scientific publications.

Committee Members

NADEZHDA GERMAN, Ph.D. | *TTUHSC*
Research Advisory Committee / Chair
Assistant Professor, Department of Pharmaceutical Sciences

ULRICH BICKEL, M.D. | *TTUHSC*
Research Advisory Committee / Ex Officio Member
Associate Dean, Office of Sciences
Professor, Department of Pharmaceutical Sciences

HIRANMOY DAS, Ph.D. | *TTUHSC*
Research Advisory Committee / Member
Professor, Department of Pharmaceutical Sciences

RONALD HALL, Pharm.D. | *TTUHSC*
Research Advisory Committee / Ex Officio Member
Associate Professor, Department of Pharmacy Practice

YOUNG LEE, Pharm.D. | *TTUHSC*
Research Advisory Committee / Member
Associate Professor, Department of Pharmacy Practice

DEVIN LOWE, Ph.D. | *TTUHSC*
Research Advisory Committee / Chair-Elect
Assistant Professor, Department of Immunotherapeutics and Biotechnology

TREY PUTNAM, Ph.D. | *TTUHSC*
Research Advisory Committee / Past Chair
Professor, Department of Pharmacy Practice & Department of Pharmaceutical Sciences
Center Director, Clinical Pharmacology and Experimental Therapeutics Center

HEATHER GRUBB | *TTUHSC*
Research Advisory Committee / Staff Support
Unit Manager, Office of Sciences

NEELY HUDSON, Pharm.D. | *TTUHSC*
Research Advisory Committee / Resident Representative
Resident PGY2, Department of Pharmacy Practice

SAEIDEH NOZOHOURI, Pharm.D.| *TTUHSC*
Research Advisory Committee / Graduate Student Representative
Graduate Student, Department of Pharmaceutical Sciences

Distinquished Speakers

Michael P. Blanton, Ph.D

University Distinguished Professor
Professor, Senior Associate Dean | Graduate School of Biomedical Sciences
M.D. / Ph.D. Program Director
Texas Tech University | Lubbock, TX

Guy Loneragan, Ph.D.

Professor and Dean | School of Veterinary Medicine
Texas Tech University | Amarillo, TX

Tedd L. Mitchell, M.D.

Chancellor | Texas Tech University System | Lubbock, TX

Lori Rice-Spearman, Ph.D.

President | Texas Tech University Health Sciences Center | Amarillo, TX

Invited Speaker

Klementina Fon Tacer, DVM, Ph.D

Assistant Professor | Department of Reproductive Biology and Oncology
Texas Tech University | School of Veterinary Medicine | Amarillo, TX

Protective Effects of Dental Pulp-Derived Stem Cells on Murine Astrocytes in an In Vitro Model of Astrogliosis

Derek Barthels, Saeideh Nozohouri, Heidi Villalba, Yong Zhang, Thomas Abbruscato and Hiranmoy Das

Department of Pharmaceutical Sciences, Jerry H. Hodge School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, Texas

Astrocytes have been implicated in mediating the complication of a number of central nervous system (CNS) injuries, such as stroke and spinal cord injuries. They have been also shown to play critical roles in chronic conditions like Alzheimer's disease and Parkinson's disease. Astrogliosis (gliosis) is a necessary mechanism of recovery after CNS trauma, but, when uncontrolled, can cause impairments in both healing and function of the CNS. Better preservation of astrocyte health and tighter regulation of the gliosis process could help mitigate further injury in the aftermath of acute trauma and during long-term dysfunction, as one astrocyte can affect up to two million neural synapses. Herein, we demonstrate the protective effects of dental pulp-derived stem cells (DPSCs) when co-cultured, without direct contact, above astrocytes in an in vitro model of induced gliosis. Immunofluorescent staining shows that DPSCs mitigate the production of reactive oxygen species (ROS) in astrocytes and preserve mitochondrial membrane integrity. The preservation of original astrocyte morphology, which changes drastically during the gliosis process, is also observed with the co-culture of DPSCs. The immunofluorescent stains also show a decrease in the expression of autophagy-related proteins, which serve as indicators of overall cell stress. Additionally, we demonstrate via quantitative real-time PCR (qPCR) the decreased expression of autophagy genes as well as gliosis-related genes in astrocytes when co-cultured with DPSCs. Lastly, mitochondrial respiration rates, collected using Agilent's Seahorse protocol, demonstrate the DPSC-mediated preservation of mitochondrial function.

In sum, it appears that the implementation of DPSC co-cultures provides a beneficial signaling microenvironment for astrocytes, exhibiting the potential of adult human stem cell transplants as an effective future treatment strategy for CNS disorders.

Effect of an Educational Video Mini-Series on Interprofessional Preceptor Development

Herman J. Johannesmeyer, Edward J. Bergman, Jongpil Cheon, Craig D. Cox

TTUHSC Jerry H. Hodge School of Pharmacy, Pharmacotherpay Resident

Purpose: To determine if an interprofessional video mini-series is a viable method of preceptor development for healthcare professionals, elicits positive reactionary and knowledge-based results, promotes long-term positive behavioral changes, and to determine what the impact age or experience could have on these outcomes.

Methods: Texas Tech University Health Sciences Center health profession faculty preceptors were recruited to view and provide feedback on the 12-episode video mini-series. Subjects completed a survey within 30 days of completion of the series to assess short-term outcomes, and an additional survey 3 months later to assess long-term impact.

Results: A total of 33 preceptors completed all 12 episodes of the mini-series. Analysis showed all healthcare preceptors viewed the mini-series as a viable form of preceptor development. All participants reported positive reactionary results that improved preceptor confidence. The short-term and long-term surveys showed increased preceptor knowledge at both time points. The mini-series format appeared to be more popular with the younger participants. Evaluating favorable response regarding reactionary results and confidence showed that pharmacy reported a more positive impact than did nursing or medicine.

Conclusion: An educational video mini-series to teach preceptor development can be an engaging medium that can improve preceptor confidence and promote both immediate and long-term retention of preceptor skills.

Kruppel Like Factor 2 (KLF2) Reduces Osteoclast Differentiation by Regulating Mitochondria, its Function, and Mitophagy

Ripon Sarkar, PhD; Hiranmoy Das, PhD

Texas Tech University Health Sciences Center Jerry H. Hodge School of Pharmacy

Osteoclasts and osteoblasts are two pecialized cells play critical role in bone remodeling which is essential for maintenance of bone homeostasis. Activation of the osteoclast cells are responsible for bone pathogenesis. The mechanisms of maintenance of osteoclast activation and differentiation has remained unclear. Kruppel-like factor 2 [lung] (KLF2), a transcription factor, has been identified to play critical roles in the regulation of inflammation and myeloid cell differentiation. Herein, we investigated the mechanisms by which KLF2 regulates the osteoclast differentiation. As autophagy plays an important regulatory role in recycling damaged molecules within the cells during osteoclastic differentiation as well as in pathological conditions, we first investigated whether KLF2 plays any role in trafficking of the autophagic vesicles from early endosomes to the lysosomes. Our confocal microscopic investigation revealed that the co-localization of autophagic molecules both in early endosomes (EEA1) and lysosomes (LAMP1) were present during the osteoclastic differentiation, however, induction of KLF2 reduced osteoclastic differentiation by limiting co-localization of both early endosomal and lysosomal autophagic molecules (ATG5, ATG7 and LC3B). We also showed that the generation of superoxides are essential for osteoclast differentiation, however induction of KLF2 reduced the generation of superoxide during osteoclast differentiation, determined by DCFDA staining and glutathione peroxidase activity assays. KLF2 also enhanced mitochondrial activity, and mitochondrial membrane potential, determined by mitotracker red, mitosox staining and JC1 staining respectively. Further, we showed that the induction of KLF2 reduced osteoclastic differentiation through inhibiting mitophagy. Moreover, KLF2 reduced the osteoclast differentiation by regulating mitochondrial functions (mitochondrial and glycolysis stress) and reducing mitochondrial fission, assessed by Flux analysis, real time PCR, and Western blot analysis respectively. All together, these data provide first evidence of KLF2 mediated osteoclast differentiation by regulating mitochondria and its function along with mitophagy.

Urea-Based Analogs as Therapeutic Option for Brain Metastasized Triple Negative Breast Cancer

Sadisna Shahi[1], Wei Wang[2], Racheal G. Akwii1, Paul C. Trippier[3-5], Constantinos M. Mikelis1, Ruiwen Zhang[2], Nadezhda A. German[1,6]

[1]Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center, [1]Jerry H. Hodge School of Pharmacy, Amarillo, Texas

[2]College of Pharmacy, University of Houston, Houston, Texas

[3]Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE

[4]Fred & Pamela Buffett Cancer Center, University of Nebraska Medical Center, Omaha, NE

[5]UNMC Center for Drug Discovery, University of Nebraska Medical Center, Omaha, NE

[6]Center of Excellence for Translational Neuroscience and Therapeutics, Texas Tech University Health Sciences Center, Lubbock, Texas

Triple-negative breast cancer (TNBC) is an aggressive breast cancer type lacking the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) genes. Therefore, it renders hormonal therapy and HER2-based treatment ineffective. Epidemiological studies suggest that TNBC is more common in younger women, primarily of African American and Hispanic descent. TNBC is characterized by higher metastatic and reoccurrence rates, as approximately 28% of TNBC patients suffer from brain metastases, leading to decreased survival rates compared to other breast cancer types. At the same time, TNBC shows a strong response to chemotherapy, and the search for novel anticancer agents is vital.

Recently, we identified a novel class of anticancer agents with cytotoxicity against MDA-MB-231, high ability to cross the blood-brain barrier in vitro and in vivo, optimized toxicological profile, and the ability to reduce tumor growth in vivo by > 95%. We synthesized and analyzed a library of about 50 compounds to elucidate the structural requirements for the observed anticancer activity. Here, we report the current state of structure-activity relationship studies for this class of compounds and proposed mechanisms of action associated with their anticancer activity.

Combination of Immune Checkpoint Inhibitor and Alendronate for the Treatment of Melanoma

Md. Rakibul Islam,[1] Jalpa Patel,[1] Hilary Shmeeda,[2] Claire Shudde,[1] Rajareddy Kallem,[3,4] Indhumathy Subramaniyana,[3,4] Vindhya Edpuganti,[3,4] Robin Rajan,[1] William C. Putnam,[3,4,5] Alberto A. Gabizon,[2,6] Ninh M. La-Beck[1,3]

[1]Department of Immunotherapeutics and Biotechnology, Jerry H. Hodge School of Pharmacy, Texas Tech University Health Sciences Center, Abilene, Texas 79601, USA

[2]Nano-oncology Research Center, Oncology Institute, Shaare Zedek Medical Center, Jerusalem 91031, Israel

[3]Department of Pharmacy Practice, Jerry H. Hodge School of Pharmacy, Texas Tech University Health Sciences Center, Abilene, Texas, USA

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[5]Department of Pharmaceutical Science, Jerry H. Hodge School of Pharmacy, Texas Tech University Health Sciences Center, Dallas, TX 75235. USA

[6]Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

Background: Although blockading antibodies against the PD-1 immunoinhibitory coreceptor (anti-PD1) are approved for the treatment of advanced melanoma, the overall response rate is only 20%-30%. A major mechanism of treatment resistance is active immunosuppression in the tumor microenvironment (TME) by myeloid cells and regulatory T cells. To address this problem, we developed a pegylated liposomal formulation of alendronate (PLA), an amino-bisphosphonate that abrogates inhibitory activity of myeloid cells and stimulates antitumor responses in T cells but is rapidly excreted in free form. We postulate that PLA will improve the antitumor efficacy of anti-PD1 therapy. Methods: In vitro cytotoxicity studies were performed on B16-OVA melanoma and primary bone marrow-derived cells. B16-OVA melanoma tumors were implanted in C57BL/6 mice for in vivo biodistribution and tumor growth studies. For tumor growth studies, animals were randomized to one of four different treatments: PLA at a dose of 4 mg/kg alendronate with anti-PD1 at 10 mg/kg, PLA with isotype IgG control, anti-PD1 with vehicle control (5% dextrose), or IgG with vehicle control. Results: In vitro, PLA and anti-PD1 lacked direct cytotoxicity in melanoma and myeloid immune cells. In vivo, PLA accumulated in tumor, draining lymph node, spleen, and liver. PLA and anti-PD1 significantly reduced tumor growth to a greater extent than either monotherapy. Inspection of the tumor tissue revealed that PLA reduced infiltration of macrophages and regulatory T cells, and prevented upregulation of CTLA-4, an immunoinhibitory coreceptor, in response to anti-PD1. Conclusion: We demonstrated that liposomes delivered alendronate to tumors and draining lymph nodes where PLA reversed the immunosuppressive TME and enhanced the antitumor efficacy of anti-PD1. These data support the clinical development of PLA in combination with anti-PD1, and suggest that PLA can enhance efficacy of other immunotherapies.

Poster Presentation Schedule

Basic Sciences Posters Presentation Thursday, June 10, 2021

Sciences Posters Group 1 (Lowe & Al-Ahmad)

Present Time	First	Last	Level	Mentor	Order
3:00 PM	Naana	Quagraine	Jr Grad	German	1
3:15 PM	Behnam	Noorani	Sr Grad	Bickel	2
3:30 PM	Hadi	Shiva	Sr Grad	Karamyan	3
3:45 PM	Sejal	Sharma	Jr Grad	Abbruscato	4
3:50 PM	Bret	Bessac	faculty	NOT JUDGED	5

Sciences Posters Group 2 (Das & German)

Present Time	First	Last	Level	Mentor	Order
3:00 PM	Iqra	Pervaiz	Jr Grad	Al-Ahmad	1
3:15 PM	Mariam	Oladejo	Jr Grad	Wood	2
3:30 PM	Joanna	Kocot	Post-Doc	Karamyan	3
3:45 PM	Sabrina	Archie	Jr Grad	Abbruscato	4
3:50 PM	Yong	Zhang	faculty	NOT JUDGED	5

Friday, June 11, 2021

Sciences Posters Group 1 (Lowe & Al-Ahmad)

Present Time	First	Last	Level	Mentor	Order
8:30 AM	Daniela	Rolph	Sr Grad	Das	1
8:40 AM	Siavash	Shahbazi	Jr Grad	German	2
8:50 AM	Shreyas	Gaikwad	Jr Grad	Srivastava	3
9:00 AM	Sounak	Bagchi	Sr Grad	Karamyan	4

Sciences Posters Group 2 (Das & German)

Present Time	First	Last	Level	Mentor	Order
8:30 AM	Ali	Sifat	Post-Doc	Abbruscato	1
8:40 AM	Saeideh	Nozohouri	Sr Grad	Abbruscato	2
8:50 AM	Yeseul	Ahn	Jr Grad	Bickel	3
9:00 AM	Ehsan	Nozohouri	Jr Grad	Bickel	4

Pharmacy Practice Posters Presentation Thursday, June 10, 2021

PP Posters Group 1 (Jaramillo & Haase)

Present Time	First	Last	Level	Mentor	Order
3:00 PM	Ganiat	Animashawun	PGY2	Chastain	1
3:10 PM	Katie	Calkins	PGY1	Cloud	2
3:20 PM	Olusegun	Adeshole	PGY2	Covington	3
3:30 PM	Kelly	Moline-Posthumas	PGY1	Craddock	4
3:40 PM	Sheena	Antony	PGY1	Lee	5
3:50 PM	Abby	MacCauley	PGY2	Nelson	6

Thursday, June 10, 2021 *(continued)*

PP Posters Group 2 (Putnam & Zhong)

Present Time	First	Last	Level	Mentor	Order
3:00 PM	Alaina	Van Dyke	PGY2	Chastain	1
3:10 PM	Satwinder “Sony”	Kaur	PGY1	Cloud	2
3:20 PM	Adam	Hilgemeier	PGY1	Lee	3
3:30 PM	Chenyuan “Helen”	Zhou	PGY1	Mullen-Lee	4
3:40 PM	Roberto	Galindo	PGY1	Philmon	5
3:50 PM	Caitlin	Burton	PGY2	Price	6

PP Posters Group 3 (Lee & Notturno-Strong)

Present Time	First	Last	Level	Mentor	Order
3:00 PM	Jordan	Armstrong	PGY1	McCarrell	1
3:10 PM	Chinedu	Diokpa	PGY2	Price	2
3:20 PM	Zach	Stephens	PGY1	Seifert	3
3:30 PM	Neely	Hudson	PGY2	Seifert	4
3:40 PM	Kaden	Ridley	PGY1	Whitworth	5

Friday, June 11, 2021

PP Posters Group 1 (Jaramillo & Alvarez)

Present Time	First	Last	Level	Mentor	Order
8:30 AM	Emily	Buatois	PGY2	Whitworth, Putnam	1
8:40 AM	Lincoln	Riley	PGY1	Lee	2
8:50 AM	Robert	Ojukwu	PharmD	Lee	3
9:00 AM	Goravpaul	Chatrath	PGY1	McCarrell	4
9:10 AM	Julia	Smith	PGY1	Mullen-Lee	5
9:20 AM	Karly	Hood	PGY1	Whitworth	6

PP Posters Group 2 (Putnam & Zhong)

Present Time	First	Last	Level	Mentor	Order
8:30 AM	Shaina	Varughese	PGY2	Price	1
8:40 AM	Matt	Mohr	PGY1	Lee	2
8:50 AM	Lakshmi	Pillai	PGY1	McCarrell	3
9:00 AM	Amika	Alibhai	PGY1	Mullen-Lee	4
9:10 AM	Carly	Oberdieck	PGY1	Philmon	5
9:20 AM	Valeria	Perez	PGY1	Philmon	6

PP Posters Group 3 (Lee & Notturno-Strong)

Present Time	First	Last	Level	Mentor	Order
8:30 AM	Nicole	Moreno	PGY2	Whitworth	1
8:40 AM	Maryam	Yassa	PGY1	Seifert	2
8:50 AM	Carol	Baby	PGY1	Mullen-Lee	3
9:00 AM	Nicole	Northcutt	PGY1	Mullen-Lee	4
9:10 AM	Ryan	Kellerman	PGY1	McCarrell	5
9:20 AM	Nida	Khan	PGY2	Selby	6

Impact of Expanded Public Health Emergency Telehealth Provisions on Chronic Disease Management and Follow-Up

Olusegun I Adeshola, Les P Covington, Evelyn S Sbar, Nicole D Lopez, Diego Regalado, Meghan Connolly, Rodney B Young, Eric J MacLaughlin

Texas Tech University Health Sciences Center School of Medicine and Jerry H. Hodge School of Pharmacy, Amarillo, Texas

Purpose: Non-adherence to outpatient clinic appointments reduces clinic and provider productivity as well as efficiency. However, pursuant to the COVID-19 health emergency, the Centers for Medicare and Medicaid Services (CMS) authorized lifting geographic and originating site restrictions to furnishing telehealth services for Medicare beneficiaries. Since telehealth may eliminate some of the barriers to in-clinic follow-up, this project aims to evaluate the impact of telehealth expansion on patient adherence to scheduled follow-up during the COVID-19 pandemic public health emergency compared to the 2 previous years before telehealth expansion. Secondary aims include assessing changes in surrogate health outcomes (e.g. A1c, blood pressure, etc.)

Method: This study has been approved by the Texas Tech University Health Sciences Center (TTUHSC) Institutional Review Board and is being conducted at the TTUHSC Department of Family and Community Medicine clinic, in Amarillo Texas. This study is a retrospective and prospective cohort study. Patient electronic medical record are being reviewed in a retrospective manner from March 5, 2018, through March 5, 2020, and prospectively from March 6, 2020, through March 6, 2021. Descriptive statistics will be used to analyze patient demographics. Linear regression will be used to evaluate differences in continuous variables (e.g., number of appointments, A1c, eGFR, and BP) and Wilcoxon signed-rank test for nominal data (e.g., sex).

Result: Data collection and analysis currently in progress.

Conclusion: The results of this study will be presented following data collection and analysis.

Evaluation of the Impact of a Pharmacist-Led Transitions of Care Service

Amika Alibhai, PharmD and Natasha Harrigan, PharmD

VA North Texas Health Care System
Texas Tech University Health Sciences Center Jerry H. Hodge School of Pharmacy

Purpose: Evaluate the impact of a pharmacist-led transitions of care (TOC) service on post-discharge acute care utilization for three targeted disease states: diabetes, heart failure, and chronic obstructive pulmonary disease.

Methods: The pharmacist-led TOC service implemented at the VANTHCS Dallas campus in late 2019 provides comprehensive medication reconciliation as well as personalized bedside patient education. Designed as a retrospective, single-center, observational chart review, this study evaluated trends in post-discharge acute care utilization, with a focus on the first 30-days post-discharge. Patients were compared from the time after implementation of the TOC service (post-TOC) to a similar cohort of patients admitted during the same time frame the year before (pre-TOC).

Results: After screening over 800 patients for eligibility, there were 133 patients included in the pre-TOC group and 137 patients in the post-TOC group, with no differences found in baseline demographics. There was a significant difference in the distribution of primary diagnosis codes, with the post-TOC group favoring COPD admissions (47.4%, p=0.02) compared to the pre-TOC group, which was divided more evenly. The majority of eligible patients in the post-TOC group (98.5%) had a documented assessment completed by a TOC pharmacist, with 85% of patients receiving medication counseling. There were 24 patients (17.5%) in the post-TOC group and 34 patients (25.6%) in the pre-TOC group that were found to have instances of acute care utilization within the first 30-days after discharge, p=0.18. All subanalyses showed decreases in acute care utilization in the post-TOC group across all timeframes within 30 days and in both hospital readmissions and emergency department visits, though statistical significance was not found.

Conclusion: Pharmacist-led TOC services can reduce post-discharge acute care utilization, though a larger sample size may be required to indicate statistical significance.

Heart Failure Outcomes in Veterans with Heart Failure with Reduced Ejection Fraction and Type 2 Diabetes Mellitus

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Background: Veterans with both heart failure (HF) and type 2 diabetes mellitus (T2DM) are associated with an increased risk of mortality compared to patients with either condition alone. Empagliflozin is a selective sodium-glucose cotransporter-2 (SGLT-2) inhibitor approved for the treatment of T2DM which has also shown to have beneficial cardiovascular outcomes (CVD and heart failure). The EMPA-REG OUTCOME trial found significantly lower rates of death from cardiovascular causes, hospitalization for heart failure, and death from any cause in the empagliflozin group compared to placebo. The EMPEROR-Reduced trial assessed the use of empagliflozin in patients with established heart failure, with or without T2DM and found the primary composite outcome of hospitalizations for heart failure and rate of death from cardiovascular causes in the empagliflozin group to be lower compared to standard of care (HR 0.75; 95% confidence interval [CI], 0.65 to 0.86; P<0.001).

Purpose: To evaluate the effects of empagliflozin on safety and efficacy of heart failure outcomes in individuals being treated with at least two oral antidiabetic agents for the treatment of type 2 diabetes mellitus (T2DM) who also have a diagnosis of reduced ejection fraction heart failure (HFrEF) in the Veteran population.

Methodology: This was a prevalent new user historical design with data recorded retrospectively from the institution's electronic records of Veterans with T2DM and HFrEF receiving 2 or more oral antidiabetic medications at the VA North Texas Health Care System (VANTHCS) from July 1, 2017 to July 31,2020. Institution IRB approval was obtained. The efficacy outcomes were the rate of CHF admissions, all-cause and CV-related deaths, nonfatal stroke and nonfatal myocardial infarction (MI). Secondary outcomes include changes in A1C, change in eGFR, admission warranting amputation, and treatment for urinary tract infection (UTI) or genital infection.

Results: Research in progress.

Conclusion: Research in progress.

Impact of an Interdisciplinary Heart Failure Clinic Versus Usual Care on Patient Outcomes

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Studies involving interdisciplinary outpatient Heart Failure (HF) clinics at VA medical centers or at international healthcare facilities have shown a reduction in hospitalizations and mortality while other studies have found no difference with interventions. Hendrick Medical Center (HMC) has had an interprofessional outpatient HF clinic for more than 5 years. The purpose of this study is to investigate whether the interdisciplinary efforts of the HMC outpatient HF clinic has a significant impact on reducing readmission rates by comparing outcomes to a matched cohort of HF patients who received usual care post hospital discharge. HMC inpatient and outpatient services utilize the Allscripts electronic medical records system. This resource was accessed for data collection from the required time period of January 1, 2016 to January 1, 2019 to review patient data from time of clinic admission to subsequent follow-up visits within a 12-month period to the heart failure clinic. Data from a matched cohort of heart failure patients who were discharged with usual care and not referred to clinic were analyzed as well. Preliminary results show that 14% of the clinic population compared to 10% (p=0.4) of the hospital-discharged patients required heart failure related hospital readmission within the following year. Data is pending further analysis by matching for age, gender, severity of heart failure and comorbidities. Possible explanations for why there was a higher rate of heart failure readmission in the clinic group could be due to loss of follow up in the hospital group. Patients in the clinic group are more closely followed healthcare professionals, potentially leading to more heart failure related hospital readmissions as well.

A Retrospective Analysis of Emphasizing Single Location Medication Delivery Instead of Multiple Location Medication Delivery for Patient-Specific Medications

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To determine if emphasizing single location medication delivery over multiple location medication delivery for patient-specific medications improves delivery times. Medications used to be delivered to multiple locations throughout the hospital. Now, pharmacy technicians deliver medications to one location at a time and return to the pharmacy between each location. We expect that emphasis of this delivery method will reduce average delivery times by 10%. Using data collected from the hospital's electronic medical records, we compared how average delivery times changed when emphasizing single location medication delivery instead of multiple location medication delivery.

Effects of Sertraline on Antidiabetic Medication Adherence in Patients with Uncontrolled Diabetes Mellitus and Depression

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Purpose: Studies have shown that there is a bidirectional association between diabetes mellitus (DM) and depression. Uncontrolled depression can have a profound adverse influence on quality of life and overall function leading to reduced exercise, self-care, and nonadherence to medications. This can lead to worse outcomes of chronic medical conditions like DM. This study will examine the effects of antidepressant therapy on antidiabetic medication adherence in patients with concurrent, uncontrolled DM and depression.

Methods: The study design is a single center, retrospective cohort study. It will include patients between 18-80 years of age with hemoglobin A1c (HbA1c) >8% and antidiabetic medication adherence <80%. Only those patients that have started and continued an antidepressant medication regimen for at least 3 months with >80% adherence will be included. These patients will then be evaluated for antidiabetic medication adherence post-antidepressant maintenance. The primary outcome measure is a change in antidiabetic medication adherence. Efficacy measures include changes in HbA1c, Patient Health Questionairre-9 and General Anxiety Disorder-7 scores, and body mass index and weight. Subjects will be serving as their own controls, which allows for paired t-test as the appropriate method of analysis of primary and secondary outcomes.

Results: 36 patients with a mean adherence to sertraline at 97.4% were analyzed. Antidiabetic medication adherence significantly changed from 49.87% to 68.18% after starting sertraline ($p < 0.001$). HbA1c also improved significantly from 9.96% to 9.04% ($p = 0.0012$). In patients without changes in antidiabetic medication rgimen, HbA1c still improved significantly from 9.31% to 8.8% ($p = 0.039$)

Conclusion: In certain patients with uncontrolled DM and depression, starting sertraline significantly improved antidiabetic medication adherence and HbA1c. This study shows the important of addressing underlying mental health disorders in this patient population. Future studies are needed to determine long-term effects of antidepressants on DM and effects of other antidepressants.

Using the HyFlex Model to Deliver a Capstone Seminar Course for Fourth-Year Pharmacy Students

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Background: The "HyFlex" model is a hybrid course structure that allows students to attend class in-person or synchronously via remote videoconferencing technology. The TTUHSC School of Pharmacy implemented the HyFlex Model in its Grand Rounds (GR) course during the COVID-19 pandemic. This study determined the impact of the HyFlex model on student engagement. The secondary aim was to describe student satisfaction with the HyFlex model.

Methods: All fourth-year pharmacy students enrolled in GR were eligible. The GR Engagement Assessment Tool (GREAT) was used to measure engagement three times during the semester. The tool contained 18 statements, which students rated using a five-point Likert scale (1 = "not true at all" and 5 = "completely true"). Statements were divided into four domains: importance, boredom, elaboration, and engagement. Free-text responses were collected for qualitative analysis. Basic descriptive statistics and Wilcoxon rank-sum tests were used for statistical analysis.

Results: Completed surveys included 128 responses from 88 unique students. There were no differences between remote and in-person attendance for any statement in the boredom and elaboration domains. In the importance domain, in-person students felt the material was more practical (median 4, IQR [4,5]) than remote students (median 4, IQR [3,4]; p=0.0023). In-person students also thought the material was more applicable to other situations (median 3, IQR [3,5]) compared to remote students (median 3, IQR [2,4]; p=0.0363). There were no differences in engagement, except in-person students reported listening more intently (median 4, IQR [3,4]) than remote students (median 3, IQR [3,4; p=0.0324). Preliminary qualitative analysis of free-text responses demonstrated five themes related to student satisfaction: safety, flexibility, convenience, technology, and professionalism.

Conclusions: There was no significant loss in student engagement or satisfaction in GR using the HyFlex model. This study may be used to expand similar courses to other universities where remote instruction is needed.

Outcomes of Buprenorphine/Naloxone Assisted Treatment in Veterans with Opioid use Disorder

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Background: Previously published studies for OUD primarily compare different pharmacotherapy options, but, outcomes from combined pharmacotherapy and psychotherapy have not often been assessed. With the addition of psychotherapy interventions, some studies have shown improvement in outcomes, however, other studies have reported no difference. Established in April 2015, the Suboxone (buprenorphine/naloxone, or BUP/NAL) clinic involves a three part treatment plan: witnessed urine drug screens (UDSs), group therapy, and pharmacotherapy with BUP/NAL. Patients enrolled in the BUP/NAL clinic begin treatment at level one (weekly check ins) and can progress to level four (8 week check ins). Expectations of the BUP/NAL clinic include agreements to remain abstinent from illegal drugs, alcohol, and non-VA prescribed medications.

Objectives: The objective of this study is to compare opioid use and treatment engagement in Veterans with OUD who receive BUP/NAL and psychotherapy (as part of the structured BUP/NAL clinic) versus BUP/NAL alone. The primary outcome of this study is percentage of negative UDSs for opioids. Secondary outcomes include relapse rates, days on BUP/NAL treatment, reported side effects, and positive UDSs for substances other than opioids.

Results: No significant difference was found between treatment groups in percentage of negative UDSs ($p = 0.18$), relapse rates ($p = 0.455$), side effects ($p = 0.58$), or days on BUP/NAL treatment ($p = 0.13$). Ten patients in the BUP/NAL plus psychotherapy arm subsequently had their BUP/NAL tapered by provider for violation of clinic agreement due to positive UDSs for other substances. After taper of BUP/NAL by provider: 1 patient re-enrolled in the BUP/NAL clinic in the future, 3 patients were admitted to the inpatient MH ward or domiciliary for opioid use, 3 patients continued to follow up with MH, but were not resumed on BUP/NAL, and 3 patients were lost to follow up.

Optimization of Misoprostol Utilization for Induction of Labor in a Major Labor and Delivery Hospital

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Purpose: To determine optimal prescribing regimens of misoprostol to provide a major labor and delivery hospital, Texas Health Harris Methodist, the safest and most efficacious therapy for induction of labor (IOL). Despite the increasing prevalence, international organizations have not formed a consensus on the ideal route, dose, and frequency of misoprostol for IOL, making the proper regimen selection unclear for providers and pharmacists alike.

Methods: Using the institution's electronic health records, a retrospective review of all misoprostol doses from January 2019 until November 2020 was conducted. The primary outcome was time to delivery with oral versus vaginal misoprostol. Secondary outcomes were use of additional agents such as oxytocin or use of balloon catheter, use of additional doses of misoprostol past the initial dose, successful induction via vaginal delivery, and neonatal outcomes including APGAR scores and NICU admission. Safety outcomes included maternal hyperstimulation and postpartum hemorrhage/bleed.

Results: A total of 410 patient encounters were analyzed, of which 28% (n=115) were included. Patients were most frequently excluded due to administration of balloon catheter prior to misoprostol (n=88). Only 34 encounters of vaginal misoprostol were eligible for inclusion. The time to delivery with oral misoprostol was 23.9 hours compared to vaginal at 21.6 hours (p=0.538). The total dose for oral was 100mcg compared to 50mcg with vaginal misoprostol (p <0.001) and both routes required two doses for induction (p=0.532). There was not a statistically significant difference in maternal outcomes, use of additional agents, or APGAR scores.

Conclusion: While this study was unable to meet power, it does appear oral misoprostol may be as safe and effective for induction of labor compared to vaginal. Based on this analysis, gestational age and indication may be factors in selecting oral versus vaginal misoprostol. Further research is warranted.

Evaluation of Prophylactiv VS Higher Than Usual Anticoagulation Doses in Covid-19 Patients Admitted to the ICU

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Purpose: It is a well-known fact that COVID-19 induces a hypercoagulable state. Standard prophylactic doses of enoxaparin fail to inhibit Xa adequately, which may be due to an increase in the levels of heparin-binding proteins.1 This may explain, the incidence of venous thrombotic events (VTE) in patients despite receiving standard prophylaxis enoxaparin. The advent of decreased utility of standard doses of enoxaparin has spawned "higher than usual" or "half-therapeutic" doses usually defined as 0.5 mg/kg. The safety of this dosing strategy has yet to be determined, and this retrospective analysis aims to answer this question.

Methods:A retrospective chart review will be performed on patients with a COVID-19 diagnosis receiving enoxaparin who were admitted to the ICU were retrospectively analyzed to assess safety outcomes dependent on what dosage of enoxaparin-19 they received. If patients received both dosing strategies, they were assigned to the dosage group for which they received for the majority of their stay

Results: Results are currently pending

Conclusion: A conclusion is currently pending based on the results of this retrospective analysis

A Comparison of Prazosin and Topiramate for the Treatment of Alcohol Use Disorder in Veterans with PTSD

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Background: Alcohol use disorder (AUD) affects millions of Americans. Treatment of alcohol use disorder can be complicated by other comorbid psychiatric conditions like post-traumatic stress disorder (PTSD). Symptoms of PTSD can also lead to increased substance abuse and alcohol consumption, further complicating treatment. Available data observing the use of medications to treat substance use disorders may have low applicability by excluding patients with comorbid psychiatric conditions like PTSD. Few studies have evaluated the use of topiramate or prazosin for the treatment of both PTSD and AUD. The aim of this study is to add to existing evidence and evaluate the efficacy of topiramate and prazosin for AUD in PTSD.

Objectives: The objective of this study is to assess treatment outcomes in Veterans with PTSD and determine which medication intervention, topiramate or prazosin, significantly improves alcohol use disorder outcomes. The primary outcome is change in standard drinks per week. Secondary outcomes include alcohol cravings, change in drinking days per week, incidence of relapse, alcohol related hospital admissions, change in PTSD symptoms measured by the PTSD Checklist (PCL), blood ethanol, incidence of hypotension, and other medication side effects.

Methods: Data for outpatient Veterans with a prescription for prazosin or topiramate between September 1st, 2015 and September 30th, 2020 were collected from the institution's electronic records. Outcomes relating to alcohol use disorder and PTSD were evaluated.

Outcomes: Baseline characteristics were similar between groups. No statistically significant differences were detected in the primary or secondary outcomes after data analysis. Prazosin seemed to have had a greater effect than topiramate on decreasing standard drinks per week (6.75 and 2.52, respectively). Decrease in drinking days were comparable between the two treatment arms. More side effects were reported in the prazosin group including dizziness, lethargy, and headache.

Evaluation of an Anticoagulation Dosing Strategy for Venous Thromboembolism Prophylaxis in Hospitalized COVID-19 Patients

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Purpose: To evaluate the efficacy and safety of an anticoagulation dosing strategy in preventing venous thromboembolism (VTE) in hospitalized COVID-19 patients

Methods: This is a retrospective study to assess the efficacy and safety of an institution-specific VTE prophylaxis dosing algorithm for COVID-19 patients admitted to Texas Health Presbyterian Hospital Dallas (THD). Patients included were adults (≥18 years old) admitted to THD for a confirmed COVID-19 infection, received VTE prophylaxis in accordance with the THD algorithm, and had a D-dimer ≥1 mcg/mL for 72 hours. Excluded patients were those receiving anticoagulation for an indication other than VTE prophylaxis for COVID-19, those without D-dimer testing within 24 hours of admission, pregnancy, acute coronary syndrome, active bleeding, and those with a high risk of bleeding. Primary outcomes of the study were the incidence of VTE and incidence of major bleed. Secondary outcomes evaluated were incidence of non-major bleed, hospital length of stay, ICU length of stay, and in-hospital mortality.

Results: A total of 107 patients were evaluated. VTE was identified in 2 patients (1.9%) and a major bleed occurred in 7 patients (6.5%). Five patients (4.7%) developed a non-major bleed. The median hospital and ICU length of stay were 12 days (IQR 8-20) and 10 days (6-18) respectively. Incidence of in-hospital mortality was 7.5%.

Conclusions: The utilization of our institution-specific dosing protocol appears to be an effective and safe approach in preventing VTE in hospitalized COVID-19 patients.

Clinical Outcomes Between Vancomycin AUC-Based vs. Through Concentration-Based Dosing

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Purpose: Vancomycin treatment must balance efficacy against nephrotoxicity. Historically, vancomycin had been dosed based on serum vancomycin trough (Vt) values, but in 2020 an update to the dosing guidelines recommended using the proportion of area under the curve (AUC) of vancomycin levels to mean inhibitory concentration (MIC) instead. This study compared the incidence of vancomycin-induced nephropathy in patients treated with AUC-based dosing and Vt-based dosing by exploring trends in serum creatinine between treatment groups, as well as relevant secondary endpoints.

Methods: This retrospective, single-center, cohort study reviewed charts of patients receiving vancomycin under Vt (Vt group) and AUC dosing schedules (AUC group). The primary outcome was incidence of vancomycin-induced nephropathy (VIN). Secondary outcomes included time to clinical cure, time to microbiologic cure for applicable disease states, percentage of patients achieving therapeutic goals, length of stay, duration of therapy, hospital mortality, and mean daily vancomycin dose.

Results: Preliminary results include an analysis of 25 patients in each arm. VIN incidence was 44% in the VT group and 28% in the AUC group (p=0.327). Average length of stay was 11.48 days in the VT group and 8.04 days in the AUC group (p=0.139). Duration of therapy was 8.69 days in the VT group and 7.15 days in the AUC group (p=0.489). Average vancomycin per day was 29.15 mg/kg/day in the AUC group and 21.5 mg/kg/day in the AUC group (p=0.021). In-hospital mortality incidence was 1 patient in the VT group and 2 patients in the AUC group; time to clinical cure was 5.31 days in the VT group and 3.23 days in the AUC group.

Conclusion: Preliminary results did not detect significant difference in VIN incidence between dosing regimens. However, there was an absolute difference of VIN incidence of 16% between the dosing regimens; this may warrant investigation with larger sample size.

Influence of Patient Characteristics on Provider Deviation from Guideline Based Treatment of HFrEF Within Outpatient Family Medicine and Internal Medicine Clinics

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Purpose: The purpose of this study is to identify possible HFrEF treatment gaps in academic teaching clinics. This study will compare provider adherence rates to GDMT of HFrEF between different patient subsets along with looking at medication choice, and dosing.

Methods: This study is a retrospective, two center, chart review of outpatients seen at Texas Tech Family Medicine and Internal Medicine clinic between 01/01/2018 and 02/29/2020. Patients selected were >18 years old with a diagnosis HFrEF, and an EF< 40%. Patients that were pregnant, on hospice, on dialysis, or prisoners were excluded. Patients are stratified based off of their characteristics (race, sex, age, insurance status, distance from clinic), severity of HFrEF and, between these patient subsets, the rates of provider adherence to HFrEF GDMT will be analyzed. Subset analysis will determine if specific patient characteristics influence provider deviation from GDMT of HFrEF and the percentage of patients on optimal and suboptimal HFrEF therapeutic regimens independent of patient characteristics. Patient demographic information and baseline characteristics will be analyzed via descriptive statistics and the primary and secondary objectives will be analyzed using Chi-Square or Fisher's Exact test, where appropriate.

Results: 121 patient charts were reviewed with a total of 25 patients with a charted EF <40% within the last 3 years. Data for the primary objective wasn't found to be statistically significant between the 6 subgroups analyzed. The subgroups compared males to females, Caucasian race to other races, private insurance holders to Medicare/Medicaid, those <10 miles from clinic to >10, family medicine to internal medicine patients, and patients >65 to <65 year olds. Within these subgroups the percentage of patients on triple therapy, dual therapy, or single agent therapy were compared. The secondary objective found that 0% of patients were on optimized GDMT and most patients were on single agent therapy.

Conclusion: Research in progress.

Evaluation of Thromboelastography (TEG) Utilization During Massive Transfusion Activations

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Objective: To examine if utilizing TEG during massive transfusion protocol (MTP) activations in trauma is associated with a different amount of blood product utilization and a difference in in-hospital outcomes. TEG allows specific clotting parameters to be obtained, allowing targeted blood product administration compared to the historical standard of care.

Methods: This is a single-center, retrospective chart review designed to evaluate the use of TEG vs. no TEG during MTP activations at University Medical Center in Lubbock, Texas, a Level-1 trauma center. Charts and blood bank records were reviewed for inclusion criteria from January 1, 2018-December 31, 2020. The primary outcome is to evaluate whether TEG utilization during MTP affects the composite number of units of blood products administered. Secondary outcomes include evaluating the difference in individual units of blood product administration between the groups (packed red blood cells, fresh frozen plasma, platelets, and cryoprecipitate), the effect of TEG usage on in-hospital morality, hospital length of stay, and ICU free days. Additionally, the usage of prothrombin complex concentrate and antifibrinolytic agents will be analyzed in relation to patient outcomes and units of blood product administration.

Results: Pending

Conclusion: Pending

Implementation of the PEN-FAST Penicillin Allergy Screening Tool in the Emergency Department During Medication Reconciliation

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Purpose: The purpose of this study was to implement the PEN-FAST Penicillin Allergy Screening Tool in the ED to identify patients with low risk penicillin-related allergies to transition to a beta-lactam. Newly published, validated, penicillin allergy clinician decision tool allows providers to identify low risk penicillin allergies with a NPV of ≥96%. This quick, 5-question tool allows providers to efficiently identify patients who would test negative if a formal penicillin allergy test was performed.

Methods: During routine medication reconciliations, pharmacists will identify patients who have a documented penicillin-related allergy in the EMR and use the PEN-FAST screening tool. Patients meeting inclusion criteria will have their penicillin-related allergy updated in the EMR based upon their assessed risk of very low, low, moderate, or high. The primary outcomes for this study are the percentage of patients screened that were classified as "very low and low risk" and percentage penicillin-related allergies updated. The secondary outcomes are the percentage of patients that required antibiotic therapy (post-allergy update) that were transitioned to a beta-lactam, inpatient broad-spectrum antibiotic usage before and after allergy update, and time spent interviewing each patient.

Results: A total of 59 patients were interviewed using the PEN-FAST Tool. The results for the primary outcomes indicate 92% (n=54) of patient allergies updated in the EMR, 24% (n=13) of patients classified as "very low risk" and 34% (n=18) of patients classified as "low risk". Results for the secondary outcome showed out of the 36 patients that were on non-beta lactams during allergy update, 72% (n=26) of those patients were transitioned to a beta-lactam. The average time to complete the PEN-FAST Tool was 4.2 minutes.

Conclusion: The results support the use of the PEN-FAST Tool in updating patient's allergies in the EMR and identifying low risk patients who may be eligible for beta-lactam therapy.

Evaluation of Risk Factors for Methicillin-Resistant Staphylococcus Aureus and Pseudomonas Aeruginosa Community-Acquired Pneumonia at BSA Health System

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This project will investigate the historical incidence of community-acquired pneumonia (CAP) with positive cultures for methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa (PSA). The patient population will be adults who were diagnosed with CAP at Baptist Saint Anthony's Hospital (BSA) in Amarillo Texas. We will attempt to assess differences in risk factors identified in literature for CAP caused by MRSA and PSA separately. This project will be a step towards identifying local risk factors for these infections, as suggested by the American Thoracic Society (ATS) and Infectious Diseases Society of America's (IDSA) 2019 CAP practice guidelines

Evaluation of Therapeutic Efficacy of Weigh-Based Versus Non-Weight-Based Dosing of Norepinephrine in A Cardiopulmonary ICU

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Norepinephrine is the first line vasopressor recommended by the SCCM guidelines for the treatment of septic shock. Literature on dosing of norepinephrine includes weight-based and non-weight-based dosing recommendations. Clinical practice guidelines do not comment on the optimal dosing strategy, which has led to a divide in practice. The purpose of this study was to evaluate the dose of norepinephrine in microgram per kilogram per min required to achieve a goal mean arterial pressure (MAP) of 65 mm Hg in critically ill patients receiving weight-based versus non-weight-based doses of norepinephrine for septic shock. This study can help elucidate which dosing strategy is the most efficacious and safest for critically ill patients.

This was a single center, retrospective, observational, cohort study of adult patients admitted to the cardiopulmonary ICU at the North Texas Veterans Affairs Health Care System and received norepinephrine for presumed septic shock between November 2018 and November 2020. In November of 2019, the North Texas Veterans Affairs Health Care System switched from non-weight-based dosing to weight-based dosing of norepinephrine. Patients were divided into two comparator groups based on the institution-guided dosing protocol. Between November 1, 2018 and October 31, 2019 patients received non-weight-based dosing of norepinephrine, versus between November 1, 2019 and October 31, 2020 patients received weight-based dosing of norepinephrine. Data points collected for comparison included patient demographics, sequential organ failure assessment (SOFA) scores, APACHE II scores, Charlson Comorbidity Index scores, hemodynamic parameters, doses of norepinephrine, fluid boluses, length of stay, mortality, and initiation of renal replacement therapy.

Data collection is complete, and analysis is currently in process. Final data will be presented at Research Days

Implementation of Therapeutic Drug Monitoring in Patients on Dual Atypical Antipsychotics in a Correctional Setting

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Background: To overcome poor response rates to antipsychotic therapy, clinicians often use antipsychotics at higher doses than recommended or initiate a second antipsychotic in hopes of achieving better symptom control. Evidence for enhanced efficacy with combination second generation antipsychotic (SGA) therapy is poor and may cause greater harm than standard-dose monotherapy. A strategy that may prove useful in these patients is therapeutic drug monitoring (TDM), which allows clinicians to identify the lowest effective dose, thereby preventing unnecessary adverse effects and allowing better individualization of treatment.

Objective: Determine if pharmacist-managed TDM allows for narrowing to a single antipsychotic in at least 50% of patients on more than one SGA.

Methods: Reports of correctional patients prescribed more than one SGA were pulled to identify candidates for TDM clinic from July 2020 to January 2021. After enrollment, serum levels of SGAs were collected and the clinical pharmacist conducted visits with patients to assess efficacy and side effects. Using serum drug levels and the pharmacist's clinical evaluation of the patient, adjustments to the antipsychotic regimen were made. Patients were followed in TDM clinic until their release from jail or optimization of their antipsychotic regimen.

Results: Of the 13 patients enrolled in TDM clinic, 10 (77%) were narrowed to a single antipsychotic. Four of 10 reported reduction or resolution of hallucinations and 6 of 10 reported improvements in mood. Side effects were highly variable but trended towards improvement.

Conclusions: The clinical pharmacist-run TDM clinic was successful in transitioning patients to a single antipsychotic in most cases. Serum drug levels were useful for guiding dose adjustments and evaluating adverse effects. While this project was limited by a small sample size, it is likely that this type of TDM clinic could be useful in other correctional settings or settings in which dual SGA therapy is frequently seen.

Evaluating the Implementation of IV Insulin Dosing Software in the Critically Ill and in Patients with Hyperglycemic Crisis

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Purpose: Although IV insulin is the preferred method for the management of hyperglycemia in the critically ill, there exists the risk of causing hypoglycemia that can be dangerous and potentially fatal. One strategy to reduce the incidence of hypoglycemia is the use of IV insulin dosing software which utilizes mathematical modeling to create patient specific dosing. This study will compare the effectiveness and safety of IV insulin dosing that is dosed using IV insulin software compared to IV insulin dosing based on the hospital's previous protocol.

Methods: This study is a retrospective, single-center, cohort study looking at patients receiving IV insulin in the critically ill and in patients experiencing hyperglycemic crisis. We will be comparing data obtained from October 1 2019 to December 31, 2019 (previous protocol) to data obtained from October 1, 2020 – December 31, 2020 (EndoTool protocol). Prisoners, pregnant females, age less than 18 years, and those not admitted to the specified units will be excluded. Patients will be identified to either the IV insulin protocol using an insulin dosing software or the previous IV insulin dosing protocol at Hendrick Medical Center. The primary outcomes include percent of time blood glucose values were within target range, time to reach target blood glucose range after initiation of insulin protocol and the number of level 1 and level 2 hypoglycemic episodes. Secondary outcomes include total time on insulin drip, number of blood glucose drops > 100mg/dL within 1, our, and length of stay in the specified units. Data collection includes demographic information, baseline characteristics, comorbidities, diagnostic codes, laboratory values including blood glucose values, anion gap, medications, duration of treatment, length of stay, and nutrition source(s). Nominal data will be analyzed by chi-square or Fisher's exact test and secondary outcomes will be analyzed by multivariate regression.

Results: N/A

Conclusions: N/A

Predictive Factors for Invasive Fungal Infection in Hospitalized COVID-19 Patients

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Background: Invasive fungal infections (IFI) are associated with high mortality rates despite antifungal treatment. Early data suggests similar mortality risks in COVID-19 patients with IFI. Risk factors for fungal infections are well known and prediction tools have been established for hospitalized patients. Patients with COVID-19 carry many known risk factors and may have additional risk due to associated immunosuppression and prolonged hospital course. Steroid use is common in hospitalized COVID-19 patients as they have been associated with improved outcomes. However, higher doses or prolonged therapy may increase risk of IFI due to immunosuppression and risk of hyperglycemia that further favors immune dysfunction. The impact of these and other potentially modifiable factors is unknown in this patient population.

Purpose: To identify factors associated with IFI in hospitalized patients with COVID-19 and to characterize rates of fungal positivity, receipt of antifungal therapy, and outcomes in these patients. Additionally, to determine the relationship between steroid dose, duration of use, and likelihood of positive fungal cultures in COVID-19 patients.

Methods: This is a retrospective cohort study of adult patients with COVID-19 who were admitted to two tertiary care hospitals between March 2020 and February 2021. The cohort includes a randomized sample of subjects with COVID-19, with a 2:1 allocation based on presence or absence of at least one positive fungal culture. Patient demographics, documented risk factors for IFI, including antibiotic use, location and duration of lines and tubes, need for mechanical ventilation, parenteral nutrition, hemodialysis, and surgery will be collected. Other potential risk factors will be characterized, including dose and duration of steroids, hyperglycemia, and lymphopenia. Fungal cultures, use of antifungal therapy, and patient outcomes will also be described. A logistic regression model will be developed to determine significant predictor variables associated with fungal positivity in this population.

Results/conclusion: Data collection and analysis is currently in progress.

Change in Empagliflozin Efficacy in Type 2 Diabetes Patients with Renal Function Declining to Stage 3b CKD or Lower

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Purpose: To determine the change in efficacy of empagliflozin in veteran patients that experience a decline in eGFR below 45 mL/min/1.73m2. Current manufacturer labeling recommends discontinuing empagliflozin if the eGFR remains persistently below 45 mL/min/1.73m2. Data suggests that empagliflozin may have moderate HbA1c reductions in patients with moderate CKD (eGFR 30 to 60 mL/min/1.73m2), however, the data is limited in assessing HbA1c below the cutoff of 45 mL/min/1.73m2.

Methods: This retrospective observational study was conducted at the VA North Texas Health Care System (VANTHCS). Electronic health records were reviewed for patients with Type 2 Diabetes whose eGFR declined below 45 mL/min/1.73m2 while taking empagliflozin. The primary outcome was to assess the change in HbA1c from baseline, defined as the last A1c prior to the decline in eGFR, versus the follow-up A1c, defined as the first A1c recorded as of the drop in eGFR <45 mL/min/1.73m2, on empagliflozin. The secondary outcomes include assessments of change in weight, blood pressure, and adverse drug events. Descriptive statistics were utilized to assess demographic data while paired t-test analysis was utilized to assess for primary and secondary outcomes.

Results: A total of 1438 patient were screened for inclusion of this study with a total of 65 patients included for analysis. Subjects had a mean age of 69 years (41-83), 100% male, and 72% Caucasian. Mean baseline A1c was 7.88% and the follow-up A1c 7.89% resulting in a mean change of 0.02% (P = 0.91). No significant differences were found in the secondary outcomes for weight and blood pressure.

Conclusion: No significant change was found in A1c among patients on empaglizlozin with an eGFR declining below 45 mL/min/1.73m2 suggesting that empagliflozin may continue to hold benefit in declining renal function to Stage 3B CKD or lower. HgA1c did not significantly increase but instead was similar between baseline and follow-up.

Analysis of A Direct Oral Anticoagulant Indication-Of-Use Policy: Impact on Dosing Accuracy and Patient Outcomes in a Tertiary Care Hospital

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Background: All direct oral anticoagulants (DOACs) have multiple indications, each of which have specific dosing recommendations. Dosage adjustments may also be required for renal function, age, and weight. As such, proper dosing of DOACs can be problematic.

Purpose: To evaluate the impact of a hard-stop, required indication for electronic order entry of DOACs on dosing accuracy and adverse outcomes.

Methods: Single-center, retrospective, pre-post intervention study. Texas Health Presbyterian Hospital Dallas (THD) implemented a required DOAC order indication protocol on July 8, 2020. Pre-intervention data was collected for the prespecified month of March 2020 and post-intervention data was collected for the prespecified month of October 2020. Adult patients > 18 years old were included if they were admitted to THD for over 24 hours and initiated or re-initiated on a DOAC during admission. Patients were excluded if they were missing age, weight, or serum creatinine in the electronic medical record or if a DOAC was ordered, but not administered during admission.

Results: Retrospective data collection was completed for 283 patients, with 202 patients included in analysis [55% (n = 111) pre-protocol vs. 45% (n = 91) post-protocol]. Prior to implementation of the required indication protocol, 30% (n = 33/111) patients had DOAC orders that did not match the recommended dose. This was reduced to 18% (n = 16/91) after protocol implementation (difference 12%, p = 0.049). There were no differences in incidence of major bleeding or new thromboembolic events.

Conclusion: Implementation of a required indication field in the electronic health record significantly increased the likelihood of DOAC dosing that matched package insert recommendations for indication.

Identifying an Appropriate Unfractionated Heparin (UFH) Dosing for Patients with Body Mass Index (BMI) ≥18.5 Kg/M2 Study

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Purpose: UFH is a commonly used anticoagulant in venous thromboembolic events (VTE), acute coronary syndromes (ACS) and many other indications. Heparin is primarily distributed in the plasma, therefore, clinicians should exercise caution to prevent bleeding complications while maintaining therapeutic anti-Xa levels. The study objective is to find a safe and effective UFH weight-based dosing protocol for patients with a BMI of 18.5-24.9 kg/m2 (group 1), 25-39.9 kg/m2(group 2), and ≥40 kg/m2(group 3).

Methods: A single-center, randomized, retrospective chart review was performed during the period of January 2013 to December 2019. The primary outcome was to measure the mean infusion rate of UFH (units/kg/hr) at the first therapeutic anti-Xa for BMI of 18.5-24.9 kg/m2, 25-39.9 kg/m2, and ≥40 kg/m2. Secondary outcomes included the time to reach the first therapeutic anti-Xa, number of dose adjustments to reach therapeutic anti-Xa, duration of hospital stay, major bleeding event, and new thromboembolic event while on UFH.

Results: Preliminary results revealed 97 patients in total met the inclusion criteria [BMI of 18.5-24.9 kg/m2 (n=22), 25-39.9 kg/m2 (n=69), and ≥40 kg/m2 (n=6)]. Primary outcome of UFH rate at therapeutic anti-Xa was 12.3 u/kg/hr, 13.3 u/kg/hr and 15 u/kg/hr for BMI groups 18.5-24.9 kg/m2, 25-39.9 kg/m2 and ≥40kg/m2, respectively.

Conclusions: Preliminary results warrant to further investigate a different dosing strategy in patients with a BMI >25kg/m2.

Efficacy of an Insulin Protocol for Treatment of Hypertriglyceridemia Induced Acute Pancreatitis (HTG-AP)

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Purpose: To determine efficacy of an insulin protocol on time to a serum triglyceride value ≤500 mg/dL in patients with hypertriglyceridemia induced acute pancreatitis (HTG-AP).

Methods: This is a retrospective analysis of before and after an insulin protocol was employed in medical ICU patients for the treatment of HTG-AP. This protocol was implemented in June 2020 and has a goal insulin dose of 15 units/hour while maintaining a blood glucose of 120-180 mg/dL. Inclusion criteria were age ≥18 years, admission to Texas Health Presbyterian Hospital Dallas or Texas Health Harris Methodist Hospital Fort Worth, a triglyceride level >1000 mg/dL, and a diagnosis of hypertriglyceridemia and acute pancreatitis. Exclusion criteria were any causes of acute pancreatitis other than hypertriglyceridemia. Patients with no follow up triglyceride reading were also excluded. The pre-protocol patients were admitted from January 2019 to May 2020 whereas the post-protocol patients were admitted from June 2020 to November 2020. The primary outcome of the study was hours to a serum triglyceride level ≤500 mg/dL. Data regarding triglyceride level, treatment used, concurrent anticoagulation or fenofibrate, and fish oil medication use, length of time to resolution, and comorbidities were also collected.

Results: After screening 115 patients with a triglyceride level >1000 mg/dL, 27 patients were included. Sixteen (59.3%) patients were treated prior to implementation of the insulin-based protocol compared to 11 (40.7%) patients treated with the protocol. Time to resolution of hypertriglyceridemia was 84 ± 67.6 hours pre-protocol vs. 49 ± 28.5 hours with the use of the protocol (difference 35 hours; 95% CI, -9.6 to 79.6 hours; p=0.12). Analysis of other outcomes is pending.

Conclusions: There was a trend towards a significantly shorter time to resolution of HTG-AP in patients treated with an insulin-based, disease specific protocol. The statistical analysis is limited by small sample size and **further analysis is** pending

Retrospective evaluation of the safety of remdesivir use in COVID-19 patients with renal dysfunction (REM-RENAL)

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Remdesivir is an FDA approved medication for the treatment of SARS-COV-2 infection. The FDA label for use of remdesivir recommends against the use of remdesivir in patients with an eGFR of less than 30 mL/min. This recommendation was made due to the presence of the excipient sulfobutylether-beta-cyclodextrin (SBECD). Extrapolated from studies with other medications containing this excipient, it is understood that SBECD is renally cleared and can accumulate in patients with decreased renal function. Although recommended against use in patients with an eGFR less than 30 mL/min, the use of remdesivir is not contraindicated in this population and therefore, has been used in these patients within our institution. Limited guidance is available on the safety of remdesivir usage in patients with renal dysfunction. The purpose of this retrospective safety analysis is to provide guidance for the further use of remdesivir in patients with renal dysfunction. A retrospective chart review will be conducted on all patients on the medical floors with a documented diagnosis of Covid-19 and either acute kidney injury or chronic kidney disease. Patients excluded from this evaluation include those within critical care units, pediatric patients (< 18 years of age) and patients on dialysis. Safety outcomes in terms of renal function will be compared between patients that received remdesivir versus patients who did not receive remdesivir. To measure this, we will adopt the Kidney Disease: Improving Global Outcomes (KDIGO) guideline criteria for acute renal dysfunction which defines a clear bump in serum creatinine as ≥0.3 mg/dL within 48 hours or increase in serum creatine ≥1.5 times baseline value within the prior 7 days. For secondary outcomes, we will also analyze the rate of recovery in patients receiving remdesivir versus those that did not in this population. This will be measured by time to discharge or time to mortality.

Preferred COVID-19 Vaccine Setting: Patient Survey at a Community Pharmacy

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TTUHSC/Community Pharmacy PGY1 Community-Based Residency Program

Background: Pharmacists are the most accessible healthcare professional in the United States with nearly 9 in 10 Americans living within 5 miles of a community pharmacy, and they can have a great effect administering the COVID-19 vaccination now that it is available. Pharmacists may administer influenza vaccines in all 50 states; however, state regulations govern which additional vaccines may be administered based on the specific protocol that must be followed and different minimum age restrictions. In the 2015 – 2016 flu season, pharmacies were the second most common place for adult vaccines (24.8%) following a doctor's office (33%). In September of 2020, the Department of Health and Human Services (HHS) authorized pharmacists to order and administer COVID-19 vaccines to patients without physician supervision. However, pharmacies are limited by many obstacles still in place including lack of reimbursement, cost of personal protective equipment, and allocation to vaccine.

Methods: This study was approved by the TTUHSC Amarillo IRB. A written survey was conducted at Community Pharmacy in Denton, TX and TTUHSC Pharmacy in Lubbock, TX. The survey was available for patients 18 and older who visited the pharmacy during data collection. About 50 surveys were collected in November 1, 2020 through January 31st, 2021. Patients who visited the pharmacy to receive their COVID-19 vaccine in January were excluded from the survey. The study identified willingness to receive a COVID-19 vaccine when available, why the patient did or did not want the COVID-19 vaccine, the preferred setting to receive a COVID-19 vaccine, where the patient typically receives vaccines, and if the pandemic has influenced their decision to receive the influenza vaccine for the 2020—2021 flu season. The primary endpoint was to identify the preferred setting for COVID-19 vaccinations when they become available. Secondary endpoints were to identify if the pandemic influenced their decision to receive an influenza vaccine in the 2020—2021 season, identify if patients are willing to receive the COVID-19 vaccine when available, and to identify why patients do or do not want the COVID-19 vaccine.

Results: In progress.

Conclusion: In progress.

Impact of Clinical Pharmacist Interventions on Gestational Diabetes in a Collaborative Practice Clinic

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Pharmacotherapy Residency

Purpose: To assess the effect of clinical pharmacist education on glycemic control in gestational diabetes patients as compared to non-pharmacist management practices in an interprofessional obstetrics and gynecology clinic at Texas Tech Health Sciences Center. This data may expand the role of future clinical pharmacists.

Methods: Data was retrospectively collected utilizing the clinic's electronic health records for this single-center cohort. Glycemic control and other endpoints were compared between patients diagnosed with gestiational diabetes who were seen by a clinical pharmacist vs. usual care (non-pharmacist). The primary outcome was to assess effect of clinical pharmacist education on glycemic control compared to the non-pharmacist group. Key secondary oucomes include change in hemoglobin A1c and effects on maternal and fetal outcomes.

Results: An interm analysis of 25 patients was perfomed. All baseline characteristics were found to be similar between groups. There was found to be no statistical difference between mean post-visit fasting blood glucose ($p= 0.3285$) or mean post-visit 2-hour post-prandial blood glucose ($p= 0.4196$) when coparing the pharmacist and non-pharmacist intervention groups. Not enough patient data has yet been collected to evaluate the secondary endpoints.

Conclusion: This study addresses a unique niche in how clinical pharmacists can provide patient care utilizing their drug and disease state expertise to affect glycemic outcomes in patients with gestational diabetes mellitus. Continued evaluation of the roles of clinical pharmacists is recommended.

Imapct of Vasopressors on Mechanically Ventilated Patients with Addition of Continuous Ketamine Infusion

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Purpose: Propofol has been a standard of care sedative used for continuous sedation in mechanically ventilated (MV) patients. However, in patients who require use of vasopressors and/or positive inotropes and/or requiring concurrent pain control, propofol often is not the best option. Ketamine offers up unique properties that not only provide continuous sedation in patients, but also provide analgesia properties that can result in decreased opiate usage. Currently, there are limited studies evaluating the use of a continuous ketamine infusion (CKI) on sedation in mechanically ventilated patients requiring more favorable hemodynamic responses. Additional research is needed to study what the effect of continuous ketamine infusion has on vasopressor usage.

Methods: It is a retrospective, single-center, pre-/post-comparison study conducted in Intensive Care Unit (ICU) patients on continuous ketamine infusion (CKI) and vasopressors. Patients receiving CKI and vasopressors will be identified by their electronic medical record from 8/1/2019 to 8/31/2020. Exclusion: Prisoners, pregnancy, age < 18, and age > 89. Vasopressor requirements for all patients meeting inclusion criteria will be evaluated prior/post initiation of CKI. CKI criteria will be based on protocol at Hendrick Medical Center. Primary outcome is change in norepinephrine (NE) equivalent doses 1 hour after the initiation of CKI. Secondary outcomes include: change in NE equivalent doses at hours 2, 4, 6, 24, and 48 hours, changes in sedation dose after initiation of CKI, and duration of vasopressors used. Data collection includes: demographic information, initial dose of CKI, vasopressors used, dose of vasopressor, Richmond Agitation-Sedation Score (RASS), Critical Care Pain Observation Tool (CPOT), Sequential Organ Failure Assessment (SOFA) score, length of ICU stay, ICU mortality, mechanical ventilation duration, vasopressor duration, and CKI duration. Statistics will include: descriptive statistics, paired t-test, and a repeated measures regression.

Results: N/A

Conclusions: N/A

Evaluation of Outcomes Based on Outpatient Parenteral Antibiotic Regimen In Staphylococcal and Enterococcal Bacteremia and Endovascular Infections: Comparing Daptomycin to Conventional and Alternative Therapies

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Purpose: Hospitals have increasingly utilized outpatient parenteral antimicrobial therapy (OPAT) to facilitate discharges nd improve patient convenience for those requiring extended IV therapy. Daptomycin is currently utilized as drug of choice (DOC) for bacteremia and endovascular infections in OPAT due to minimal monitoring requirements, perceived safety, and convenience at this facility. However, daptomycin is not the first-line guideline recommended therapy for bacteremia and endovascular infections. The purpose of the study is to determine if the use of daptomycin for these infections is effective as compared to conventional and alternative therapies.

Methods: This study was a retrospective cohort design that included patients treated for staphylococcal and enterococcal bacteremia or endovascular infections in OPAT setting from October 2010 to November 2020. The primary outcome was to determine success of therapy for all patients treated for these infections. Success of therapy was defined as completion of therapy without relapse of infection with relapse defined as re-initiation of antibiotics for the same infection within 30 days of end of treatment. The secondary outcomes included incidence of readmission or emergency department visit related to infection during therapy or within 30 days of end of treatment, change of therapy required due to treatment failure or intolerance, and death. Descriptive statistics and chi-squared was used to analyze the categorical data while the continuous data was analyzed with T-test.

Results: Of the 64 patients in the daptomycin group and the 82 patients in the conventional and alternative therapies group, therapy was successful in 73.44% and 73.17%, respectively. Additionally, there were no significant differences in ED admissions/readmission or required changes in therapy (p=0.85, p=0.99). There was a significant difference found between number of deaths between two groups (p=0.03) with 7 deaths in the daptomycin group and 2 deaths in theother group. Exploratory cost analysis comparing medications is pending.

Retrospective Assessment of Antibiotic Utilization in Clostridioides Difficile Infection Before and After Implementation of Two Step PCR and Toxin Testing Algorithm

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Purpose: Clostridioides Difficile infection (CDI) is a common healthcare associated infection in hospitalized patients in the United States. Currently, utilization of rapid diagnostic tests help to identify patients with CDI, but sensitivity and specificity comes into question when used alone. The purpose of this study was to evaluate if the utilization of antibiotics for the treatment of CDI at University Medical Center in Lubbock, TX had decreased with implementation of reflexive toxin testing after a confirmed positive PCR (polymerase chain reaction) test, specifically in PCR+/toxinpatients. Historically, PCR testing was completed for patients suspected of CDI and treatment given without knowledge of toxin presence per prescriber discretion and patient presentation.

Methods: This was a single centered retrospective chart review of those tested for CDI at University Medical Center in Lubbock, TX for 1 year previous to reflexive toxin testing (01/01/2019 – 12/31/2019) and for 10 months after implementation of reflexive toxin testing (01/01/2020 - 10/31/2020). Pre-implementation patients were obtained from ICD 10 codes, and the post implementation population obtained from Clostridioides difficile isolates identified from microbiology lab results. Results: Preliminary analysis shows a statistically significant decrease in patients receiving no antibiotic therapy from pre implementation to post implementation from 0.5% (1/198) of patients in the pre implementation receiving no antibiotics, to 9% (13/135) of patients post implementation receiving no antibiotics ($p<0.0001$). There was a slight decrease in median duration of days of antibiotics from pre to post implementation from 11 days (10 – 15) to 10 days (9 – 12) (p 0.48 CI 0.65 – 1.22).

Conclusion: The number of patients who received CDI antimicrobial therapy decreased with the implementation of the reflex toxin assay. Preliminary results also show a potential to have a larger detectable decrease in median duration of days of antibiotic therapy with further studies.

Evaluation of Renal Function in Veterans with Type 2 Diabetes Mellitus and Heart Failure on Empagliflozin

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Type 2 diabetes mellitus (T2DM) is a major risk factor for the development of cardiovascular disease (CVD), including heart failure, and nephropathy. Empagliflozin is a selective sodium-glucose cotransporter-2 (SGLT-2) inhibitor approved for the treatment of T2DM which has also shown some benefits in improving cardiovascular outcomes as well as slowing the progression of kidney disease. The EMPEROR-Reduced trial has found that the rate of decline in estimated glomerular filtration (eGFR) is slowed by the addition of a SGLT2 inhibitor. Currently, limited studies exist that specifically assess the safety and efficacy outcomes of empagliflozin in the older adult or veteran population. The purpose of this study is to determine if empagliflozin improves renal function and glycemic outcomes in Veterans with T2DM and heart failure. Data were recorded from electronic medical records of Veteran patients ages 18 years and older with T2DM and heart failure receiving at least two oral antidiabetic medications from July 1, 2017 to July 31, 2020 at the Veteran Affairs North Texas Health Care System (VANTHCS). The primary outcome was a composite consisting of renal function endpoints (decline in renal function from baseline of at least 50% or progression to end stage renal disease [ESRD]). The secondary outcome was glycemic control, noted by change in A1c from baseline. Safety outcomes included admission for ketoacidosis, admission warranting amputation, and treatment for urinary tract infection (UTI) or genital infection.

A Retrospective Study Evaluating the Role of Atomoxetine In Improving Outcomes in Patients with Attention Deficit Hyperactivity Disorder and Comorbid Substance use Disorder

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VA North Texas Health Care System and Texas Tech University Health Sciences Cente

Background: There are higher rates of substance use disorders (SUD) in adults with attention deficit hyperactivity disorder (ADHD) as compared to adults without ADHD. Stimulant use disorder is a type of substance use disorder involving the use of stimulants such as cocaine, amphetamines and methamphetamines. Increased impulsivity and potential behavioral problems associated with ADHD may increase the chance for illicit stimulant use. Current first line treatment for ADHD include stimulant medications such as amphetamines or methylphenidate. Many clinicians are reluctant to prescribe stimulants to patients with SUD due to the potential for abuse, diversion, and reduced treatment outcomes. Atomoxetine, a nonstimulant medication, is thought to have less abuse potential than stimulants while being effective in treating ADHD symptoms. This study will evaluate outcomes for ADHD and stimulant use disorder in adults receiving treatment with atomoxetine and methylphenidate.

Methods: This study will consist of adults who have concurrent ADHD and stimulant use disorder receiving treatment with atomoxetine or a stimulant medication (methylphenidate) for ADHD. Demographic variables, current psychotropic medications, comorbid disorders, dosing regimen, and concurrent substance use disorders will be collected. ADHD outcomes will be evaluated using subjective patient reports collected via chart review in the computerized patient record system. SUD outcomes will be evaluated through urine drug screens, time to relapse, and reported drug cravings.

Results: The results of this study show half of the patients with stimulant use disorder receiving atomoxetine for ADHD relapsed on illicit stimulants. This suggests that the choice of atomoxetine or methylphenidate may not influence sobriety. Patients were also more likely to discontinue atomoxetine due to tolerability or were more likely to be prescribed atomoxetine if presenting with a recent drug use. ADHD outcomes were similar among the two groups.

An Evaluation of Outcomes Pursuant to Emergency Department Treatment of Deep Vein Thrombosis After Single-Dose Anticoagulant Administration

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Purpose: Patients with venous thromboembolism (VTE) are often treated in the inpatient setting despite being appropriate candidates for outpatient management. The reverse is also true. The primary endpoint of this study is to evaluate therapeutic outcomes following acute management of deep vein thrombosis (DVT) in the ED followed by outpatient management, compared to inpatient management, by evaluating hospital visits for recurrent VTE. Secondary outcomes include evaluating the appropriateness of DVT management in the ED by evaluating factors such as recurrent ED visits and readmissions for VTE, anticoagulation complications, and the potential relation of these to patient cost barriers.

Methods: This is a retrospective, single-center cohort study of patients with confirmed DVT managed in either outpatient or inpatient settings at University Medical Center between January 2017 and September 2020. A total of 200 patient charts were reviewed, half treated in the inpatient setting, the other half in the outpatient setting. Those treated in the outpatient setting received single-dose anticoagulant in the Emergency Department (ED), and were then discharged.

Results: There was no significant difference between both groups with regards to readmission for VTE in outpatient and inpatient arms, respectively (20.2% vs 17.9%, p 0.68). The majority of patients treated in the outpatient setting had lower extremity DVT diagnosis (78.6%, $p<0.0001$), and the majority were managed acutely with LMWH or a DOAC (64.6% and 38.6%), respectively. More patients with a history of hypercoagulable states were treated in the outpatient setting (68.7% vs 48.4%, p 0.0067). Other endpoints were not statistically different.

Conclusions: Appropriate candidates for the management of VTE in the outpatient setting often have successful treatment outcomes. Others do not due to numerous barriers. In appropriate candidates for outpatient management, the involvement of a pharmacist at discharge to establish follow-up will assist in overcoming barriers, prevent VTE recurrence and assist in maintaining the appropriate monitoring associated with anticoagulation treatment

Assessing Change in Renal Function Between Empagliflozin and Liraglutide in Veterans with Renal Impairment at Baseline

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Type 2 diabetes mellitus is a chronic condition that leads to microvascular complications including neuropathy, retinopathy, and nephropathy. When diabetes is left uncontrolled, damage to the kidneys can lead to chronic kidney disease. Certain classes of antidiabetic medications have been theorized to protect the kidneys and help slow the progression of kidney disease. The sodium-glucose co-transporter 2 (SGLT2) inhibitor empagliflozin and the glucagon-like peptide 1 (GLP-1) agonist liraglutide are two such medications. There have been promising results in clinical trials that indicate these medications help reduce incident and worsening nephropathy. However, the primary focus in existing clinical trials have been on cardiovascular, rather than renal outcomes. The purpose of this study is to investigate empagliflozin and liraglutide to determine the change in renal function in Veterans who are renally impaired at baseline.

A retrospective cohort study will be conducted in Veterans with type 2 diabetes and renal impairment who received care from the VA North Texas Health Care System. Specific study inclusion criteria include Veterans 18 years of age or older with a type 2 diabetes diagnosis and an eGFR of 45-59 mL/min, who have been using either empagliflozin or liraglutide for at least 3 months. Baseline, outcome, and adverse effect data will be collected from the Computerized Patient Record System (CPRS) on patients initiated on either study medication from May 1, 2016 to September 1, 2020. The primary outcome is the percentage change in eGFR at 3, 6, 9, 12, and 18 months. Secondary outcomes include absolute change in microalbumin to creatinine ratio from baseline, initiation of hemodialysis (HD) or continuous renal replacement therapy, and/or doubling of serum creatinine from baseline. A student's t-test will be conducted for all numerical outcomes and a chi-square test for all discrete data with a p-value of less than 0.05 indicating statistical significance.

Effect of Isoflurane Anesthesia on Ceftazidime Brain Uptake

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Isoflurane is a volatile anesthetic that has been widely used in clinical settings. Our group recently showed that it changes the fluidity of lipid membranes of brain endothelial cells, which may affect the permeability of the blood-brain barrier (BBB). Accordingly, our in vivo studies in mice indicated a two-fold increase in BBB permeability of the permeability marker, sucrose, under 30 min isoflurane exposure. Here we used ceftazidime, an antibiotic drug known to cause neurotoxicity in patients, particularly with renal impairment, to investigate the change in brain uptake clearance value (Kin) under isoflurane anesthesia compared to ketamine:xylazine in a mouse model. A liquid chromatography-tandem mass spectrometry (LC-MS/MS) method was established to analyze ceftazidime in biological fluids and brain tissue. For in-vitro permeability studies, a monolayer of induced pluripotent stem cells (iPSCs) derived brain endothelial cells (BMEC) was seeded on the trans-well system. To measure the brain uptake in vivo, ceftazidime was injected via the jugular vein in two groups, one anesthetized with isoflurane (n = 6) and the other group with ketamine:xylazine (n = 5). Blood samples were collected up to 30 min after the injection, and then the mice were sacrificed to collect the brains. The trans-well model using BMEC showed low permeability (6.706 ±1.40×10−7cm/s), which is close to the permeability of sucrose (4.744±0.315×10−7cm/s). Both brain concentration (Cbr) and brain uptake clearance (Kin) were significantly higher in the isoflurane group compared to the ketamine group (Kin of 0.0572±0.0066 µL g−1 min−1 and 0.0328±0.0021 µL g−1 min−1with p-value = 0.0001 and Cbr of 0.0195 ± 0.0018 %ID/g and 0.0152 ± 0.0023 %ID/g with p-value = 0.0068, respectively). This study suggests that the use of isoflurane as an anesthetic in patients could increase the brain uptake of ceftazidime and, as a result, increase the chance of causing neurotoxicity

Effect of Prenatal E-cigarette Exposure on Postnatal Blood Brain Barrier and Behavioral Outcomes

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Background: Electronic cigarette (e-Cig) is considered as a safer alternative to tobacco smoke and therefore has gained popularity among all age groups and sex. Harmful effects of tobacco smoke exposure during pregnancy are well documented for both pregnant and neonatal health however there is lack of preclinical and clinical studies to evaluate the long-term effects of prenatal e-Cig exposure on neonatal health. Therefore, the aim of our study is to evaluate the effect of maternal e-Cig smoking on blood-brain barrier (BBB) and behavioral outcomes in offspring at adolescence and adult age.

Method: In this study, pregnant CD1 mice (E5) were exposed to e-Cig vapor (2.4% nicotine) till postnatal day (PD) 7. Weight of the offspring was measured at PD0, PD7, PD15, PD30, PD45, PD60 and PD90. Structural elements of BBB, tight junction proteins (ZO-1, Claudin-5, Occludin), astrocyte (GFAP), pericyte (PDGFRβ) and basement membrane (Laminin α1, Laminin α4) level were analyzed using western blot in 7day old offspring. Long-term motor and cognitive functions were evaluated using open field test, novel object recognition test and morris water maze test at adolescence (P 6 weeks) and adult (P 3 months) age.

Results: Reduced body weight was observed in e-Cig exposed offspring at all time points till PD90 days compared to control ($P < 0.05$). Significantly reduced expression of Claudin-5, ZO-1 and GFAP was observed on PD7 e-Cig exposed group ($P < 0.05$). Additionally, prenatally e-Cig exposed female adolescent and adult offspring showed impaired locomotor, spatial learning, and memory function compared to control female offspring ($P < 0.05$).

Conclusion: Our findings suggest that prenatal e-Cig exposure affects neonatal blood brain barrier function and impairs motor and cognitive function at adolescence and adult age. Our ongoing work includes evaluation of prenatal e-Cig exposure on BBB at postnatal day 23, 45 and 90. Support: NIH R01DA049737 and R01DA02912.

Method Development for Simultaneous Quantification of Serotonin, Dopamine, and Norepinephrine by LC-MS/MS

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Introduction: Stroke remains one of the key contributors to worldwide mortality and long-term disability with the necessity of new therapeutic strategies. Studies have shown that enhancing the presence of local neurotransmitters (NTs) led to improved cortical plasticity, eventually helping in motor recovery after stroke. The study is designed to develop a robust and sensitive liquid chromatography-mass spectrometry (LC-MS) method to be able to quantify three essential NTs, serotonin (5-HT), dopamine (DA), and norepinephrine (NE) in artificial cerebrospinal fluid (aCSF), with the future objective to extend the methodology to be pertinent for rodent brain tissue.

Method: The quantitative analysis of three NTs DA, 5-HT and NE were executed using a reversed-phase Raptor Biphenyl column (100 × 2.1 mm, 2.7µm) coupled to an API-QTRAP 5500 (AB SCIEX) mass spectrometer under a gradient mode, using a 0.2% formic acid in water and 0.2% formic acid in methanol at a flow rate of 0.2 mL/min. Data acquisition and processing were performed with the Analyst software (version 1.7). Calibration curves of the analytes were established by plotting the peak area ratios of each analyte to IS (internal standard) versus analyte concentrations. Linearity was evaluated by the correlation coefficient (r).

Result: The multiple reaction monitoring (MRM) was optimized for all three neurotransmitters 5-HT (m/z 177.07→160.00), DA (m/z 154.04→137.00), and NE (m/z 152.06→106.90) using the positive ion mode. All the three NTs were well separated within 6 mins runtime for aCSF method. The linearity for 5-HT, DA achieved from 0.781ng/ml- 100 ng/ml and 1.562ng/ml – 100ng/ml for NE with r2 value > 0.99.

Conclusion and on-going studies: This work demonstrated a sensitive, selective, and simple (LC-MS) method for quantitating 5-HT, DA, and NE in aCSF. Currently, we are developing a method to determine the levels of NTs in brain homogenates of CD-1 mice (sham/ischemic stroke).

Is Diminazene an Activator of ACE2?

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The aim of this study was to verify a recently reported effect of anti-trypanosome agent diminazene (DMZ) on activity of Angiotensin-Converting Enzyme 2 (ACE2) and extend it to other zinc-endopeptidases from the same family of enzymes. For this purpose, we evaluated concentration-dependent effect of DMZ on ACE2 activity, in a well-established enzymatic assay. Initial velocities of ACE2 in the presence of increasing concentrations of DMZ were ascertained by assessing the extent of fluorescence upon hydrolysis of a fluorogenic substrate. To determine the kinetic parameters for recombinant human and mouse ACE2 in the presence of DMZ, fluorescence-based kinetic assays were performed with saturating concentrations of substrate. Surprisingly, DMZ did not enhance activity of ACE2 in assay conditions replicating that of the original study reporting activation of the peptidase with this agent. Additionally, we observed inhibition of ACE, neurolysin, thimet oligopeptidase and neprilysin at high micromolar concentrations of DMZ. Furthermore, DMZ did not substantially affect Vmax or Km values of substrate hydrolysis at 10 and 50 µM assay concentrations. To validate the observations with the synthetic substrate, we replicated the lack of ACE2 activation by monitoring hydrolysis of angiotensin II by ACE2 using LC-MS/MS. No significant difference was observed in the amount of angiotensin-(1-7) formation or angiotensin II hydrolysis. To verify that the observed discrepancy was not because of the recombinant ACE2 used in our study, additional experiments were performed to confirm identity of this enzyme. In this set of experiments, we confirmed concentration-dependent activation of ACE2 by NaCl and inhibition of the enzyme by well-characterized inhibitors DX600 and MLN-4760. Moreover, identity of ACE2 was confirmed by immunoblotting using a specific polyclonal antibody against the peptidase. While we continue our studies to clarify the noted discrepancy, our current data indicate that DMZ does not enhance the catalytic activity of ACE2.

Use of HDX-MS to Characterize Interaction of Dipeptide His-Tyr With Recombinant Neurolysin

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Peptidase neurolysin (Nln) has been recognized as a cerebroprotective enzyme functioning to protect the brain in acute neurodegenerative disorders. With the use of a structure-based discovery approach we have recently identified dipeptide His-Tyr to enhance catalytic efficiency of recombinant Nln. The goal of the current study was to use hydrogen/deuterium exchange mass spectrometry (HDX-MS) to characterize interaction of His-Tyr and Nln, and potentially identify the binding site of the activator.

For HDX, Nln was pre-incubated with or without His-Tyr and underwent HDX reaction at 37oC (up to 10 min), followed by analysis of 322 peptides covering 83.36% of Nln primary sequence. Binding of His-Tyr caused significant changes in deuterium uptake across two fragments of Nln: a decrease in HDX was observed in region spanning amino acid residues 223-236, while a.a. 204-220 region showed an increase in HDX, indicating that the former one may be involved in ligand binding. Using molecular simulation model of Nln from our published study and contact analysis, it was determined that three amino acid residues (Asn-203, Lys-204, Asn-207) had the most favorable properties to interact with His-Tyr. To experimentally verify whether His-Tyr binds to any of these amino acid residues, we produced and purified three single mutant hNln constructs (N203A, K204A and N207A) as well as one double mutant - N203A/N207A, and evaluated concentration-dependent effect of His-Tyr on catalytic activity of wild type and mutant Nlns. Our results indicate that the documented decrease in HDX in the noted sequence of Nln is unlikely to be because of direct binding of His-Tyr but rather it is due to conformational change of the peptidase induced by binding of the dipeptide.

Since, small molecule activators of Nln could become important research tools to study its functional significance, identification of the activator binding site and mechanism remain the subject of our ongoing efforts.

Blood-Brain Barrier Permeability is not Globally Compromised in the Tg2576 Mouse Model of Alzheimer's Disease

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive dysfunction and loss of neurons, associated with the deposition of extracellular amyloid β (Aβ) protein and formation of neurofibrillary tangles from hyperphosphorylated tau protein. Despite reports on the loss of endothelial tight junction proteins and dysregulated transport function at the blood-brain barrier (BBB), the effects of AD-related pathological events on the global barrier function remain debated. We recently introduced a novel LCMS/MS method for the paracellular permeability markers sucrose and mannitol as a very useful tool in quantifying BBB integrity in different in vitro and in vivo disease models. Here we conducted a quantitative pharmacokinetic study to investigate the BBB permeability of sucrose and mannitol in both sexes of aged Tg2576 mice, one of the most widely used and well-characterized transgenic mouse models of AD. Interestingly, we found no difference when we compared the brain uptake clearance (Kin) of mannitol and sucrose between aged (16 months old) AD and wild type mice. Kin values of mannitol for the hippocampus region of aged wild type and AD mice (n = 7 per group) were 0.151 ± 0.042 and 0.148 ± 0.038 μl g−1 min−1, respectively. Similarly, the sucrose Kin value was 0.056±0.016 and 0.062±0.013 μl g−1 min−1 for the hippocampus region of the aged wild type and AD mice. Similar results were found for olfactory bulbs, cortex, and cerebellum, which confirmed the absence of widespread BBB disruption in the aged Tg2576 model. Overall, based on the high sensitivity of our LCMS/MS method, this finding strongly suggests a lack of global BBB impairments in the TG2576 mice, despite significant amyloid pathology at advanced ages.

Isoflurane Affects the Blood-Brain Barrier Permeability for Gentamicin

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Isoflurane has been known to change the blood-brain barrier integrity, thereby altering the permeability function of the barrier. An increase in permeability across the blood-brain barrier was previously observed using [13C12] sucrose marker, which showed 2-fold higher brain uptake clearance values (Kin). The change in the permeability across the BBB for gentamicin, a neurotoxic antibiotic was tested in this study with similar attributes to [13C12] sucrose marker using in vitro and in vivo BBB models. Human BMEC monolayer was used as in vitro model, while 2 groups of male C57Bl/6J mice anesthetized with isoflurane and ketamine: xylazine respectively was used to test in vivo permeability. A highly sensitive and robust UPLC-MS/MS method was developed and validated for the quantification of gentamicin in biological samples. Gentamicin was found to have low in vitro permeability with a permeability coefficient in the range of 8.05 ± 1×10-7 cm/s. Gentamicin was found to be approximately 2- folds more permeable across the BBB under the 30 min exposure to clinical levels of isoflurane anesthesia as compared to ketamine: xylazine (Kin was 0.052 ± 0.014 and 0.10 ± 0.03 µl g−1 min−1 for ketamine and isoflurane group respectively). Future studies should investigate whether it can cause increased neurotoxicity in patients when using a clinical dose of gentamicin IV, under the influence of isoflurane anesthesia.

Glutamate Buffering Activity and Blood-Brain Barrier Protection of Opioid Receptor Agonists Biphalin And Nociceptin

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Opioids play crucial roles in the regulation of many important brain functions including pain, learning, memory, neurogenesis and hemodynamics. Activation of opioid receptors is reported to have neuroprotective effects following ischemic reperfusion injury. Here we aimed to understand the role of biphalin and nociceptin, non-selective opioid receptor agonists, on blood-brain barrier (BBB) integrity during ischemic stroke.

In this study, we measured the effect of biphalin and nociceptin on astrocytic glutamate uptake and the expression of excitatory amino acid transporter (EAAT) to study the indirect role of astrocytes on opioid receptor-mediated BBB protection. Further, we used mouse brain endothelial cells, bEnd.3 and primary astrocytes as monoculture and co-culture in-vitro BBB models. Restrictive BBB properties were evaluated by measuring [14C] sucrose paracellular permeability and the redistribution of the tight junction proteins. The protective effect of biphalin and nociceptin on BBB integrity was assessed after exposing cells to oxygen-glucose deprivation (OGD) (1% O2, 2 hours) and glutamate (2mM). Respective opioid receptor antagonists were used to determine opioid receptor dependent activity of biphalin and nociceptin. It was observed that the combined stress (2mM glutamate and 2 hours OGD) significantly reduced glutamate uptake by astrocytes however, biphalin and nociceptin treatment increased glutamate uptake in primary astrocytes. This suggests a role of increased astrocytic buffering capacity in opioid meditated protection of the BBB during ischemic stroke. It was also found that the combined stress (2mM glutamate and 2 hours OGD) significantly increased [14C] sucrose paracellular permeability in bEnd.3 cells as well as in a co-culture cell model. Biphalin and nociceptin treatment attenuated the effect of the combined stress, which was reversed by the opioid receptor antagonists, suggesting the role of opioid receptors in both biphalin and nociception's BBB modulatory activity.

Characterization and Therapeutic Targeting of CD105 in Renal Cell Carcinoma

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Renal cell carcinoma (RCC) arises from the renal parenchyma and accounts for approximately 85% of all kidney cancers. It is highly metastatic and invasive with a 5 year overall survival rate of 13% when diagnosed with metastasic lesions present. This metastatc form of RCC is resistant to chemotherapy and radiotherapy and moderately responsive to anti-angiogenic therapy. CD105 (endoglin), a TGF beta co-receptor involved in angiogenesis, is highly expressed in RCC and this expression corellates with disease severity. Interestingly, CD105 is highly expressed in both the RCC tumor vasculature and the RCC tumor cells, with limited understanding for it's role in tumor cells. To characterize the role of CD105 in RCC tumor cells, we have generated a CD105 deficient cell line from the parental RENCA cell line utilizing CRISPR/Cas9 technology. This CD105 deficient cell line interestingly demonstrates increased motility and metastatic potential in an in vitro wound healing assay but no difference in growth rate in vitro. However, after subcutaneous implantation in syngeneic male mice, CD105 deficient tumor cells initially present with a rapid appearance of tumor formation but progress very slowly subsequently. In comparison, mice receiving control tumor cells developed slower initial tumor formation but, ultimatlely, significantly higher tumor burden than mice receiving CD105 deficient tumor cells. As our characterization studies suggest CD105 potentiates the tumor phenotype and is, therefore, a viable RCC target, we pursued therapeutic targeting of CD105 with a Listeria-based immunotherapy (Lm-LLO-CD105). Treatment of mice bearing RCC tumors with Lm-LLO-CD105 resulted in a significant decrease in tumor burden in comparison to control Listeria treated animals in both subcutaeneous and orthotopic mouse models of RCC. Overall, our studies suggest CD105 expression by RCC tumor cells contributes to the malignant phenotype and this expression can be effectively targeted therapeutically with tumor immunotherapy.

Brain Microvascular Endothelial Cells are Sensitive to Hypoglycemia and Partially Rescued by Ketone Bodies

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Introduction: Glucose represents the main source of energy of the central nervous system (CNS), as 20% of daily glucose intake is directed towards the brain. Glucose transport inside the CNS is occurring mostly via the blood-brain barrier (BBB) via the presence of several glucose transporter isoforms (GLUTs). Although glucose metabolism has been mostly investigated in the lens of astrocyte-neurons axis, the fate of glucose and its metabolism at the BBB remains elusive. GLUT1 deficiency syndrome (GLUT1DS) is a autosomal dominant haploinsufficiency characterized by mutations in SLC2A1 resulting in impaired GLUT1 expression and/or activity. Patients suffering from GLUT1DS suffer from epileptic seizures, intellectual disabilities, and movement disorders. As of today, medical intervention involving the adoption of a ketogenic diet (KD) remains the main course of action with satisfactory clinical outcomes. Yet, the effect of hypoglycemia and ketone bodies on the BBB function (including its glucose metabolism) remains unclear. This study investigates the effect of hypoglycemia and ketone bodies on the barrier function and glucose metabolism in vitro.

Methods: CTR90F and CTR65M iPSC derived BMECs were used in this study. Changes in GLUTs expression was assessed by immunofluorescence and flow cytometry, change in glucose uptake was assessed using 14Cglucose, change in glycolytic flux using SeahorseXF24 flux analyzer, and changes in the barrier function by transendothelial electrical resistance (TEER) and permeability to fluorescein. Cells were supplemented ketone bodies (KB, 4microM beta-hydroxybutyrate and 1mM acetoacetate) for 24 hours.

Results: Our data suggest that a decrease in glucose level upregulates the expression of GLUT1 and GLUT3 isoforms in our BMECs monolayers, such decrease was accompanied by a decrease in glucose uptake, alterations in tight junction complex, as well as a decreased cell metabolic activity and glycolytic flux resulting in a partial recovery of the barrier function under mild hypoglycemia and a partial recovery of the glycolytic flux. No significant changes in glucose uptake was observed in our model following treatment with KB.

Discussion: Our study suggests that BMECs may rely on glycolysis as the main source of energy, a decrease in blood glucose may have a detrimental effect on the barrier function. Supplementation with KB partially relieved such symptoms.

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Potentiation Activity of Urea-Based Analogs in the Treatment of Triple Negative Breast Cancer

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Triple-negative breast cancer (TNBC) is an aggressive subtype of cancer that makes up 15-20% of breast cancer patients. Characterized by the lack of response to estrogen (ER), Human Epidermal Growth receptor 2(HER2), and progesterone (PgR), TNBC remains a challenging therapeutic target. Current anticancer agents on the market are efficacious in their treatment, but continued use can lead to resistance in tumors. Combination therapy, in which two or more therapeutic agents are administered for a single condition, is currently used in clinical settings. This therapeutic approach has been validated for use in the treatment of resistant tumors.

As previously published, a novel urea-based compound synthesized in our lab has shown promising efficacy in treating MDA-MB-231 originated TNBC in vitro and in vivo. In this work, we have evaluated the therapeutic potential of the combination of doxorubicin and our lead urea compound using MDA-MB-231 cells. Our data show that combined treatment has IC50 in the low nanomolar range. The efficacy of this drug combination in vitro decreased the original IC50 values of doxorubicin by 10-20 fold.

Ferutinin Promotes Expression of Functional and Structural Osteogenic Molecules in Dental Pulp Stem Cells

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Osteoporosis is a skeletal disease characterized by loss of bone density and increased susceptibility to fractures. At a cellular level, it occurs when bone resorption by osteoclasts outpaces bone formation by osteoblasts. It is a common disease and is associated primarily with aging, especially in post-menopausal women. Stem cell-based regenerative therapies have received attention in recent years as potential therapeutic agents for the treatment of degenerative diseases. In this study, we demonstrate that dental pulp stem cells (DPSCs) treated with the phytoestrogenic compound ferutinin are capable of producing the functional and structural molecules necessary for osteogenesis and proper osteoblastic function.

In this study, we show that ferutinin promotes BMP2 pathway expression in DPSCs. Using qPCR and western blot analysis, we demonstrate that BMP2, Runx2, and Smad1/5/8 are significantly enhanced at the gene level as well as the protein level. Using classical differentiation with β-glycerophosphate and L-ascorbic acid as a positive control, we further confirm that ferutinin promotes osteogenesis. Moreover, we demonstrate using qPCR methods that ferutinin significantly increases expression of genes that encode functional molecules, including PTHLH, SPP1, IBSP, and SP7. Furthermore, significant increases in collagen 1a1 and osteocalcin expression in ferutinin-treated DPSCs are observed via ICC. Further transwell studies demonstrate that ferutinin-treated DPSCs not only have osteogenic potential, but that they remarkably attenuate induced osteoclastic differentiation of monocytes. By western blotting, we also demonstrate that ferutinin induces DPSC expression of osteoprotegerin, a protein which is important for the regulation of osteoclastic differentiation and activity in bones. These findings demonstrate that ferutinin-treated DPSCs function much like osteoblasts in vitro and indicate that they have potential to positively impact osteoporotic bone within the skeletal microenvironment.

Design and Synthesis of Gliotoxin Analogs as Selective KOR Antagonists for Treatment of Chronic Pain

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Gliotoxin is a sulfur-containing mycotoxin produced by many fungal species including Aspergillus, and Candida. It crosses the blood-brain barrier and has selective inhibitory action against histamine H1 receptors. Previously, we used the structure of this natural product as a template for designing compounds with selective binding to the kappa-opioid receptor (KOR). Such ligands were shown to be active in neuropathic pain model in rats, where intraperitoneal administration (3 mg/kg) of the lead molecule resulted in the modulation of sensory and emotional pain-related behaviors in animals. Here, we present the design and synthesis of the next generation of piperazine-based KOR ligands as a part of the ongoing structure-activity relationship study.

Mechanism of Metformin Transport Across Bbb in Normal Physiological Condition and Ischemic Brain Injury

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Metformin is a first-line anti-diabetic therapy. Past studies have shown metformin to cross the BBB, accumulate in different parts of the brain and exert its neurotherapeutic action. However, it is important to decipher brain pharmacology of the drug including its potential interaction with transporters expressed at the BBB. Studies from a cellular model of the human epithelium showed that luminal transporters contribute to intestinal accumulation and absorption of metformin. Three types of organic cationic transporters- OCT1, OCT2 and OCT3 that belong to the SLC22 families have been identified at the luminal membrane of BBB. In our study, we investigated the potential involvement of OCT1, 2, and 3 transporters in metformin transport by using transporter-specific inhibitors in a brain microvascular endothelial cell line hCMEC/D3. Furthermore, we used RT-PCR to confirm the mRNA-expression of OCT1-3 relative to 18s rRNA in the cell line. In presence of inhibitors, amantadine at 500 µM (OCT 1/2) and prazosin at 100 µM (OCT1/3), the amount of transcellular permeability of metformin was significantly decreased suggesting involvement of OCT transporters. Additionally, with self-inhibition studies, the permeability decreased suggesting saturation of the transporters. Furthermore, our real-time PCR data showed low OCT1, OCT3 and but no OCT2 expression suggesting OCT1 and OCT3 might be potential transporters for metformin brain entry. Our preliminary findings support involvement of OCT1 and OCT3 transporters for metformin brain uptake. To test the in vivo blood to brain uptake of metformin, we plan to administer the metformin at multiple times to determine a suitable time point at which brain concentration is optimum. Furthermore, we will use OCT transporter inhibitors to study the role of these transporters in brain uptake of metformin. Lastly, we will utilize metformin administration coupled to the stroke conditions, and TS/e-Cig exposure to decipher metformin's maximal neuroprotective efficacy.

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Cerebrovascular Effects of Juul Electronic Cigarettes by Analyzing Blood and Brain-Based Biomarkers

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Electronic cigarettes (e-Cigs) have been rapidly gaining popularity in the general population. Juul is an e-Cig brand which is extremely popular in adolescent population. The short and long-term health effects of these alternative cigarette products are mostly unknown and warrant extensive research. We aimed to study the cerebrovascular effects of Juul exposure by analyzing different plasma and brain biomarkers in comparison with tobacco smoke (TS) exposure. We exposed male C57 mice to TS/Juul vapor for 14 days. Open field test was performed to study the locomotor activity of the mice. LCMS/MS was used to measure brain and plasma nicotine and cotinine level. Middle cerebral artery occlusion (MCAO) followed by reperfusion was induced in mice to mimic ischemic stroke after Juul/TS exposure. Enzyme-linked immunosorbent assay was done to investigate plasma biomarkers and western blot to study brain biomarkers. Juul/TS-exposed mice had reduced weight compared to control. Also, TS-exposed mice showed significantly increased activity compare to control/ Juul groups. Interestingly, Juul exposed mice had higher brain/plasma ratio of nicotine compared to TS and Blu e-Cig-exposed mice. MCAO increased plasma IL-6 and decreased plasma thrombomodulin level, but no significant effect of TS or Juul was observed for these biomarkers. Brain injury after MCAO was significantly worsened with Juul/TS pre-exposure. We also found reduced brain tight junctional proteins (ZO-1, occludin) expression with Juul and TS exposure after MCAO. The inflammatory marker ICAM-1 was increased in the brain while MMP-9 was decreased with Juul and TS exposure. Further, the antioxidant marker Nrf2 was decreased after MCAO in TS-exposed group. These results indicate that Juul exposure could exert similar level of cerebrovascular injury compared to TS. Further studies are needed to characterize the neurotoxic effects of Juul e-Cig exposure. Support: NIH R01DA0497 and R01DA029121

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C-Fiber Neuron ANO1 in Nociception

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Anoctamin 1 (ANO1 or TMEM16A) is a Ca2+−gated Cl^- channel expressed in a variety of tissues. In C-fiber neurons, ANO1 is emerging as a molecular component of peripheral pain transduction. C-fiber neurons have cytosolic Cl^- concentration ($[Cl^-]i$) of ~40mM and thus Cl^- electrochemical equilibrium (ECl-) is excitatory at ~ -30 mV. Whole-cell patch-clamp (current-clamp) electrophysiology recordings of C-fiber neurons from mouse dorsal root ganglia demonstrated robust action potential responses to ANO1 activation by application of E-act (N-aroylaminothiazole reagent, 10µM) with 40mM $[Cl^-]i$ (via recording pipet perfusion); but at low $[Cl^-]i$ (10mM) (thus inhibitory ECl-) E-act did not trigger action potentials. E-act induced current to voltage (I-V) curves (in voltage-clamp) were consistent with other ANO1 recordings. ANO1 is activated by local cytosolic Ca2+ ([Ca2+]i). C-fiber neuronal noxious-stimuli receptors often increase [Ca2+]i, including the noxious heat sensor, TRPV1 (transient-receptor-potential vallinoid 1). At 40mM $[Cl^-]i$, application of TRPV1-activator, capsaicin (15µM), induced action potentials in mouse C-fiber neurons that were diminished with co-application of ANO1 inhibitor, T16A[inh] (20µM). In contrast, at 10mM $[Cl^-]i$, E-act co-application inhibited capsaicin-induced action potentials, T16A[inh] co-application restored action potentials. Thus, depending on $[Cl^-]i$, ANO1 amplifies the TRPV1 response in nociceptors. To not disrupt TRPV1 carried-Ca2+, recordings were in perforated-patch (Amphotericin−B) configuration. Nociceptor action potentials signal to the brain for pain perception. Thus, subcutaneous injections of E-act (5mM) or capsaicin (50µM) into mouse hind paws induced dramatic nocifensive behavioral responses. Reponses were attenuated by co-injection with T16A[inh] (1.3mM). In summary, ANO1-activation induced $[Cl^-]i$-dependent nociceptor action potentials and mouse nocifensive behaviors; thus, direct ANO1 activation can induce pain perception. ANO1 inhibitor attenuated TRPV1-triggering of action potentials and capsaicin-induced nocifensive behaviors, which indicate that TRPV1 carried [Ca2+]i activates ANO1 channels, which in turn facilitates TRPV1 triggering of action potentials in nociceptors. Reagents inhibiting ANO1 are currently being examined as analgesics.

Brain Distribution and Potential Neuropsychological Significance of SARS-Cov-2 Entry Receptor ACE2

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Growing evidence shows that neuropsychological symptoms are common in COVID-19 pandemic patients. The viral pathogen SARS-Cov-2 has been reported in postmortem brain tissues. In addition, approximate 30% of recovering patients experience lasting neuropsychological disorders. Knowledge the receptor responsible for brain entry for SARS-Cov-2 is key to understand the transmission and pathogenesis of the pandemic. ACE2 is the primary entry receptor for SARS-Cov-2, besides its role in cardio-cerebro-vascular regulation, immunoregulation and neurogenesis. However, current studies on brain distribution of ACE2 and brain entry of SARS-Cov-2 remain incomplete, inconsistent and controversary. In this study, we systemically examined the spatial and cell-specific distribution of ACE2 in mouse brains. Our IHC data showed ACE2 unevenly distributed throughout the brain with high expression in microvascular walls, modest in subventricle zones, hippocampus, hypothalamus, rostral migratory streams and olfactory bulb, but low in cortex, thalamus and large blood vessels. Co-stain of ACE2 with cell-specific markers revealed strong expression of ACE2 in pericytes, modest in neurogenic cells and astrocytes near cerebral microvessels and ventricles, but undetectable in mature neurons and endothelial cells. Cell-specific ACE2 expression was validated with primary astrocytes, neurons and endothelial cells. The extreme low ACE2 in endothelial cells suggests crossing blood-brain-barrier route is less likely to account for SARS-Cov-2 brain entry in healthy adults. Alternatively, the retrograde olfactory route could be an option. Olfactory and hippocampus distribution of ACE2 may be related to the common neuropsychological symptoms including anosmia, mood disorder and deeper cognitive impairment. ACE2-positive pericytes and astrocytes near microvessels and ventricles may involve potential cardiocerebrovascular dysfunctions. Finally, the new finding of ACE2 in neurogenic cells may explain the lasting neuropsychological disorders in recovering patients. Taken together, our study highlights a good correlation between ACE2 brain distribution and acute and long-term clinical manifestations, providing new insights into the brain entry and pathogenesis of SARS-Cov-2.

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