The Effect of Imaging Modality on the Selection of Hemodialysis Access Type

Objective: The selection of hemodialysis access type (arteriovenous fistula versus graft) has clinical implications for patients requiring dialysis. Currently, there are no recommendations for the use of pre-operative contrast venography (CV) or intra-operative duplex ultrasound (DUS) as the most effective imaging modality for selection of hemodialysis access type. The purpose of this study was to determine whether intra-operative duplex ultrasound (DUS) changed the selection of hemodialysis access type recommended after pre-operative contrast venography (CV).

Methods: We conducted a retrospective cohort study in which we identified 48 patients who had hemodialysis access creation with intra-op DUS after having had pre-op CV. We determined the percentage of cases in which intra-op DUS changed the selection of hemodialysis access type after pre-op CV and the percentage of cases in which the change yielded the selection of more favorable access types.

Results: Of our 48 patients, 42 (87.5%) had arteriovenous fistula creations while 6 (12.5%) had graft insertions. Intra-op DUS changed the selection of hemodialysis access type in 20 (41.7%) of our patients with selection of more favorable access type in 13 (27.1%) of these patients. Access failed in 4 of these 20 patients with only 2 patients ultimately requiring the access type recommended prior to intra-op DUS.

Conclusions: Our study shows that intra-op DUS changed the selection of hemodialysis access type recommended after pre-op CV and that in most of these cases, intra-op DUS yielded the selection of more favorable access types. Further research is required to establish the most effective imaging modality for the selection of hemodialysis access types.

Connective Tissue Growth Factor: An important extracellular cue in retinal progenitor cell growth and differentiation

The mouse retina is an established model for investigating the mechanisms of progenitor cell proliferation and cell fate specification. During development, multipotent retinal progenitor cells (RPC) give rise to seven major classes of retinal cell types that organize into three layers. The outer nuclear layer contains the cell bodies of the light-sensing rod and cone photoreceptors. The inner nuclear layer contains the cell bodies of various interneurons and Müller glia. Finally, the ganglion cell layer contains retinal ganglion cells (RGCs), which send their axons to the brain. Major efforts have been deployed to develop stem cell-based therapies to replace lost or deficient retinal cells causing blindness. However, transplantation of multipotent RPC or mature cells into the adult retina did not achieve significant integration. Although extracellular matrix (ECM) proteins play significant roles in adhesion, migration, proliferation, and differentiation, their role in RPC differentiation and lineage specification is unknown. This study focuses on the connective tissue growth factor (CTGF), a multimodular ECM protein involved in different cellular and biological events. In this study, we examined the role of this protein in retinogenesis using lineage tracing and mouse genetics. Using a green fluorescent protein (GFP) transgenic mouse under the CTGF promoter control, a proxy for endogenous CTGF expression, we found that the CTGF:GFP signal is dynamic within a subset of RPCs and RGCs. The GFP expression is co-expressed with the molecular markers of these cells (e.g., Sox2, CHX10 and Brn3) at embryonic stage E14. Concordantly, CTGF deletion resulted in reduction of both retinal thickness and cell proliferation and lower levels of RGC and CHX10+ cells compared to wild-type embryos. These data underscore the important role of CTGF, as an extracellular cue, in driving RPC growth and differentiation and possibly retinal tissue regeneration in inherited retinal diseases.
Absorption and Tissue Uptake of Folate Forms in a Rat Model: Implications for the Treatment of Folate Receptor Autoimmune Disorder in Pregnancy and Autism.

Folate is an essential vitamin whose cellular transport is mediated by folate receptor alpha (FR) and reduced folate carrier (RFC) once absorbed in the gut by the proton-coupled folate transporter. The specificity and affinity of the transporters for various forms of folate is thought to influence absorption and cellular uptake. Therefore, the aim of this study is to compare absorption and tissue distribution of folate forms available and evaluate the effect FR antibodies (FRAb) on this distribution. Four forms of folate L-Folinic acid (Fusilev, Levofolinate, LFol); DL-Folinic acid (Leucovorin, DLFol); L-Methylfolate (MTHF) and folic acid (FA) were orally administered (dose 4mg/kg) to adult male rats, GD14 pregnant rats, and PND21 male rats and measured intestinal absorption, maternofetal transport, and brain uptake respectively. Where applicable, pregnant rats received 200ug FRAb IP, 24 hours prior to folate administration and young pups received 100ug of FRAb. Results of tissue absorption in adult male rats showed peak absorption of all folate forms at 1 hour. While half of FA is converted to MTHF by 4 hours, most of LFol and DLFol are absorbed unconverted. In either maternofetal transport and brain uptake, LFol emerges as the form that is better absorbed, transported, and distributed in the presence of FRAb. Currently, pharmacologic doses of DLFol are used in clinical trials to treat children with autism. The D-Form is metabolically inactive, clears slowly, and can interfere in folate dependent reactions. Since LFol transport is via RFC only, LFol appears as the folate form of choice to treat fetal and brain folate deficiency due to FRAb interfering with folate transport. These results support the use of LFol to treat autism and other developmental disorders where FRAb are present and to prevent fetal folate deficiency during pregnancy. The use of LFol to fortify food products would also negate the issue of unmetabolized folic acid.

Tropism and Proliferation of Colon and Pancreatic Cancers Using an in-vivo Zebrafish model

Xenotransplantation in zebrafish embryos has been used in numerous studies to understand how different tumors undergo vascular invasion and localize to specific organs that are analogous to their activity in humans. These studies have been carried out in transgenic zebrafish previously with GFP (green fluorescent protein) labeled blood vessels or specific organs. We aim to create a model of tropism and proliferation of various colon cancer and pancreatic cancer cell lines. We will use fluorescently labeled cells injected into zebrafish embryos that will be followed for 1 week to evaluate early and late metastatic activity using fluorescent microscopy. We will also use immunofluorescence to check various cell markers including Ki-67 to establish area where tumor cells implant and actively divide and compare the various cell lines for qualitative and quantitative differences in tumor metastasis. Using these preliminary studies we aim to develop a transgenic zebrafish model to evaluate specific markers and interactions that are involved tumors that display perineural invasion.
Dynamic Volume Changes of the Brain’s Extracellular Space Underlying Seizures

It has been established that during seizures the brain’s extracellular space (ECS) undergoes a long lasting shrinkage of about 30%, which is likely a consequence of the increased neuronal activity during this pathological state. This shrinkage is believed to help synchronize and excite neurons through amplifying pro-excitatory factors in the brain, such as excitatory neurotransmitters and ions. The problem with these volume measurements of the ECS is that their time resolution is too long to directly detect ECS shrinkage during individual local field potentials. By using a technique called relative volume monitoring (RVM) to continuously track relative changes in ECS volume, we have determined that the ECS undergoes a fast shrinkage of up to 13% (on top of the previous 30%), then slow recovery during each synchronous neuronal discharge that occurs during epileptiform activity. Because these dynamic volume changes (DVCs) of the ECS are likely dependent on the development of osmotic gradients between the intracellular and extracellular compartments, we decided to pharmacologically block channels and transporters that were likely to be involved. This would help us determine if stopping these DVCs is a possible way to stop epileptiform activity. Pharmacological blockade of the NBCe1 transporter, an astrocytic sodium-bicarbonate cotransporter, led to the elimination of both DVCs and epileptiform activity. Based on the effect of blockade, we determined that it was likely because of the elimination of DVCs that the epileptiform activity was halted. Based on these results, DVCs likely represent a force that helps promote excitability and synchrony and therefore may serve as a possible target for seizure treatment.

Renal Cell Carcinoma in Dialysis Patients: Criteria for Transplant Wait List Inclusion

Introduction: End-stage renal disease (ESRD) patients on long-term hemodialysis have higher incidence of renal cell carcinoma (RCC) in their native kidneys than the general population. Most cancer diagnoses require a cancer free period before transplantation. Yet, low-stage RCC (tumors <5 cm) does not, based on the now disproven belief that RCC <5 cm do not metastasize. Histologic subtype and tumor grade are also not considered in the eligibility criteria. Long time dialysis patients, those most likely to develop RCC, are therefore among soonest transplanted. We reviewed our 15-year history of RCC diagnoses and correlated subtype, grade and stage with clinical outcomes for ESRD patients and sporadic tumors. Our intention was to find evidence for or against instituting a watch and wait period for RCC before transplant.

Methods: We reviewed charts and tumor slides for all RCC diagnosed from 2002-2017. Pathologic characteristics assessed were: histologic subtype; tumor size; grade; and staging. Clinical data recorded were: ESRD status; renal failure cause; dialysis time; transplanted or not; immunosuppressive medication; symptomatic or incidental; treatment; and recurrence. 87 patients were identified. Analyses were based on differences between patients with and without ESRD, while correlating tumor subtype, size and grade with patient outcomes. The outcome of interest was recurrence.

Results: There were no differences in tumor staging or grading between ESRD and non-ESRD groups. Yet, further analysis showed overall recurrence was more frequent in higher grade tumors (67% vs. 22%, p=0.038). Among ESRD patients with recurrence, there was increased total dialysis time (18yrs vs. 6yrs, p=0.024). In subanalysis of ESRD patients with clear-cell (CC) histology and <5 cm tumors, recurrence was more frequent compared to non-ESRD patients (33% vs. 0%, p=0.048).

Conclusions: CCRCC subtype should require a wait period before transplant regardless of tumor size at diagnosis.
Florenal Joseph

**YPK9, a homolog of Parkinson’s associated PARK9, has a role in peroxisomal proliferation**

Mutations in ATP13A2, a putative divalent cation transporter located in lysosomes, have been implicated in the aging disorder, Parkinson’s disease. Yeast PARK9 (YPK9), an ortholog of human ATP13A2, suppresses alpha-synuclein toxicity in yeast. The accumulation of alpha-synuclein into Lewy bodies is a hallmark of Parkinson's. We speculated YPK9 loss affects chronological lifespan and oxidants, such as hydrogen peroxide, exacerbates it. We found ypk9 and wildtype growth rates were nearly identical. However, growth was severely impaired and peroxisomes proliferated when ypk9 was treated with hydrogen peroxide. Double deletions of YPK9 and genes regulating peroxisomal proliferation yielded insight into YPK9's role in this process. Together, these results suggest YPK9 negatively regulates peroxisomal proliferation and plays an important role in hydrogen peroxide detoxification.

Erica Griffith

**Modeling Cell Types in the Claustrum**

An unsupervised machine learning classifier was previously used to classify claustrum neurons based on their intrinsic electrophysiological properties, namely the firing patterns and action potential waveforms elicited in response to a sequence of current steps. Here we use this in vitro data to construct in silico models of the major cell types identified by this classifier. Each cell type was modeled with a single-compartment conductance-based model, which used biologically-based current mechanisms to maintain membrane potential and to create spiking behavior. Every model used leak, fast sodium, and slow potassium current mechanisms, while others included additional mechanisms such as M currents that were used to modulate more complex properties such as adaptation. All single-cell models were instantiated using NetPyNE. Each of these models contained several parameters that were optimized in order to replicate certain properties of the cell. These cell properties included subthreshold dynamics, firing rate, and spike frequency adaptation. All parameters were optimized using a multi-objective evolutionary optimization algorithm that employed python’s inspyred module. To optimize the passive parameters, this algorithm explored different parameter combinations, generated simulated subthreshold voltage traces, and directly compared these simulated voltage traces with the experimental traces. To optimize the active parameters, the simulated and experimental F-I curves were compared. In cell types with adaptation, adaptation curves (instantaneous firing rate vs. time) were compared at each current step. In the future, we aim to expand these single cell models to include morphological reconstructions, and to also use these models in conjunction with emerging connectivity data in order to explore network dynamics in the claustrum.
Sphingomyelin synthase gene family has mammalian phospholipase C activity

Mammalian specific phospholipase C (PLC), such as phosphatidylcholine-PLC (PC-PLC) and phosphatidylethanolamine-PLC (PE-PLC), plays an important role in lipid signaling and cell membrane structure formation. The product, diacylglycerol (DAG), is well known as second massager mediating many biological functions. However, so far, the gene(s) which is(are) responsible for mammalian specific PLC activity is not known. We hypothesized that the SMS gene family members have specific PLC activity since they have the ability to do so. SMS family has three members: SMS1, SMS2, and SMSr, they use ceramide with PC/PE to produce sphingomyelin (SM) and ceramide-phosphatidylethanolamine (CPE), respectively. Utilizing both cell lines and specific knock-out mouse models, we indicate that SMS1/2 have PC-PLC activity and SMSr has PE-PLC activity. Furthermore, SMS1/SMS2/SMSr triple deficiency on hepatocytes significantly increase PC and PE levels, whereas significantly decrease DAG levels. Thus, SMS1/2/r genes are responsible for PC-PLC activity, PE-PLC activity, and DAG level. Their biological function deserve further investigation.

Of Mice and Men: Depot Specific Enzyme Differences in Adipose Tissue

Since the identification of the thermogenic role of Brown Adipose Tissue in 1961, it has been understood that adipocytes are not all functionally equivalent. Research has shown that brown, white, and beige fat have different genetic markers and different cells of origin. It is now known that adipocytes have varying morphology depending on the location within the body (known as depots). These differences are implicated in obesity and various metabolic conditions. However, little work has been done to elucidate the molecular basis for these depot differences. Our research focused on two enzymes, Sphingomyelin Synthase (SMS) and Lysophosphatidylcholine acyltransferase (LPCAT3), both of which are integral in synthesis of cell membrane proteins. The integrity of these membranes is vital for signal transduction and regulation of apoptosis. The goal of our research was to assess for the presence of any difference in SMS and LPCAT3 activity in visceral (VAT) as compared to subcutaneous (SQAT) adipose tissue. We VAT and abdominal SQAT samples from humans and mice. We measured enzyme activity using thin layer chromatography (TLC) to determine SMS and LPCAT activity. We used PCR spectroscopy to measure mRNA levels of SMS and LPCAT. TLC consistently revealed differences between visceral, specifically retroperitoneal, adipose and subcutaneous adipose in terms in LPCAT 3 and SMS activity. PCR spectroscopy data similarly showed significant differences in mRNA expression among the various depots. This data not only further demonstrates that adipocytes are functionally distinct in different depots, but also offers a molecular explanation for some of the previously documented morphologic differences.
Aparajita Bhattacharya  
Advisor(s): Jin Montclare  

**Engineering and characterizing a clickable micellar block protein CE2 conjugated to a bimodal fluorescent/PET probe for theranostic applications.**

Theranostic agents are being developed for their ability diagnose disease and improve drug delivery at target tissue site. Traditional chemotherapeutic drug delivery has been inefficient due to factors such as drug insolubility, tissue indiscriminate cytotoxicity, their inability to stimulate release and their lack of direct monitoring. So, we have engineered a nature-inspired smart protein nanofiber-based theranostic agent by rational design from a construct based on COMPcc (cartilage oligomeric matrix protein) and ELP (elastin-like protein), combined to form a block protein called CE2. CE2 has previously been shown to self-assemble into micellar structures and consist of hydrophobic pores in its COMPcc domain, capable of carrying hydrophobic chemotherapeutic drug molecules such as doxorubicin. Its ELP domain imparts the CE2 a thermo-responsive nature. Next, we aim to perform residue-specific incorporation of a non-natural amino acid analog to replace methionine with AHA (azidohomoalanine), to give rise to clickable azide-functionalized CE2 protein. This property would then be used to perform its conjugation to a PET (positron emission tomography) agent named BODIPY leading to a 18F-labeled BODIPY-F1 azide, imparting the compound the added ability to be used as a dual modality PET probe.

After validating the expression of the protein by E. Coli and measuring the incorporation of AHA into CE2 via MALDI-TOF (Matrix assisted laser desorption ionization- time of flight), we have been working on biophysical characterization of the CE2-AHA micelles via CD (circular dichroism), DLS (dynamic light scattering), TEM (transmission electron microscopy). CE2-AHA showed maintenance of alpha-helical structure, sized to be 20-30nm in diameter, that would facilitate their interaction with cells by EPR (enhanced permeation and retention), and their micellar character and size was validated using TEM. These results show that CE2-AHA holds promise for being used as a theranostic agent.

Rachel Irizarry  
Advisor(s): Mark Stewart  

**Seizures induce obstructive apnea in DBA/2 audiogenic seizure-prone mice: lifesaving impact of tracheal implants**

Patients with epilepsy suffer from a higher mortality rate than those without (Becker 2000), and sudden unexplained death in epilepsy (SUDEP) accounts for the majority of deaths during epileptic episodes (Walczak et al. 2001). Previous studies have shown that seizures can induce laryngospasm that leads to a sequence of obstructive apnea, cardiopulmonary dysfunction, and death (Nakase et al. 2016). However, these findings were obtained with anesthetized animals. In this study, we examined whether a novel tracheostomy procedure protected awake mice from fatal audiogenic (not drug-induced) seizures. Sixty-eight animals were implanted with a tracheal T-tube that provided either a closed or an open alternative airway. All animals were then exposed to loud noise to trigger audiogenic seizures, and the outcome “death vs. survival” was recorded. Twenty-seven animals each with either a closed or an open T-tube displayed a tonic-clonic seizure with full hindlimb extension during noise testing. Only one animal with a closed T-tube survived, whereas 13 animals with an open T-tube survived, indicating that the odds ratio for survival was more than twenty times higher with an open T-tube (Fisher's exact test, p < 0.001). Our results support the hypothesis that upper-airway obstruction due to laryngospasm is the proximal cause of death from audiogenic seizures and highlight the importance of airway management during epileptic episodes.
Seizure-associated central apneic responses replicated by nasopharyngeal irrigation induced diving response

The spread of epileptic seizure activity to brainstem respiratory and autonomic regions can elicit episodes of obstructive apnea and of central apnea with significant oxygen desaturation and bradycardia. Previously, it has been argued that central apneic events were not consequences of respiratory or autonomic activity failure, but rather an active brainstem behavior equivalent to the diving response resulting from seizure spread. To test the similarities of spontaneous seizure-associated central apneic episodes to evoked diving responses, we used nasopharyngeal irrigation with either cold water or mist for 10 or 60 s to elicit the diving response in urethane-anesthetized animals with or without kainic acid-induced seizure activity. Diving responses included larger cardiovascular changes during mist stimuli than during water stimuli. Apneic responses lasted longer than 10 s in response to 10 s stimuli or about 40 s in response to 60 s stimuli, and outlasted bradycardia. Repeated 10 s mist applications led to an uncoupling of the apneic episodes (which always occurred) from the bradycardia (which became less pronounced with repetition). These uncoupled events matched the features of observed spontaneous seizure-associated central apneic episodes. The duration of spontaneous central apneic episodes correlated with their frequency, i.e. longer events occurred when there were more events. Based on our ability to replicate the properties of seizure-associated central apneic events with evoked diving responses during seizure activity, we conclude that seizure-associated central apnea and the diving response share a common neural basis and may reflect an attempt by brainstem networks to protect core physiology during seizure activity.

Three Dimensional Reconstruction of the NeuN Stained Carollia perspicillata Hippocampus

With the advancement of optical sectioning techniques, image processing and segmentation, and 3 dimensional (3D) reconstructive techniques, there is an increasing call for 3D representations of histologic data. Here we show a workflow for the 3D reconstruction of NeuN stained hippocampus of Carollia perspicilatta, also known as Seba’s short-tailed fruit bat, and discuss future uses for these techniques. To begin, the animals are perfused with fixative. The brains are carefully removed and further prepared for sectioning. They then are sliced with a microtome generating serial sections that cover the entirety of the brain. Next, the sections are stained using traditional tissue staining techniques. We then image the sections by optical sectioning with the Zeiss LSM 800. Images are processed and segmented utilizing the Matlab extension, Microscopy Image Browser, to process, segment, and register the sections. With this processed data, the NeuN stained hippocampus can be represented in 3D. This example serves to demonstrate the workflow of 3D reconstruction of brain structures. and to display general structural relationships that can be difficult to appreciate when serial sections are analyzed separately. Further applications of 3D reconstructions include the utilization of annotated 3D brain models that allow for the speedy alignment of experimental brain serial sections. Additionally, these annotated 3D reference models offer a way of using software to annotate the anatomy of experimental brain sections, removing a degree of the guess work involved in defining anatomical regions by eye alone. Future work will consist of the continued acquisition of images of serial-sectioned tissue using neuronal and glial markers to classify cell types and characterize their anatomic distributions. Finally, 3D reconstruction of the bat brain will allow for the compilation of histologic findings, creating a centralized framework for analyzing histologic data.
Hyperphosphorylated tau and α-synuclein aggregates coincide with diffuse axonal loss in a mouse model of traumatic brain injury

Traumatic brain injury (TBI) selectively damages white matter and increases the risk of developing neurodegenerative disorders, including Alzheimer’s disease and Parkinson’s disease. Alzheimer’s and Parkinson’s disease are characterized by aggregates of hyperphosphorylated tau (p-Tau) and α-synuclein (α-syn), respectively. Tau and α-synuclein are located in axons and presynaptic termini, respectively. This suggests that the white matter injury produced by TBI may produce subsequent changes in p-Tau and α-syn. We have begun testing this hypothesis by isolating parasagittal brain sections from C57BL/6 mice 14 days after experimental closed head injury. p-Tau and α-syn were identified by immunohistochemistry and axons were visualized by Bielschowsky silver stain. Injured mice (n=5) exhibited more axonal loss and greater levels of p-Tau and α-syn than sham-injured controls (n=3). This was noted in multiple brain areas, including the following: the cortex adjacent to the impact site, the hippocampal CA2 region, the cingulum, the ventral striatum, and the basal forebrain. These results suggest that markers of neurodegeneration coincide with diffuse axonal injury. Our laboratory previously showed that the drug combination of minocycline and N-acetylcysteine prevents white matter injury after TBI (Haber, et al., 2017; Sangobowale, et al., 2017; Sangobowale, 2018). We are currently evaluating if these treatments also prevent the emergence of p-Tau and α-syn after closed head injury.

Minocycline and N-acetylcysteine improves behavioral outcome, dendritic integrity, and Protein Kinase Mz levels when first dosed 72 hours after experimental traumatic brain injury.

Traumatic Brain Injury (TBI) produces long-term deficits in cognition and memory. There are currently no drugs to treat TBI, in part, because drugs lose potency as the time to first dose increases. The Bergold laboratory previously showed that the drug combination of minocycline plus N-acetylcysteine when first dosed 72 hours post-injury (MN72) allows mice to acquire Barnes maze when tested at either 14 or 60 days post-injury (DPI). Acquisition of Barnes maze requires one functioning hippocampus; previous studies also showed that MN72 restores long-term potentiation, a process that is needed to acquire Barnes maze, only in the hippocampus contralateral to the injury site. MAP2 and PKMz are two key proteins needed for long-term potentiation. We therefore examined the time course of MAP2 and PKMz after injury to see if MN72 alters their expression. Injured mice treated with saline or MN72 had a rapid loss of MAP2 or PKMz expression in the hippocampus ipsilateral to the injury site that remained low up to 60 DPI. MN72-treatment increased MAP2 expression in the contralateral hippocampus to sham-injured levels by 14 DPI while saline-treatment increased MAP2 expression only by 60 DPI, suggesting that MN72 accelerated the recovery of MAP2 expression. Injured animals treated with either saline or MN72 reduced PKMz expression at 3 and 7 DPI in the contralateral hippocampus. At 14 and 60 DPI, MN72 increased PKMz expression while saline treatment did not increase expression. Restoration of PKMz expression suggests that MN72 regulates key proteins that may improve deficits in synaptic plasticity, cognition and memory produced by head injury. Notably, these therapeutic effects occurred with drugs dosed in a clinically relevant time window to treat TBI.
Matthew Evrard  Advisor(s): Sheryl Smith

α4βδ GABAA Receptors Initiate AdolescentSynaptic Pruning of the Medial Prefrontal Cortex

The medial prefrontal cortex (mPFC) is the anatomical substrate for higher cognitive functions including behavioral flexibility and working memory. Clinically, abnormal higher cognitive functions are implicated in neuropsychiatric disorders of mood or anxiety that typically emerge during adolescence. During normal adolescent development, the brain undergoes a significant reduction of dendritic spines, which are compartment-like structures representing the excitatory post-synaptic terminal, which can disrupt normal function. Previously, our lab has shown that the pubertal expression of α4βδ GABA-A receptors (GABARs) initiates synaptic pruning (Afroz et al., 2016). This study looked to see if the same mechanisms were also required for synaptic pruning in layer 5 of the prelimbic cortex (PL; rodent correlate of the mPFC). We used Golgi staining to assess spine density comparing pubertal (P35) vs. post-pubertal (P56) mice. Spine density quantification and morphological subtyping were analyzed using Neurulucida 360. Spine density decreased across adolescence (~40% in females and ~50% in males) with mushroom spines showing the greatest decrease. Next, to test the role of α4βδ GABARs we assessed the pubertal expression of the α4 subunit using immunohistochemistry and confirmed the functional expression through whole cell patch clamp recordings. There was a 3-fold increase in the pubertal expression of α4 and a 4-fold increase in the holding current as a response to gaboxadon (GABA agonist selective for the α4βδ GABARs at 100 nM). Finally, to establish the role of pubertal α4βδ GABARs, we compared spine density and subtypes from post-pubertal wild-type to α4 knock-out mice. Post-pubertal densities were significantly higher in α4 knock-out mice when compared to wild-type and did not significantly differ from the pubertal wild-type densities. Taken together these data suggest that synaptic pruning in PL layer 5 is initiated by pubertal expression of α4βδ GABARs.

Benjamin Tessler  Advisor(s): Steven Fox

Optimizing Transcranial Electrical Stimulation in a Rat Model

Hippocampal theta is the largest amplitude rhythmic local field potential (LFP) in the mammalian brain. It is often associated with learning and memory due to its involvement in the timing of place cell firing. In the literature, anti-epileptic effects have been seen during theta with a dramatic reduction of epileptic discharges. Transcranial electrical stimulation (tES) techniques may provide for an advantageous method to elicit or modulate theta at low-cost and low-risk, allowing it to be easily translatable. In our lab, we tested tES methods that optimize the injected currents to target the CA1 of the hippocampus in a rat model. With 3-D reconstructions generated from MRI data that are inserted into powerful physics solvers, various electrode placements are iterated through to maximize the ratio of electric field intensity in the CA1 relative to the rest of the brain. We then validate these results by using phantom models of cleaned rat skulls filled with agar that has NaCl concentrations appropriate for the equivalent brain electrical conductivity. We have found our physics simulation results to be comparable to our phantom model results. One of the tES methods we tested is intersectional pulsing (ISP) stimulation, which is proposed to focus electric fields on deep targets by a rotation of the bipolar current injection. However, we have found ISP electric fields to be equal to the equivalent electrode placements without any rotation. The optimal tES method we have validated is temporal interference (TI) stimulation that uses two pairs of electrodes, one injecting a current of slightly higher frequency than the other causing an amplitude maximum at the difference frequency near the midline of the two pairs, thus properly targeting deeper structures. These results will guide us and other researchers to maximize the efficacy of their tES techniques when attempting to modulate neuronal oscillations of deep structures.
Veronica Sebastian  
Advisor(s): Todd Sacktor

**Hippocampal PKMzeta expression decreases with age in the APP/PS1 model of Alzheimer’s disease**

Alzheimer’s disease (AD) is a neurodegenerative disorder, which results in severe cognitive and behavioral deficits characterized by progressive memory loss. Over 5 million Americans currently suffer from AD, with an estimated 13.8 million cases projected by 2050. One possible mechanism that could explain the memory deficits seen in AD is disruption of PKMzeta expression. PKMzeta is a persistently active atypical PKC isoform that is specific to the nervous system and necessary for maintaining long-term memory. Work in our lab has shown an age-dependent decrease in PKMzeta expression in the dendrites of CA1 neurons in the APPswe/PSEN1dE9 model of AD, which shows hippocampal overexpression of amyloid-beta in cell bodies starting at 3 months and formation of amyloid plaques at 6 months. We also see abnormal increased PKMzeta expression in non-neuronal cells, which strongly co-localizes with the astrocytic marker, glial fibrillary acidic protein (GFAP). These results suggest that atypical PKCs may play a dual role in AD, involving both loss-of-function in neurons and excessive signaling in astrocytes, which may be related to astrogliosis and glial activity affecting neuronal function.

Michael Tekin  
Advisor(s): Sheryl Smith

**Sex differences in synaptic pruning of dendritic spines of mouse primary motor cortex at puberty**

The primary motor cortex (M1) is essential for motor learning. Adolescent synaptic pruning is necessary for optimal learning, yet pubertal synaptic pruning of basilar dendrites in layer 5 (L5) of M1 is not fully understood. Because gender differences in motor learning and motor flexibility are reported after puberty, I compared synaptic pruning in M1 L5 of male and female mice. Golgi staining was used to assess spine density/types in each group from z-stack projection (0.3 Åm) photomicrographs taken with a Nikon DS-U3 camera mounted on a Nikon Eclipse Ci-L microscope using a 100x oil objective. Spine density across the basilar dendrites (proximal, medial and distal segments) was compared using pubertal and post-pubertal (P35 vs. P56) mice. Using a Student T-Test, we found no significant difference in total spine density between P35 and P56. In female L5 there was a significant decrease in proximal mushroom spines (P35=0.574±0.065 spines/10 Åm, P56=0.258±0.054 spines/10 Åm, P<0.05), and an increase in proximal thin spines (P35=1.06±0.10, P56=1.55±0.18, P<0.05) and proximal long thin spines (P35=0.528±0.080 spines/10 Åm, P56=1.01±0.140 spines/10 Åm, P<0.05). In male L5, mushroom spine density did not change, but there was a significant increase in proximal thin spines (P35=1.45±0.40, P56=2.63±0.19, P<0.05). The increase of thin spines was significantly more in males (M) than females (F) (M=1.27±0.09 spines/10 Åm, F=0.49±0.24 spines/10 Åm, P<0.05), the increase of long thin spines was significantly more in females (M=0.21±0.08 spines/10 Åm, F=0.48±0.07 spines/10 Åm, P<0.05), and the decrease in mushroom spines was significantly more in females (M=0.10±0.06 spines/10 Åm, F= -0.32±0.03 spines/10 Åm, P<0.05). These results suggest that selective pubertal pruning of proximal mushroom spines in M1 L5 pyramidal cells exist in female mice but not in male mice and differences in thin and long proximal spine formation exist between male and female mice.
New ribosomal RNA expression is required during re-consolidation of memory

Long-term memories can be usually found in two different states. A labile state that happens right after the initial acquisition (of the memory) or during memory recall, and a stable state that happens after the labile state in the initial acquisition or after a recall. The initial transition from labile to a stable state after learning is called consolidation, whereas the stabilization after a recall is called reconsolidation. The purpose of such labile state after a recall is to update the original memory. It has been well studied that new protein synthesis and gene expression (Kandel, 2001) are required during consolidation and reconsolidation (LeDoux JE 2011) of memory. Most efforts to understand experience-induced changes in neuronal gene expression have focused on the transcription products of RNA polymerase II (Pol II)—primarily mRNAs and the proteins they encode. While there has been significant progress in identifying the Pol II-dependent transcripts (primarily mRNAs) required for early phase long-term synaptic plasticity, the gene products responsible for late-phase and maintenance remain elusive. In contrast, the transcription products of RNA polymerase I (Pol I), responsible for producing non-(protein) coding ribosomal RNA, have been left unexplored despite the fact that Pol I transcription constitute more than 50% of nascent RNA synthesis in a cell. Without rRNA synthesis, new ribosomes cannot be made. We recently showed that new ribosomal RNA expression (therefore new ribosomes) are necessary for consolidation of memory. We ask does reconsolidation also require rRNA expression and the synthesis of new ribosomes?

In order to approach this question, we have specifically blocked polymerase -1 activity (ribosomal RNA synthesis) before the recall and assessed whether this inhibition affects memory after a second recall. Our data suggest for the first time that new ribosomal RNA expression (therefore new ribosomes) are required for memory reconsolidation.
### Engineered Protein-Lipid Hybrid Nanomaterial For Cutaneous Gene Therapy

Gene therapy has the potential to treat various diseases of the skin, including chronic wounds associated with diabetes. However, a vehicle capable of delivering nucleic acids across the many layers of the skin does not currently exist. We have recently developed a lipoproteoplex (LPP) consisting of a super-charged coiled-coil protein (CSP) and a cationic liposomal carrier, that has the ability to condense nucleic acids and deliver them trans-dermally in-vivo. A CSP variant known as N8 has been rationally designed to improve the efficacy of the LPP compared to the parent protein via increased nucleic acid binding. The physical properties of the N8 LPP have been probed using dynamic light scattering, zeta potential measurements and transmission electron microscopy in order to see the effect the new protein variant has on the assembled vehicle. The N8 LPP maintains optimal size and charge for cellular transfection while having an increased ability to condense siRNA, leading to higher transfection efficiency.

### Interdisciplinary Education Module for Early Intervention Team for Academic Partners

The Early Intervention (EI) interdisciplinary education module combines the knowledge between the New York City (NYC) academic partnerships in various professional fields in order to enhance their expertise in collaborating effectively. The information from our module can be implemented not only in NYC, but in other areas of the country. The module will assist members in gaining the skills they need to be an adequate team member amongst participants at the American Occupational Therapy Association (AOTA) conference. The EI module supports the importance for professionals to integrate and coordinate interventions for better treatment. Within these module sessions, AOTA participants will understand roles in EI, effective collaboration, team building strategies, the individualized family service plan (IFSP), and a final session that encompasses all topics. In addition, activities will be provided within each of the five modules for members to have the opportunity to interact with each other and share their knowledge acquired throughout the sessions. Even though the module is about EI, many AOTA members can benefit from the use of this training as it can be effective in various areas of occupational therapy.
Babies’Transition From the NICU to Home: Clarifying Occupational Therapist’s Role in the Process

Occupational therapists (OTs) play an integral role in the Neonatal Intensive Care Unit (NICU) multidisciplinary team during the transition process from the NICU to home. In many instances, parents with babies in the NICU independently acquire the knowledge necessary to manage and advocate for their child’s ongoing needs after leaving the NICU. Parents often state they do not receive adequate support in the NICU and even less once they leave the hospital, leading to feelings of incompetence in their ability to care for their baby at home.

There is limited amount of literature regarding the OT’s role in transitioning parents and babies to home. The poster will present information from semi-structured interviews that were conducted to gain insight into the personal experiences of parents in the NICU, specifically regarding their preparedness to transition their baby home from the hospital. The data collected were used to analyze the factors that influence the transition process, and to begin defining the OT’s role in preparing a family's transition from the NICU to home.

Responses revealed the need for additional support and education during the transition from the NICU to home. Expanding on that, confidence was seen to be influenced by how much support parents were provided. It is clear that there were opportunities for OTs to address certain challenges parents faced when transitioning their baby home from the NICU. The findings gathered from this study contribute to the existing literature on the OTs role in transitioning a family from the NICU to home and informs the NICU community how the OT contributes to this process.

Effectiveness of a Multimodal Fall Prevention Program for Older Adults

Falls are a prevalent issue among older adults that affect performance in daily activities. The Easy-Does-It Falls Prevention, occupational therapy-based program was a quality assurance review aimed at helping participants in a group decrease their risk of falling, fear of falling, and increase their overall mobility confidence. The group was designed for adults aged 65 and older and combined education with physical activity. This taught participants strategies to improve their strength, balance, function and confidence. The sessions also incorporated movements which could be applied to activities of daily living. For example, activities include vacuuming, reaching for objects overhead, weight shifting to open heavy doors, maintaining balance on a public transportation as well as functional mobility. Essentially, the weekly sessions helped adults maximize their functions and fulfill their roles in daily life. Additionally, they emphasized the importance of body awareness while performing these occupations. The program was multi-modal, incorporating yoga, tai chi, Feldenkrais, breathing, and meditation. Feldenkrais involves slow motions and helps people develop body awareness during their daily functional activities. These movements assist people to advance their thinking, self regulation and organizational skills (1). The overall goal of this quality assurance review was to examine whether combining traditional techniques (e.g. yoga, tai chi), which have been proven to decrease fall risk, were effective when utilized as one comprehensive educational program (2). The results of this quality assurance review supplements current research on the impact of environmental, behavioral, and physical factors of fall risk and confidence among the older population.
**Group Role Play: Introducing Group Roles to OT Students**

Effective group counseling training is imperative for future OTs as activity-based group interventions continue to be an integral tool in OT mental health settings. A study demonstrated the following to be most helpful group counseling learning methods in graduate programs: group counseling practice, observation and supervision of group leadership, experiential group participation, and academic instruction. In particular, participants appreciated viewing other groups and conceptualizing the situations that can occur (1). Understanding the group roles that members take on during sessions provides valuable information to the OT, by allowing the therapist to help members develop goals, evaluate progress and outcomes, and gain meaning from the group dynamics. It will also allow the therapist to facilitate members’ reflection on behaviors and possible consequences (2). This poster will review a student-developed educational video of an activity-based group session to introduce the concept of group roles to OT students. Occupational therapy educators can utilize this video in their group theory curriculum to allow students to identify, analyze and understand functional, maintenance, and self-serving member roles that can be observed during group therapy.

**Analysis of Burnout Experienced by Occupational Therapists Employed within a Physical Disability Setting**

The purpose of this pilot study was to analyze the relationship between staff support and burnout experienced by occupational therapists (OTs) working in physical disability settings. Burnout syndrome is defined as a constellation of symptoms that occurs without any prior history of psychological or psychiatric disorders1. A longitudinal cohort study was performed in 2002 discussed how changes in healthcare facilities impacted therapists’ feelings of job satisfaction and methods used to cope2. Another cross-sectional survey was conducted on psychosocial factors that influence burnout amongst OT professionals3. OTs often work in settings with high clinical demands and minimal institutional support, and yet limited research exists that provides data correlating these factors with burnout. When conducting this study, specific inclusion criteria was utilized to select candidates, such as 1-10 years experience working in a physical disability setting and being an alumnus of SUNY Downstate Medical Center’s OT program. The analysis revealed that 72% of all respondents reported having greater than 5 types of staff support available within their facility. 76% of these participants experienced burnout, and 52%, attributed this burnout to lack of adequate staff support. This pilot study was unable to provide statistically significant correlations between burnout and the amount of staff support received within a physical disability setting. This study did, however, show that therapists believe that multiple factors may contribute to their symptoms of burnout.
Establishing an Implicit Bias Component within the SUNY Downstate Cultural Competence Education Module

The OT Program at SUNY Downstate is establishing a cultural competence module intended to educate students on the importance of cultural competence. This project’s purpose is to fill the gap within the module specifically addressing implicit bias. Twelve individuals were chosen at random and interviewed about personal client factors and activities of daily living as described in The Occupational Therapy Practice Framework 3rd Edition. First year OT students were then asked to complete an online module addressing implicit bias which consisted of a pre and posttest measuring levels of implicit bias (Implicit Association Test [IAT] ‘Gender-Career’) and three matching quizzes that were based on the responses of the interviewees. A class discussion was held and mindfulness was introduced to increase awareness of implicit bias. Based on a 2x3 contingency table chi square analysis of pre and posttest IAT scores, it was determined that there was no statistically significant correlation between administration of the proposed implicit bias cultural competence module and IAT pre and post-test scores. Qualitative feedback indicated the perceived usefulness of the class discussion and module. Further research is needed to determine the effects of the cultural competence module on implicit bias, as the sample size was small (pre-test n=23; post-test n=13).

Systematic Review of Short Thumb Spica Orthoses to Determine Best Practice Design for Individuals with Dual Diagnoses of Systemic Lupus Erythematosus and Carpometacarpal Osteoarthritis

Systemic lupus erythematosus (SLE), the most common type of lupus, is a chronic autoimmune disease affecting various parts of the body including skin, organs, and joints. Osteoarthritis (OA) is a degenerative joint disease that affects the cartilage of joints, particularly the hip, knee, and hand. Painful, swollen joints, particularly in the CMC joints of the hand, are a common symptom of both SLE and OA, which can result in a disruption of daily function. Objective: This systematic review explored articles published between 2008-2018 that compare various thumb spica orthotic designs in order to explore best practice design for those with dual diagnoses of SLE and thumb CMC OA in terms of pain reduction and increased hand function. Method: We analyzed 12 research articles that considered at least one orthotic design for individuals with CMC OA of the thumb, in terms of pain reduction and hand function. Articles were evaluated based on level of evidence and PEDro score. Results: Orthoses that are more rigid and restrictive tend to be more effective at reducing pain than their softer, less restrictive counterparts. Rigid orthoses tend to be less effective in the areas of hand function and patient preference; patients typically preferred less restrictive orthoses due to the greater amount of mobility, hand function, and comfort. Conclusion: Short thumb spica orthoses are effective in decreasing pain and improving hand function in individuals with CMC OA of the thumb; however, there is no evidence to support the effectiveness of different orthotic designs in individuals with dual-diagnoses of SLE and CMC OA. Due to the prevalence of CMC OA of the thumb in women with SLE, it is imperative to explore the multiple types of thumb spica orthoses that may benefit this population.
Ultra-large field-of-view two-photon imaging of primary visual cortex foveal region in non-human primates

In the past decade, novel microscopy methods and genetically-encoded sensors have been revolutionary to understanding neural circuits in rodents and invertebrates. Using these methods in non-human primates (NHPs) has proven difficult due to technical hurdles that are being overcome. NHP advances have brought the technology closer to use in humans, such as with high-quality cortical imaging windows that are both larger than an entire mouse brain allowing unprecedented ultra-large-scale circuit analysis that remain patent for years (periods longer than a mouse's entire lifespan), allowing for long-term all-optical interrogation of neural circuits over a time period relevant to human cognitive development. Here we show a new method for multicolor labeling of neurons in macaque area V1. We present a novel procedure for precise, deep brain injections using neurosurgical navigation without live imaging sources. We transfected cells using cortical and thalamic convection enhanced delivery (CED). The target for injections was pyramidal neurons in the primary visual cortex (V1), as well as in the lateral geniculate nucleus (LGN). Adeno-associated viruses (AVVs) encoding for 5 different fluorophores with nonoverlapping emission spectra were injected along with a GCaMP6/jGCaMP7 transgene. We transfected LGN neurons with the ChR2 optogene tagged with YFP. To image the cells, a Bruker Ultima IV two-photon imaging microscope with a MaiTai DeepSee Ti:Sash laser illuminated the cortex with a wavelength of 730 nm. To capture an entire 2-cm diameter imaging window, we tiled the window with 49 (7 x 7) 500 µm deep z-stack scans of 2.8mm on a side. We stitched the z-stacks into a single image to visualize the whole imaging window and performed a cell count with a total cell count of ~200,000 cells. Spectral analysis reveals that about 20% of the cells expressed a single-colored transgene, whereas about 80% had 2 or more multi-colored transgenes stochastically arrayed.

Evidence for decreased nucleolar PARP-1 as an early marker of cognitive impairment

Poly(ADP-ribose) polymerase-1 (PARP-1) is a nuclear protein that regulates gene expression through poly(ADP)-ribosylation, resulting in the loosening of chromatin structure. PARP-1 enzymatic activity has been shown to be necessary for the expression of several genes required for memory formation and consolidation. Previously, we showed that nucleolar PARP-1 is significantly decreased in hippocampal pyramidal cells in Alzheimer’s disease (AD). We proposed that the displacement of PARP-1 from the nucleolus results in downregulation of new rRNA expression and ribosome biogenesis, leading to cognitive impairment. To further investigate the relationship between nucleolar PARP-1 and memory impairment, we examined PARP-1 expression in the hippocampus of individuals with mild cognitive impairment (MCI) compared to control and AD cases. We used immunohistochemical techniques to examine the nuclear distribution of PARP-1 in the Cornu Ammonis (CA region) of the hippocampus. PARP-1 positive cells were then scored for the presence or absence of PARP-1 in the nucleolus. We found a significant decrease of PARP-1 staining in the nucleolar compartment of hippocampal pyramidal cells in MCI compared with Control and AD. When the four CA (CA1-4) regions were considered separately, only the CA1 region showed significant differences in nucleolar PARP-1 with Control > AD > MCI cases. In addition, measurements of the diameter of nucleolar PARP-1 positive cells in CA4 shows Control > MCI. Thus, MCI cases have lower percentage of PARP-1 nucleolar positive cells and smaller nucleolar diameter in CA1 and CA4 respectively, compared to Control and AD. Our data suggests that disruption of nucleolar form and function is an early and important step in the progression of cognitive impairment.
Histologic features of a rare disease, sialodochitis fibrinosa and its differentials

Kussmaul reported first case of sialodochitis fibrinosa in 1879, also known as Kussmaul Disease. The characteristic features of the disease are recurrent major salivary gland swelling, eosinophil-rich mucus plugs, and intense periductal eosinophilic infiltrate with peripheral blood eosinophilia. The patients often have atopic disease such as asthma, eczema, or seasonal allergy. Although over a century passed, due to lack consistent diagnostic terminology and uniform diagnostic criteria, there are only limited cases reported in English literature. A recent review recommended to use “eosinophilic sialodochitis” as diagnostic terminology to replace “allergic parotitis”, ‘sialodochitis fibrinosa’ and many other terminologies that may have been used in literature to designate the same condition such as chronic sialodochitis with eosinophilia, sialodochitis with eosinophilic inflammation, idiopathic bilateral salivary megacanal, idiopathic eosinophilic parotitis and Kausmal disease. In view of these heterogeneous names, likely reflect that the condition may be underrecognized. Due to rarity of the disease and surgical removal of gland is not primary choice of treatment modality, detailed pathologic studies are sparse. We happen to receive a specimen of right submandibular gland resection in a patient meets newly proposed diagnostic criteria for eosinophilic sialodochitis and are able to have detailed histologic picture of the condition. This case is presented as below.

KRAS Mutation, But Not Mismatch Repair Deficiency, Occurs with Increased Frequency in African American Patients with Colorectal Cancer and Predicts Poor Disease-Free Survival

The incidence and mortality of colorectal cancer (CRC) are higher in African American (AA) patients than white patients. Although socioeconomic factors are involved in this racial disparity, biological differences in CRC in different racial groups remain unelucidated. Deficient Mismatch Repair (dMMR) function has been linked to a better prognosis in CRC. KRAS mutation, another biomarker, predicts a poor response to EGFR inhibitor therapy. Here we compared profiles of KRAS mutation and MMR status in AA and white patients, and evaluated their prognostic value in CRC. All CRC cases tested for MMR (n=75) or KRAS mutation (n=110) from 2009 to 2017 at our institution were included in this study. Clinicopathologic variables were recorded for these cases. Chi-square test was used to analyze MMR status and KRAS mutations in different racial groups. Univariate survival analysis was performed with Kaplan-Meier method. Multivariate Cox regression was used to predict hazard ratio (HR) of MMR status and KRAS mutations. Due to limited size of white patient group in our study, we also utilized published data of white patients. There is no significant difference in MMR status between AA and white patients. dMMR is associated with better disease-free survival (DFS) in AA patients with CRC by univariate analysis (p=0.05). However, after adjusting for other factors by multivariate analysis, DFS in AA was not affected. Frequency of KRAS mutation was higher in AA than white patients (57% vs. 21%, p<0.001). Amongst subtypes of KRAS tested, codon 12 mutation was more frequent in AA (85% vs. 69%, p=0.02). KRAS mutation is a significant predictor of poor DFS in both AA (HR=4.67, p<0.001) and other racial groups (HR=4.18, p=0.001). KRAS mutation is strongly associated with poor DFS in CRC in all racial groups. Since frequency of KRAS mutations is higher in AA than white patients, it most likely contributes to their increased mortality.
A case of a child with coexisting growth hormone deficiency and hypophosphatasia: a therapeutic dilemma

Introduction: While growth hormone deficient-short stature is not an uncommon childhood-disorder, hypophosphatasia (HPP) is a very rare inborn-error-of-metabolism. HPP is characterized by abnormal mineralization of bone and dental tissues, caused by loss-of-function mutation(s) in the gene that encodes the tissue-nonspecific isozyme of alkaline phosphatase. Childhood HPP is widely variable clinically ranging from isolated premature shedding of deciduous teeth to physical and radiographic evidence of low bone mass, rickets and musculoskeletal manifestations. Enzyme replacement therapy (ERT) has been proven very effective in the treatment of patients with perinatal and infantile forms of HPP.

Case report: A twelve-year-old, male presented at the age of nine years with short stature. Growth hormone (GH) stimulation test was performed with the highest peak of 3 ng/ml, consistent with GH deficiency. Additionally, he was found to have consistently low serum alkaline phosphatase levels, and high serum vitamin B6. Plain x-rays of long bones showed under-mineralization; however, he had no past history of rickets, non-traumatic bone fractures, or dental problems. Past history was significant for well controlled celiac disease and traumatic fracture of the right small middle phalanx after a high-impact sports injury. Family history is significant for asymptomatic low serum level of ALP and high serum level of vitamin B6 in his mother. He was started on growth hormone replacement with improvement in growth velocity and increased serum levels of ALP and vitamin B6.

Conclusion: After review of current literature, HPP in a patient with GH deficiency has not been reported before. Treatment with GH replacement in a patient with co-existing bone mineralization defect raises the concern of potential orthopedic side effects. It is unclear whether ERT should be considered in this case given that, currently, he is growing at a normal percentile and does not exhibit any symptoms of HP.

Diabetes distress is associated with diabetes control in minority adolescents

Diabetes Distress (DD) describes emotional stress and difficulties coping with the daily burden of diabetes due to frequent blood sugar monitoring, administering insulin, pump use and carbohydrate counting. We aimed to determine the risk of DD in adolescents with diabetes (type 1 and 2) in our population and determine its association with glycated hemoglobin (A1C). We screened for DD in patients, 11-21 years old, with diabetes for more than 1 year, requiring insulin. A validated screening tool for DD, PAID-T© for ages >12 years or PAID-C© for ages 11-12 years was given to patients at their regularly scheduled endocrinology follow-up. Patients with positive scores of ≥ 44 on PAID-T or ≥ 44.6 on PAID-C were referred to mental health specialists for counseling. A1C was measured every 3 months. The groups were divided into positive distress (PD) and negative distress (ND). Statistical analysis included t-tests, Spearman correlation and linear regression modeling. A total of 34 patients were enrolled. Fifty percent of the group had DD. Baseline characteristics were similar between the two groups (age, ethnicity, diabetes type, pump vs MDI use, A1C). The mean (SD) DD score was 58.5 (9.37) in PD vs 27.3 (9.7) in ND (p<0.005). Mean A1C was 11.7% (2.85) in PD vs 10.3% (2.23) in ND (p=0.11). The correlation between DD and A1C was statistically significant (r=0.36, p=0.03) which was even more significant after eliminating outliers (r=0.52, p=0.002). Linear regression analysis to predict A1C using DD score was significant (beta coefficient =0.05). We found 50% of our group of minority adolescents with insulin dependent diabetes had DD. A significant positive correlation was found between DD score and A1C. Routine screening for DD with validated screening tools and early referral for counseling could potentially improve glycemic control of those having significant distress.
**The Effect of Hydroxyurea on Hemoglobin A2 (HbA2) Concentration in Children with Sickle Cell Disease**

Background: Sickle cell disease is due to a single mutation in the beta-globin gene that results in the production of sickle hemoglobin (HbS). In settings of low oxygen tension, HbS polymerizes, causing a change in the red blood cell (RBC) shape known as “sickling.” Sickling of RBCs is a major contributor to the sequelae of this disease, including chronic hemolytic anemia, vaso-occlusive crises, vasculopathy, and damage to organs. In 2017, Hydroxyurea (HU) received approval from the FDA to treat sickle cell disease (HbSS) in the pediatric population. Hydroxyurea increases the concentration of fetal hemoglobin (HbF), which inhibits HbS polymerization. Hemoglobin A2 (HbA2) also inhibits the polymerization of deoxy-HbS and, unlike HbF, is present in all erythrocytes.

Objectives: To compare HbA2 levels in pediatric patients with HbSS and HbS/beta0-thalassemia pre- and post-HU therapy, and to determine whether elevated HbA2 is correlated with changes in other hematologic parameters.

Methods: A retrospective cohort study of 46 children aged 9 months to 21 years with HbSS or HbS/beta0 thalassemia who were on HU for more than 6 months. Data were collected from UHB and KCHC. We used paired t-test to analyze HbA2 level concentration pre-HU therapy and post-HU therapy when the therapeutic goal had been achieved (defined as HbF ≥ 15% with ANC 1.5-4K/ul and/or ARC 100-200K/ul). Spearman correlation coefficients were used to determine the associations of HbA2 levels with hematologic parameters of hemoglobin (Hb), MCV, WBC, ANC, and HbF.

Results: There was a significant increase in HbA2 levels after treatment with HU (p=0.006). However, this elevated HbA2 level did not significantly correlate with changes in the other hematologic parameters examined.

Conclusions: Hydroxyurea increases HbA2 in addition to HbF in children with sickle cell disease. Elevation of HbA2 provides another explanation as to how hydroxyurea attenuates the complications seen in sickle cell disease.

**Placental Abnormalities Affect Fetal Development**

**Dee-Anne Cush, CUNY John Jay College; Hongjie Li, MD, Ph.D.; Virginia M. Anderson, M.D.,**

Introduction Fetal loss causes complicated grief. Understanding the cause for miscarriage helps families, and provides guidance for future pregnancies. Placental insufficiency leads to a failed pregnancy often complicated by rupture of the fetal membrane or placental abruption. Dysmorphic features of the fetus and chorionic villi reflect a genetic problem as the root cause for the perinatal loss. Retroplacental hemorrhage occurs in abruption. Normal villi occur with abruption, funisitis, or chorioamnionitis. Objectives Fetal dysmorphic features and placental abnormalities occur in pregnancy loss. An under-perfused placenta with abnormal chorionic villi occurs in genetic disease. The root cause of perinatal loss requires careful dissection of the fetus, placenta and medical record review.

Methods Fetal weight, placental weight, gross malformations and placental abnormalities were analyzed in 34 fetopies. Large hydropic dysmorphic avascular villi, trophoblastic inclusion cysts, and caps within villi were associated with malformations. Results 34 fetopies, 23 had large hydropic dysmorphic avascular villi, 10 had trophoblastic inclusion cysts and 3 had caps. Fetal findings included 15 with gross malformations of the midface, hands and feet. Ten fetuses had normal placentas; 7 with normal midface, hands or feet; 3 fetuses had facial abnormalities. Brain growth reflects facial development. Five nuchal blebs were seen with dysmorphic villi. 70% of the fetuses were either too small or too large suggests placental based fetal growth failure in small for date cases, or fetal hydrops in large fetuses.

Conclusion Abnormalities identified early in pregnancy relayed to the parents influences clinical decision making. Nuchal bleb is associated with hydropic dysmorphic villi. Facial abnormalities reflect brain development. Fetal expected weights vary drastically from normal weights in abnormal fetuses.
Intravenous Methylprednisolone vs Intravenous Methylprednisolone combined with inhaled Budesonide in Acute Severe Asthma in Children

Rationale for the study: Previous studies suggested that budesonide nebulization along with oral Prednisolone was effective in reducing admission rates in acute wheezing episodes in preschool children. Hence, we wanted to study for similar effects of use of inhaled budesonide in children admitted to pediatric intensive care. Hypothesis: Adding inhaled Budesonide to systemic steroids will lead to a reduction in the duration of continuous β-2 inhalation therapy, need for mechanical ventilation, pediatric intensive care (PICU) hours, and overall length of stay in children aged 1-18 yrs admitted with acute severe asthma. Study design: In a randomized controlled trial, we enrolled children aged 1-18 years who were admitted to PICU for acute severe asthma. Children with cardiovascular disease, neurological disease, neoplastic disease, renal disease or pregnancy were excluded from the study. Patients were randomized for treatment allocation into two groups using block randomization of 2. Group-A received only intravenous Methylprednisolone 2mg/kg/day (IV MP) and Group-B received Budesonide nebulization 0.5 mg/kg every 12 hrs as well as IV MP. Results: We enrolled 25 patients in each group. There was no statistical difference between the two groups in relation to prior use of inhaled corticosteroids, maximum oxygen requirement and need for mechanical ventilation. Number of past hospitalizations was higher in Group A (mean 4.1 vs 1.92, P-0.004). The mean duration of hours of continuous albuterol treatment in PICU (42.28 vs 33.56 P-0.24), length in hours of PICU stay (58 vs 43.6, P- 0.07) and total length of stay in hours (82 vs 71.2, P-0.06) was lower in Group B but was not statistically different. Conclusions: In our study, addition of inhaled steroids to systemic steroids in acute severe asthma showed a trend towards reduction in the mean duration of hospital and PICU stay, but not statistically different. Larger studies are recommended.

The Effectiveness and Challenges of the ASD Screening Program in the SUNY Downstate Pediatrics Clinic

Rationale: According to the CDC, 1 in 59 children are identified with Autism Spectrum Disorder (ASD) by 8 years of age. Given the high prevalence, the AAP recommends ASD screening at 18 and 24 months for early detection and intervention. The Modified Checklist for Autism in Toddlers (MCHAT) is a validated screening tool distributed at primary care visits in Downstate’s pediatrics clinic. The goal of this QI project is to evaluate the effectiveness and challenges of the screening program in place. Methods: 342 children were screened with the MCHAT between 7/1/16-6/30/17. Children with positive MCHATs are referred for further evaluation. Phone calls are made to evaluation sites to monitor if children received an evaluation, an ASD diagnosis and/or services. Results: 24 of the 342 children (7%) screened positive on the MCHAT. Of the 24 positives, 4 had already received a diagnosis of ASD. Of the 20 remaining positive MCHATs (de novo identification of possible ASD), 18 were referred, 1 was asked to follow up for a repeat MCHAT and did not return, and 1 was not referred due to history of prior evaluation for delays (no ASD evaluation was completed). Of the 18 referred, 7 (39%) were evaluated for ASD. Challenges impeding ASD evaluation included difficulties communicating between referring and evaluation sites regarding the type of evaluation needed (4), delayed follow up by parent and child “aged out” (1), no show to intake appointment (1), no show to evaluation appointment (3), parent’s denial of concerns (2), administrative delays (1), and unable to contact parent for follow up (1). Of the 7 evaluated for ASD, 2 were diagnosed. Discussion: These preliminary results outline the value of screening for ASD and the significant challenges that lie between a child screening positive and receiving a formal ASD evaluation. Future directions involve using the results to implement improvements to the program, and long-term follow up for children who screened positive.
Benign or Pathologic? Implementation of a Modified AUC criteria as a New Cost-Effective model of managing Pediatric murmurs in General Pediatric Practice. A Quality Improvement Project.

Introduction: In Pediatrics, up to 50% of children have an innocent heart murmur during childhood, but only 1% of newborns have a structural heart defect. This Quality Improvement project aimed to improve identification of innocent murmurs and implement our Modified Appropriate Use Criteria at SUNY Downstate Medical Center Pediatric Resident Continuity Clinic, and therefore decrease the amount of new referrals for innocent murmurs to the Cardiology Department.

Methods: A retrospective chart review was done of all Cardiology referrals from 2014 - 2017 in patients aged 0 - 24 months with an isolated finding of a new onset murmur. As an intervention, pediatric residents and attendings from our general pediatrics continuity clinic attended an educational session reviewing murmurs, cardiac exam, and our modified appropriate use criteria for referral. The data 6 months prior to the intervention was compared to 6 months after, to identify improvement in identification and referral rates, and data was analyzed for statistical and clinical significance.

Results: From 2014 - 2017, there were 57 referrals that met criteria, and 95% (54/57) were benign murmurs, as only 3 patients had a pathologic murmur. 6 months pre-intervention referrals were 100% (15/15) benign and 6 months post-intervention referrals were 86% (13/15) benign.

Conclusion: While our study did not yield statistical significance due to low power and small sample size, we believe our results to be clinically significant. Our study also reinforces that Pediatricians have a high rate of Cardiology referral for benign murmurs, though improvement can be made with continuing educational review and practice. Overall, during residency training education is needed to minimize negative effects of unnecessary Cardiology referrals in the future. This may also lead to decreased financial stress for the medical system and avoiding emotional stress for families.

Patient Safety Concerns as a Result of Poor Documentation in the Adolescent Primary Care Setting

The prevalence and incidence of depression has increased in recent years in the United States. Over 11% of adolescents suffer from major depressive episodes in 2014. With regard to adolescents, the U.S. Preventive Services Task Force recommends screening in clinical practices that are able to provide accurate diagnosis, effective treatment, and follow-up. The Patient Health Questionnaire (PHQ)-9 is a validated screening tool that is often used, with a sensitivity of 61% sensitivity and a specificity of 94%. As of July 1, 2019, Downstate Medical Center required the PHQ-9 be administered to all adolescents at their well child visit. A chart review was conducted of all well child visits to Downstate Medical Center Suite D of adolescents ages 12-19 from July 1, 2019 to August 1, 2019 to determine the success of PHQ-9 documentation. In the month of July, 58 visits were accessed through HealthBridge. Over two-thirds of the visits did not have a PHQ-9 value documented. Of the two-thirds, 7.7% had documented “PHQ WNL” and 7.7% had documented “PHQ neg” within the note, but a numerical number was not documented. Of the nearly 57% who did not have the PHQ-9 value documented and had no mention of it in the physician note, 12% had a history of suicide attempt and 3% had a diagnosed mental illness. This study shows that the PHQ-9 is not being documented in an overwhelming majority of adolescent well child visits in the first month of the indoctrination of its requirement. Furthermore, it demonstrates that the PHQ-9 is not being documented in high-risk patients, such as those with previous suicide attempts and those with diagnosed mental illness. The findings of this study suggest the need for a root cause analysis to look into the reason for the poor documentation to ensure adolescents with depression are being identified through screening and provided with the proper resources for treatment and follow-up.
Empiric Antibiotic Therapy in Late Onset Sepsis in Preterm Infants- An Inner-City Hospital Experience

Background: Late onset neonatal sepsis (LOS) has been associated with increased mortality & morbidities in preterm infants. Prevalence & distribution of pathogens causing sepsis vary with time & location of neonatal intensive care unit. Given the difficulty of diagnosis & the potential consequences of missed diagnosis, empiric antibiotics are most frequently used in preterm infants.

Objective: To determine the incidence of late onset sepsis in preterm infants, distribution of pathogens & susceptibility pattern to help us in identification of appropriate empiric antibiotic therapy.

Methods: All preterm infants (< 34 weeks gestation age) admitted from January 2013 to December 2018 at Kings County Hospital, who were evaluated for LOS & received empiric antibiotics were eligible for the study. Retrospective chart review of the patient medical records was done & de-identified data was collected on pre-specified study questionnaire.

Results: Blood culture confirmed LOS was seen in 45(29.4%) of the total 153 neonates with clinically suspected LOS. LOS incidence was 8.6%. The major organisms causing LOS in order of frequency were coagulase negative staphylococcus 17(37.8%), escherichia coli 6(13.3%), klebsiella pneumoniae 6(13.3%), staphylococcus aureus 4(8.9%), candida 4(8.9%), pseudomonas 2(4.4%), & streptococcus viridans 2(4.4%). The gram-positive organisms displayed a high resistance to most penicillins, cephalosporins, oxacillin & fluoroquinolones but were sensitive to vancomycin & rifampin. High resistance was noted with ampicillin & gentamycin amongst most gram negative organisms, whereas amikacin, most cephalosporins, fluoroquinolones & carbapenems were effective in most cases.

Conclusion: Based on our findings, Vancomycin & Amikacin can be an appropriate relatively narrow spectrum empiric antibiotic regimen for preterm infants with suspected late onset sepsis. But ongoing surveillance for antibiotic susceptibility will help to safeguard proper empirical therapy.

The Effect of an Educational Intervention Teaching the Systematic Approach to the Critically Ill or Injured Child on Pediatric Residents’ Knowledge Retention.

Objective: We aimed to determine the effect of an educational intervention teaching the systematic approach algorithm from the American Heart Association (AHA) Pediatric Advanced Life Support (PALS) on pediatric residents’ knowledge retention of the systematic approach steps over time.

Methods and Materials: We recruited residents from our pediatric residency program and randomized into two groups, intervention group and control group. Pre-intervention survey delineating resident demographics, experience and confidence level were collected at the beginning of the study. Along with the survey, residents also completed a baseline knowledge assessment survey adapted from the AHA PALS systematic approach algorithm with nineteen fill-in-the-blank questions. The intervention group completed the post-intervention knowledge assessment and survey 1 month from the educational session. The control group completed the knowledge assessment and survey 1 month from their initial knowledge assessment. We used two way ANOVA for statistical analysis.

Results: 70 residents were enrolled in the study (31 intervention group, 39 no intervention). Comparing the difference in score before and after intervention among the three PGY levels, the assessment score significantly improved after intervention (p = 0.034). PGY level was not associated with difference in scores between pre and post intervention. (p = 0.82)

Conclusion: Receiving educational interventions on the systematic approach algorithm may be beneficial to increase pediatric residents’ knowledge in assessing critically ill patients and identifying the need to resuscitate.
Comparison of Different Types of Intravenous Corticosteroids in the Treatment of Acute Severe Pediatric Asthma

Objective: Various intravenous steroids are available for acute severe asthma treatment, however the choice of intravenous (IV) steroids varies broadly and depends on institution, country, or physician preferences. In this study, we compared the efficacy of IV dexamethasone, methylprednisolone, and hydrocortisone in acute severe pediatric asthma during the PICU admission.

Methods: This was a prospective randomized clinical trial. Patients aged 1-21 years were included and randomized into 3 groups. Patients in Group A received iv Methylprednisolone 2mg/kg/day, Group B received IV Hydrocortisone, 5 mg/kg/day and Group C received IV Dexamethasone 0.6mg/kg/day every 6 hours. All patients received continuous beta-2 agonist treatment and ipratropium bromide nebulization every 6 hours. Duration of continuous beta-2 agonist treatment, maximum dose of beta-2 agonist, need for mechanical ventilation, PICU and hospital length of stay (PLOS/HLOS) were collected.

Kruskal-Wallis test by ranks was used to compare the three groups of treatment.

Results: 48 pediatric patients were enrolled in the study. Mean age was 7 (SD 4). 2 patients (4%) were newly diagnosed asthma, 25 (51%) were intermittent, 9 (18%) mild persistent, 11 (22%) moderate persistent and 2 (4%) severe persistent asthma. Comparing the three treatment groups. Median durations for beta-2-agonist treatment was 24 (IQR 17-31), 36 (IQR 18-42), 30 (IQR 16.5-43.5) days respectively (p-value 0.6). Median PICU stay was 24.5 (IQR18.75-36), 44 (IQR 34-62), 36 (IQR 33-48.5) days respectively (p-value 0.019). Median total hospital stay was 51.5 (37.5-95.5), 75 (53-98), 72.5 (51.5-102) days respectively (p-value 0.26).

Conclusion: PLOS was significantly less for iv Methylprednisolone group compared to iv Hydrocortisone group. All three iv steroids were similarly effective in the treatment.

Use of Nanoparticles to Deliver ALT as a Novel Mechanism to Enhance Beta-Galactosidase Activity and Decrease Proliferation in Triple Negative Breast Cancer Cells Lacking Retinoblastoma Protein

In vitro and in vivo studies have shown that an alternatively spliced variant of Breast Tumor-Related Kinase (ALT) is able to inhibit phosphorylation of the Y88 residue on p27Kip1. This hinders p27’s ability to activate cyclin D-cdk4 and cyclin E-cdk2, which play key roles in cell cycle progression. It has been demonstrated that ALT can be packaged into lipid nanoparticles (NP-ALT) and delivered to cells in vitro, where it’s been shown to decrease proliferation in various breast cancer cell lines.

Palbociclib (PD) is an FDA-approved small-molecule inhibitor of cdk4 and is the standard of care treatment for metastatic ER+, HER2- breast cancer. Patients with triple-negative breast cancer (TNBC), defined as ER-, PR-, and HER2-, respond poorly to current therapies and often develop resistance to agents including PD. One hypothesis is that growth in these cells is driven predominantly by cdk2 rather than cdk4. TNBC cells that are retinoblastoma (Rb) negative can be particularly impervious to treatment, warranting the need to develop more targeted approaches. The Rb-, TNBC cell lines, BT549 and MDA-MB-468, were treated with PD, NP-ALT, or a combination of both. Rates of proliferation were significantly decreased in TNBC cells treated with NP-ALT alone or combined with PD compared to vehicle-treated cells. Additionally, cdk2 activity was inhibited as measured by immunoblot analysis using cdk2T160 antibodies. Cell survival was not affected by 48 and 72 hours of treatment, while Beta-galactosidase (β-gal) levels were significantly enhanced. Our results demonstrate that NP-ALT is effective at reducing proliferation and increasing levels of senescence in these PD-resistant cells, and induction of β-gal activity, a well-established marker of senescence, suggests that ALT treatment causes a permanent cell exit. These data suggest that ALT may provide a novel mechanism to target TNBCs and may expand the repertoire of anti-cancer drugs for treating these patients.
Ahmed Badran

Advisor(s): Vivian Chin

**Two cases of hypoparathyroidism due to activating calcium sensing receptor mutation**

Introduction: The extracellular calcium-sensing receptor (CaSR) located throughout the body plays an important role in calcium (Ca2+) metabolism through regulation of parathyroid hormone (PTH) secretion in the parathyroid gland and Ca2+ reabsorption in the kidney. It is located on chromosome 3q. Activating mutations of CaSR can lead to hypoparathyroidism. Constitutively activated CaSR receptors lower PTH release leading to hypocalcemia and hyperphosphatemia. Hypocalcemic symptoms include paresthesia, muscle spasms, cramps, tetany and even seizures in severe cases.

Case 1: A 14 year old male presented with hypocalcemia and hyperphosphatemia on routine blood work. Physical examination showed positive Chvostek sign. Lab results revealed low Ca2+ (8.1 mg/dl), high phosphorus (6 mg/dl), inappropriately normal PTH (26.8 pg/ml) and Ca/Cr ratio 0.19. He is stable on Calcium carbonate and Calcitriol. FISH was negative for 22q11 deletion, and autoimmune polyglandular syndrome 1 was ruled out. Gene testing showed heterozygous CaSR gene mutation I822T, variant of uncertain significance. Given that his father with primary hypoparathyroidism also tested positive for the same mutation, this is likely a pathogenic mutation.

Case 2: A 1 day old 32 week preterm female found during NICU admission to have hypocalcemia 6.1 mg/dl, inappropriately normal PTH (18.5 pg/dl), high phosphorus (8.8 mg/dl) and normal renal function. There were no symptoms of hypocalcemia and her examination was unrevealing. FISH was negative. She is maintained on ergocalciferol, calcitriol and sevelamer. Genetic testing showed a variant in CaSR I832T.

Conclusion: Hypoparathyroidism due to activating CaSR gene mutation should be considered in patients who present with hypoparathyroidism.

Abin Sajan

Advisor(s): Robert DiRaimo

**Surgical Anatomy of the Carotid: Stenting vs Endarterectomy vs Transcarotid Artery Revascularization**

Objectives: To prevent stroke in at-risk patients, the surgeon may choose to treat the accumulation of atheromatous plaque in the carotid arteries from an open or endovascular approach. The height of the carotid bifurcation (HCB) is classically defined in relation to the cervical vertebral levels and it is an important operative tool that influences the decision between carotid endarterectomy (CEA) vs stenting vs transcarotid artery revascularization (TCAR). The current anatomical definitions are of limited practicality during open operative procedures because the cervical spine is not readily accessible in the surgical field. Thus, we devised a novel cadaveric approach to evaluate the best carotid surgical approach.

Methods: Neck dissections were performed on ten carotid regions and the following structures studied: common carotid bifurcation (CCB), superior thyroid artery (STA), facial vein (FV), CN IX, CN XII, and superior laryngeal nerve (SLN). The distance measures from the medial border of the clavicle (MBC) to the above structures were divided by the MBC to mastoid process distance to generate individual ratios and then compared between the right vs. left.

Results: The ratio of the distance from MBC to CCB, MBC to STA origin, and the MBC to FV origin ratio was significantly greater on the left than the right side with 0.74 vs 0.64 (p = .008), 0.70 vs 0.64 (p = .02), and 0.69 vs 0.61 (p = .004), respectively. The MBC to CN XII and STA origin to CN XII was also significantly greater on the left side than the right with 0.77 vs 0.66 (p = .003) and 0.08 vs. 0.05 (p = .02), respectively.

Conclusions: Our results suggest that the superior left CCB is a more difficult dissection and stenting or TCAR should be considered on the left given the longer common carotid. Additionally, surgeons should approach the left CCB cautiously and consider stenting or TCAR for the left if a high CCB is initially encountered on the right side.
Abin Sajan

Geniculate Artery Embolization: A new Geniculate Artery Classification System

Purpose: Geniculate Artery Embolization has demonstrated efficacy in alleviating knee pain associated with osteoarthritis. A thorough understanding of the classical anatomy and variations in branch patterns are essential in order to optimize target therapeutic selective embolization. We plan to anatomically review the geniculate arteries (GA) as there is a lack of detailed anatomy in the literature most notably at the cadaveric level.

Materials and methods: 102 cadaveric limbs were dissected for gross anatomical appearance and the presence of the descending genicular artery off the femoral artery and all 5 main branches off the popliteal artery including the superior lateral genicular artery, superior medial genicular artery, middle genicular artery, inferior lateral genicular artery and inferior medial genicular artery. The location of origin, diameter of vessels and variation in patterns of the GA were reviewed.

Results: 96 limbs were adequately preserved and reviewed. There was minimal variation in the descending genicular artery. 7 variations were observed with 3 branching patterns previously not described in the literature. Based on these observations we propose a new classification system for the branching patterns of the GA.

Conclusion: During Geniculate Artery Embolization, knowledge of the most common vascular anatomy and variations in branching is essential for safe embolization, good clinical practice, and optimal outcomes. After a detailed review of the cadaveric anatomy, we propose a new classification system for the branching patterns GA.

Tashzna Jones

The Effect of Implementing an Integrated Medical School Curriculum on Student Surgery Shelf Performance

Introduction: Recent trends in curriculum development have seen many medical schools shift to a systems-based curriculum. Although many studies have evaluated various facets of these curriculum changes, few have specifically looked at the effects on performance in clinical rotations. The surgical clerkship in particular may be affected by the integration of anatomy in the pre-clinical curriculum.

Methods: Data was collected from a single medical school that recently transitioned from a traditional to a systems-based curriculum. NBME Surgery shelf raw scores and percentiles from students two years prior to and after curriculum change were analyzed. T-Test analysis was used to compare raw scores and percentiles between the two curricula.

Results: There was no significant difference in the raw scores for the traditional (M=76.88, SD=7.96) and the new (M=76.07, SD=7.56) curricula; t(866)=1.53, p = 0.13. There was a significant difference in the percentiles for the old (M=57.54, SD=27.72) and the new (M=72.62, SD=20.72) curricula; t(846)=9.14, p = 4.49*10^-19.

Conclusion: The implementation of a systems-based curriculum improved percentile performance on the surgery NBME. The curriculum change did not significantly impact the mean scores on the exam, suggesting both curricula are comparable in preparing students. The difference in percentiles could indicate there was a change in the difficulty of the exam over the same time period. It could also be representative of a nation-wide decline in performance on the exam compared to students who were exposed to the integrated curriculum. This would explain the difference in only the percentiles. This study shows the value of education reform but also calls for more work to examine the effects of these changes on medical school education.
**Evaluation of Rater Reliability using the Neurodevelopmental Infant Screening Tool**

The Neurodevelopmental Infant Screening Tool (NIST) was developed with the purpose of identifying any developmental delays in the first year of life. The modalities tested were social-emotional behavior, receptive language, expressive language, feeding, visual/fine motor-problem solving, sensory integration, extremity tone, axial alignment and function, and gross motor examination. If any deficits are found, this would allow the child to receive early intervention and to catch up to their peers. In this study, inter- and intra-rater reliability was tested using 13 healthy controls between the ages of one month and twelve months in order to determine whether this tool can be reliably applied to the healthcare setting. We found that students trained in using the NIST obtained similar scores with Pearson r values >0.99 when rating the same child multiple times and when compared to one another. This shows that this screening tool is reliable and can be applied to the healthcare setting without concern of variability in scores due to rater differences.

**Impact of adjunct psychotherapy in adult patient with treatment-resistant Major Depressive Disorder and concurrent congenital HIV**

Major Depressive Disorder (MDD) is 2-3 times more prevalent in patients suffering from co-morbid HIV compared to the general public. Despite multiple studies disclosing the vulnerability of this patient population, clear treatment guidelines are currently lacking. In this case report, we bring attention to the effectiveness of adjunct psychotherapy for MDD in patient suffering from congenital HIV.

This is a 30 year old Guianese American male patient with a psychiatric history of MDD and medical history of congenital HIV, compliant with HAART since birth, presents to SUNY Evening Training Service (SETS) to receive adjunct psychotherapy for his treatment-resistant MDD (failing more than two adequate trials of different anti-depressant medications). At the time of presentation, patient reported feeling depressed, hopeless, anhedonia, low energy, and psychomotor retardation. Due to depression, patient declined function in social and occupational settings. Patient’s medication regimen at the time of presentation was Duloxetine 30mg PO BID for more than 3 months with no clinical improvement. This medication regimen remained constant throughout the duration of therapy. Patient received weekly eclectic psychotherapy. We focused on patient gaining insight into his cognitive distortions of excessive shame. We also explored where these cognitive distortions are stemming from via recognizing patterns within his life. After 6 months of psychotherapy, patient denied anhedonia, hopelessness, and psychomotor retardation; he also reported improvement in mood and energy. Patient also showed improvement in romantic relationships and occupational endeavors.

In this case, patient with treatment-resistant MDD with congenital HIV showed tremendous improvement through adjunct psychotherapy for 6 months after failing multiple anti-depressant medication trials. This case highlights importance of psychotherapy in this vulnerable patient populations.
Burnout in Resident and Fellow Physicians at SUNY Downstate

Introduction: Burnout is a psychological syndrome characterized by feelings of exhaustion, detachment, and reduced personal efficacy. Physician burnout is a topic both of increasing concern and widespread effects for physicians, their families, their patients, and society. We aimed to measure burnout among a diverse group of trainees at SUNY Downstate, an academic training center in Brooklyn, New York.

Methods: The study was a cross-sectional survey in which residents/fellows were asked to complete a survey of demographic information (age, sex, PGY level, subspecialty type, average weekly duty hours) and were asked to take the Oldenburg Burnout Inventory (OLBI) a 16-item survey that covers 2 areas of burnout, exhaustion and disengagement. Average scores on OLBI were compared between male and females, those under 30 and those over 31, junior level and senior level residents/fellows, surgical and nonsurgical subspecialties, and among different self-reported duty hour quartiles.

Results: Of the 960 possible residents and fellows, 235 agreed to begin the survey (24.5%) and 203 completed the OLBI (21%). Independent t-test and one-way Analysis of Variance (ANOVA) were used to compare the mean Disengagement and Exhaustion levels between different groups. There was a significant difference between females and males in the mean levels of Exhaustion (p=0.0009) and Disengagement (p=0.01), with females scoring higher on average for both disengagement (Mean (M)=2.58, Standard Deviation (SD)=0.55) and exhaustion (M=2.81, SD=0.52) compared to male counterparts's scores for disengagement (M=2.38, SD=0.53) and exhaustion (M=2.54, SD= 0.58). There was a significant difference in the mean levels of Exhaustion for the groups based on the number of reported duty hours (p=0.0001). The group with duty hours <50 had significantly lower mean for the Exhaustion subscale compared to the groups reporting 51-60, 61-70 and 71+ hours. No significant differences were found between the other groups.

An interesting case of Late-onset Gambling Disorder

Gambling Disorder (GD) is characterized by a compulsion to engage in a short-term rewarding, gambling behavior that may engender persistence despite knowledge of severe adverse consequences. Past-year prevalence rate of GD is about 0.2%-0.3% in the general population. It is an emergent public health issue, but often goes undiagnosed in the clinics because of lack of awareness among clinicians and embarrassment among patients.

We present a case of Ms. B, a 55-year-old African American woman who presented to our adult psychiatry outpatient clinic for the management of depressive symptoms and gambling behavior. On assessment, we noticed prominent depressive symptoms, and intermittent suicidal ideas, along with an urge to buy scratch lottery tickets. History of gambling behavior revealed that she first started buying scratch tickets three years ago. Over next one and half years, she started spending increasing amount of money on purchasing scratch tickets. She felt intense desire to buy and scratch the tickets and would remain preoccupied with the thoughts of winning a big prize. She accumulated a huge debt due to her habit. She kept going back to the store despite losing money. She had been trying to stop her behavior as she felt guilty, but without any success. She lied to her family about her behavior due to shame and embarrassment. She also reported that she gambled to lift her sad mood. Based on DSM-5 criteria, she was diagnosed with Gambling Disorder, severe. She had poor adherence to treatment; she refused to take treatment for GD. With motivational interviewing, she felt encouraged to attend Gamblers Anonymous (GA) meetings.

Based on the existing literature and present case study, we recommend routine screening for GD as a part of the psychiatric intake evaluation in the clinics. Its early detection may prevent significant morbidity and financial loss among patients.
"An update on role of virtual reality based treatments in child mental illness"

Last decade has been the age of computers. The ability to modulate our senses with the use of technology has grown tremendously. Virtual reality has been a part of our everyday life from looking at a computer screen or a TV to immersive experiences like Oculus rift and HTC Vive. Tele-psychiatry offers the ability to reach patients in corners of the world where physical presence of a physician may not be possible, virtual reality offers the same but overcomes certain limitations tele-psychiatry might have and gives a sense of physical presence. Virtual reality is already well established modality for treatment in PTSD and specific phobias. Numerous trials are on the way regarding its role in treatment of anxiety disorders with promising results from initial evidence. Another area of interest and exciting new research had been the use of Virtual reality in social skills training both in autism spectrum and cognitively limited domain of patients. The potential role virtual reality might play in understanding and eventually modulating altered perceptual experiences is also being explored. The ability to alter physical environment offers an opportunity to develop newer tools and screens for improving our diagnostic accuracy and tailoring treatment to the individual needs of the patient. Traditionally psychiatry has always relied on patient and family reports, virtual reality offers an opportunity to clinically examine patients reports by simulating virtual environments for. e.g a patient report of having difficulty traveling in a subway could be followed up by 5-minute virtual subway ride in your office. One of the initiative that we plan on doing in our clinic is using an app based intervention with one of the patients in our clinic and comparing it to routine therapy based on clinet report. This presentation will explore the ongoing research and far reaching implications virtual reality may have in the field of child psychiatry.

Diagnosis, medical and psychosocial management of opioid use disorder: where do we stand?

Opioid use disorder is diagnosed using the DSM-5 criteria. The severity is based on the number of criteria a person fulfills out of a total of 11: 2-3 is mild, 4-5 is moderate, and 6 or more is severe. Screening tools such as the Drug Abuse Screen Test (DAST-10) or the Screening to Brief Intervention (S2BI) can be used in the clinic to determine whether further assessment is needed. Opioid use disorder has a variety of medical treatment options. Depending on the approach, an opioid detox program may be warranted for which the withdrawal process is treated by opioid or non-opioid interventions followed by maintenance therapy. These Medication Assisted Treatments (MAT) include methadone, buprenorphine and naltrexone, each having its advantages and limitations. While MAT is the main intervention, several psychosocial interventions have been identified for the treatment of opioid use disorder, with varying degrees of evidence supporting their efficacy. These include brief intervention, referral to treatment, office-based counselling, motivational interviewing, cognitive behavioral therapy, contingency management, harm reduction, mindfulness, yoga, and technology-assisted therapies (e.g. text messaging, video-conferencing and video games). Some of these measures can be delivered in primary care facilities, while others may require more intensive substance use specialized programs for implementation. In this poster, we review the updates in diagnosis, medical and psychosocial management of opioid use disorder.
**Airway resistance caused by sphingomyelin synthase 2 insufficiency in response to cigarette smoke**

**Rationale:** The effects of cigarette smoke exposure on ceramide, a major sphingolipid, has been extensively studied in pulmonary diseases but its subsequent impact on sphingomyelins (SGM), the second most abundant phospholipid in mammalian plasma, remains elusive. SGM synthase (SGMS) is an enzyme responsible for the production of sphingomyelin from ceramide. Here, we examine the effect of chronic cigarette smoke exposure on SGMS activity and evaluate the impact of one isoforms of mammalian SGMS, Sgms2, deficiency on pulmonary function.

**Methods:** Sgms2 knockout and wild type control mice were exposed to cigarette smoke for 6 months and pulmonary function testing was performed. SGMS2-dependent signaling was investigated in these mice and in human monocyte derived macrophages (MDM) from nonsmokers and human bronchial epithelial (HBE) cells isolated from healthy nonsmokers and chronic obstructive pulmonary disease (COPD) subjects.

**Results:** Here, we demonstrate that chronic cigarette smoke reduces SGMS activity and SGMS2 gene expression in mouse lungs. Sgms2 deficient mice exhibited enhanced airway resistance following chronic cigarette smoke exposure, but have similar levels of emphysema compared to smoke exposed wild type mice. Sgms2-/- mice had greater AKT phosphorylation and protease activity in their lungs following smoke inhalation. Similarly, we identified reduced SGMS2 expression and enhanced phosphorylation of AKT and protease production in HBE cells isolated from COPD subjects. Selective inhibition of AKT activity or overexpression of SGMS2 reduced production of several matrix metalloproteases in HBE cells and MDM cells.

**Conclusions:** Our study establishes that smoke-regulated Sgms2 gene expression influences airway resistance, AKT signaling and protease production. Modulating SMS activity and its downstream pathway may represent a therapeutic approach in smoke induced lung disease.

**Dyspnea in a Patient with Sarcoidosis.**

Lungs and lymph nodes are involved in more than 90% of patients with sarcoidosis with obstructive and restrictive disease pattern being the most common pulmonary manifestations. Although pulmonary hypertension, pulmonary muscle weakness and fibrotic lung are other pulmonary manifestation, however it is not common to consider pulmonary embolism (PE) among the pulmonary manifestations of sarcoidosis. We report a 64 year old male with no significant past medical history, no known risk factor who came to the emergency department for shortness of breath and cough with productive thin white sputum for two weeks leading to the new diagnosis of sarcoidosis and concomitant PE. Unprovoked thrombosis in patients with sarcoidosis has been reported by some studies. The mechanism responsible for the occurrence of venous thromboembolism is not well described and seems to be multifactorial. Hasday JD reported that the BAL fluid from patients with pulmonary sarcoidosis possesses procoagulant activity. Alveolar macrophages from patients with sarcoidosis exhibit greater tissue factor activity than do macrophages from healthy control subjects. Circulating and BAL levels of fibrin degradation products have also been found by investigators to be elevated in patients with pulmonary sarcoidosis. Thus, sarcoidosis, via inflammatory or other biochemical mechanisms, likely predisposes to PE therefore PE should be considered while evaluating a case of sarcoidosis flare.
S-Nitrosylation of Hemoglobin: A Potential Biomarker in Sepsis

Sepsis, defined as life threatening organ dysfunction caused by a dysregulated host response to an infection, causes millions of deaths globally a year. Yet despite this prevalence relatively few biomarkers and clinical scores exist to assist with diagnosis, assessing severity, monitoring treatment response, with no consensus on a gold standard. Considering the pathophysiology of sepsis, we wanted to look at S-Nitrosylation as a potential biomarker. We took blood samples from 25 patients presenting with sepsis and 25 healthy controls, as well as repeating bloodwork from the 25 subjects after resolution of sepsis. A Cayman biotin switch assay was used to detect S-Nitrosylation on a Western Blot. We see that S-Nitrosylation levels are higher in septic subjects as compared to resolved subjects and controls, indicating that S-Nitrosylation may indeed serve as a biomarker in sepsis, potentially assisting with diagnosis and monitoring response to treatment.

Expression and Impact of Protein Phosphatase 2A (PP2A) B Subunit in COPD

Introduction: Protein phosphatase 2A (PP2A) is the primary serine-threonine phosphatase of eukaryotic cells and changes in its activity play a major role in the regulation of airway inflammation and protease responses. PP2A consists of a dimeric core enzyme composed of a structural A and catalytic C subunit, and a variable regulatory B subunit. While C and A subunit sequences are conservative, the regulatory B subunits are more heterogeneous and their expression in the airways are not characterized. The aim of this study was to characterize the B subunit expression profiles in epithelial cells from COPD and healthy subjects and document the subsequent changes on cigarette smoke-induced responses.

Methods: Primary human small airway epithelial (SAE) cells from healthy and COPD subjects were used to screen and characterize the B subunit expression profile. Cells were exposed to cigarette smoke extract (CSE) and B subunit genes were characterized for expression. B subunit genes were silenced to examine their effect on PP2A activity and their subsequent impact on inflammation.

Results: Gene expression profiles were characterized for all the PP2A B subunits in SAE cells from healthy and COPD subjects. Expression of PPP2R2B and PPP2R2C were decreased in COPD cells in comparison to healthy cells; while expression of PPP2R5D and PPP2R5E were increased in COPD cells. Similarly, exposure to CSE reduced PPP2R2B and increased PPP2R5D gene expression in healthy cells. Importantly, loss of PPP2R5D influenced airway PP2A activity by increasing CSE-induced IL-6, caspase-3, MAPK, and NF-kappaB activities.

Conclusions: This data supports a distinct PP2A regulatory subunit profile in COPD that acts upon the activity of PP2A, which impacts the immune and proteolytic responses in cigarette smoke mediated diseases.
Immune System And Diagnosis of Sepsis: Promising New Biomarkers

Despite being one of the leading causes of morbidity and mortality within our healthcare system, Sepsis remains a diagnostic and therapeutic dilemma. One of the difficulties in the diagnosis of sepsis is that a major underlying pathophysiologic mechanism of sepsis revolves around host immune system activation and dysregulated response involving many biomarkers. Despite this overwhelming burden on healthcare and besides a few scoring systems, there is no consensus on a gold standard diagnostic biomarker. Focusing on the host immune dysregulation, we looked at various inflammatory biomarkers during sepsis. Samples of 16 subjects presenting with sepsis before and after treatment/resolution of sepsis were compared to healthy controls using a human cytokine 29-plex panel chemokine and cytokine assay. We found that Interleukin-8 (IL-8), interferon-induced protein 10 (IP-10), and monocyte chemoattractant protein 1 (MCP-1) levels were significantly elevated in the serum of sepsis patients as compared to controls indicating their potential as biomarkers in the diagnosis of sepsis. We also found that MCP-1 levels were significantly decreased in the serum after sepsis resolution. This implies the potential for MCP-1 to be useful as a biomarker in both diagnosis and monitoring response to therapeutic interventions.

Patterns of Care and Outcomes of Adjuvant Chemoradiation for Node-Positive Pancreatic Adenocarcinoma

Background: The superiority of adjuvant chemoradiation (aCRT) over adjuvant chemotherapy (aC) for resected node-positive (N1) pancreatic cancer (PC) has been debated. Both options are in the NCCN guidelines. We aimed to compare the two treatments using the National Cancer Database (NCDB).

Methods: For the years 2006-2014, patients (pts) with resected N1 PC and negative margins treated with aC or aCRT were identified in the NCDB. Radiation therapy dose was limited to 4500-5400cGy and the cohort excluded those who lived <3 months or received any neoadjuvant therapy. Multiple factors were compared between those who received aC vs aCRT. Univariable and multivariable logistic regression was performed to assess for predictors of aCRT use. The Kaplan-Meier method was used to assess overall survival (OS) and univariable and multivariable Cox regression was used to assess impact of covariables on OS.

Results: 3,609 pts met study criteria; 2,988 (82.8%) received aC and 621 (17.2%) aCRT. Median follow-up for living pts was 33.8 months (IQR 22-51). 2-year OS was 44.9% vs 42.6% for aC vs aCRT (p=0.169). On multivariable analysis, pts were less likely to receive aCRT over aC if they were treated at an academic facility (p<0.001), had more recent years of diagnosis 2009-2014(p<0.001) and had the highest median income quartile (p=0.009). Pts treated in the South were more likely to receive aCRT (p=0.002). On multivariable OS analysis, age group ≥60 (p=0.021), Black race (p=0.034), and Charlson-Deyo comorbidity score ≥1 (p<0.05) were associated with worse OS. Treatment at an academic facility (p<0.001), highest median income quartile (p=0.010) and more recent years of diagnosis 2009-2014 (p<0.05) were associated with improved OS. The treatment variable of interest was not associated with any differences in OS.

Conclusions: aC alone following surgery for PDAC is the predominant treatment of choice among US hospitals. There was no OS benefit noted in those who were treated with aCRT.
Comparing Perioperative Outcomes of Uterine Fibroid Embolization and Hysterectomy: A Retrospective, Mult-center Database Study

Purpose: This study sought to identify the 30-day readmission, 15-day complication, and minimum 1-year surveillance time reintervention rates of patients undergoing uterine fibroid embolization (UFE) or hysterectomy (H) for uterine leiomyoma.

Material and methods: Patients from the New York State’s Statewide Planning and Research Cooperative System database admitted from 2009-2013 that were over 18 years old, diagnosed with uterine leiomyoma, and who underwent non-radical hysterectomy or UFE were retrospectively reviewed. 1:1 propensity match was carried out, followed by a univariate analysis comparing demographics, complications, readmissions, and reintervention rates. Multivariate binary stepwise logistic regression models identified independent predictors of outcomes.

Results: 682 patients were identified (H: n=341; UFE: n=341). No significant differences were identified between H and UFE demographics, complication (2.90% H vs 2.60% UFE, p=0.816) or readmission rates (4.40% H vs. 3.80% UFE, p=0.700). 0.3% of UFE patients had a reintervention UFE and 2.60% of UFE patients had reintervention hysterectomy. H patients had a significantly longer average length of stay (2.42 vs 1.63 days, p<0.001). For UFE, Deyo score (OR: 18.25 [95% CI: 1.496 – 222.576], p=0.023) and obesity (OR: 4.294 [95% CI: 1.228 – 15.013], p=0.022) positively predicted readmission within 30 days. Deyo score (OR: 94.571 [95% CI: 7.651 – 1168.911], p<0.001) also positively predicted complications for UFE.

Conclusion: Patients undergoing hysterectomy had significantly longer hospital stays. For UFE patients, Deyo score and obesity positively predicted readmission within 30 days, and Deyo score positively predicted complications. Our findings support the safety and efficacy of both hysterectomy and UFE for uterine leiomyoma.

Hypomethylation of the Dual Specificity Phosphatase (DUSP22) promoter in cell-free DNA (cf-DNA) is associated with rheumatoid arthritis, joint narrowing and neuropathic pain in Hispanic individuals.

Objective: Ethnic and racial health disparities have been observed in rheumatoid arthritis (RA), but limited studies have investigated biomarkers in minority populations in RA. DUSP22 regulates intracellular pathways that underly inflammation and pain sensitization. Dysregulation of these pathways is described in seropositive RA. Previous studies uncovered an association between DUSP22 DNA methylation changes in peripheral mononuclear cells (PMC) and erosive RA disease. We conducted a pilot study to investigate plasma cell-free DNA (cfDNA) DNA methylation in DUSP22 of Hispanic RA patients and healthy controls. We also investigate DUSP22 DNA methylation associations with RA clinical characteristics. Methods: DNA was isolated from plasma from 27 RA patients who satisfied the ACR criteria, and 18 healthy controls. DUSP22 DNA methylation was determined by pyrosequencing. Statistical analysis identified group differences and associations with RA clinical measures.

Results: RA patients had lower cfDNA DUSP22 DNA methylation when compared to controls (36.47±16.17% vs. 47.05±10.28%, p=0.025). Loss of DNA methylation at a specific site in DUSP22 was correlated with increased joint narrowing (p=0.04). For seronegative RA patients, lower DUSP22 DNA methylation was significantly correlated with an increase in neuropathic pain (p=0.02) and likelihood of neuropathy (p=0.04). Conclusion: Our pilot study is the first to investigate DNA methylation biomarkers in Hispanic RA patients, suggesting that cfDNA hypomethylation might be an important biomarker. This hypomethylation correlates with joint space narrowing in RA, and among seronegative patients, correlates with increased neuropathic pain and likelihood of having peripheral neuropathy. Further studies are needed to compare DUSP22 DNA methylation from cfDNA to traditional methods (ie. PMC); and to explore its feasibility as a biomarker of prognostic value in RA.
**Disseminated Invasive Aspergillosis in Patient With SLE**

Introduction: Opportunistic infection including invasive aspergillosis is a major cause of mortality in patients with SLE who are immunocompromised. High index of suspicion, early diagnosis and treatment is the key for better outcome of patient with IA. Case presentation: A 41 yr. old woman PMH of SLE on Mycophenolate, H/O IV Methylprednisolone and Cyclophosphamide for nephritis presented to the ER for SOB and hemoptysis. Initially she was hemodynamically stable but became hypoxic, spiked fever, AMS and intubation. The patient was given IV prednisone in suspicion of SLE flare and antibiotic in concern of sepsis. But her condition deteriorated. Culture of CSF, blood, urine and sputum were negative. Galactomannan test was positive. MRI brain showed diffusion restriction. She was started on caspofungin but she failed all the treatment and expired. Autopsy revealed severe disseminated invasive in the multiple organs.

Discussion: Patient with SLE are prone to develop for IA for the disease process and immunosuppressive drugs. Patient may present with non specific symptoms such as fever, cough, chest pain, hemoptysis. They may be treated for SLE flare or bacterial infection. For diagnosis we can do tissue biopsy for histopathological diagnosis or culture to grow fungal hyphae. But most of the time the result is inconclusive. So high suspicion should be there when patient continue to deteriorate with antibiotic. We can do HRCT chest, galactomannan or beta D glucan test. If the result is suggestive of IA empiric antifungal should be initiated.

Conclusion: Our patient was immunocompromised due to SLE and the medication. She presented with non specific symptoms. But initiation of antifungal treatment was delayed and we ultimately faced fatal outcome. When an immunocompromised patient presents with nonspecific symptoms which are not responding to antibiotics, empiric antifungal should be initiated if suspicion is high with suggestive radiological feature and positive galactomannan.

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**The Use of Medical Cannabis for Treatment of Chronic Neuropathic Pain: An Integrative Research Review (IRR)**

Rationale: Chronic neuropathic pain is a common problem that affects patients globally and treatment includes a substantial use of opioids. With the growing epidemic, alternative options are being sought. Medical cannabis use as treatment for chronic pain is increasing in popularity as an alternative for opioids. The purpose of this IRR was to explore the efficacy of medical cannabis for chronic neuropathic pain treatment.

Methods: An Integrative Research Review. Included in the IRR were articles published in 2010 to 2018 in the US, Canada, and Australia. Subjects were 18 years and older. Ten articles were included: four systematic reviews of randomized controlled trials, one randomized-controlled trial, two cross-sectional observational studies, one secondary data analysis, one prospective cohort study, and one historical cohort study. PubMed and Google Scholar were used for literature search engines. Keywords used were efficacy, medical cannabis, medical marijuana, non-cancer chronic pain, neuropathic pain, opioids, substitution, and treatment. Pain was measured by the Visual Analog Scale (VAS), Descriptor Differential Scale (DDS), numerical rating scale, Brief Pain Inventory (BPI), and/or quality of life.

Data analysis: Results from the 10 articles in the IRR indicated that cannabis was associated with opioid use reduction/cessation in the US and Canadian articles, prescribing patterns and in Medicare enrollees’ spending in states where medical cannabis laws were implemented. Cannabis adverse effects found were short-term neurocognitive decline and psychiatric illness worsening. Implications: Medical cannabis was an effective treatment for chronic neuropathic pain and increased quality of life, except for an Australian prospective cohort study. Clinical practice should include medical cannabis as a treatment option for long-term management of chronic neuropathic pain in countries with medical cannabis laws.
Risk Perceptions and Knowledge of Fentanyl Exposure among New York State First Responders

Background: The current opioid epidemic and abuse of fentanyl in the United States has led to an increased risk of exposure to first responders. Law enforcement, fire, and emergency medical services are receiving misinformation on fentanyl health and safety risks and have led to miscommunication. Understanding the risk perceptions and knowledge of first responders regarding fentanyl can help identify training gaps.

Methods: A 15-item 6-point Likert scale online questionnaire was developed by researchers at John Jay College and SUNY Downstate, and distributed to firefighters, police officers, and emergency medical technicians, regarding perceptions of fentanyl exposure, and additional questions concerning knowledge. The link to the online questionnaire was sent to 15 associations and agencies of national and New York State first responders with 3 associations acknowledging and distributing the survey. Each association was sent a mailed and emailed letter. Flyers were posted in the two lead authors’ universities.

Results: Of the 245 participants, 185 served New York State. 90 worked in law enforcement, and the other 95 worked in either fire, emergency medical service, or a dual role. 147 of the respondents selected slightly agree, agree, or strongly agree that briefly touching fentanyl could be deadly. 92 respondents selected that they did not have appropriate access to personal protective equipment to address hazards to fentanyl exposure versus 75 that selected that they did. 18 of the responses indicated they were unsure.

Conclusion: New York State first responders generally agreed with expert risk perceptions in the pilot study. However, items pertaining to using hand sanitizer, selecting glove type, and dermal exposure to fentanyl did not align with expert beliefs. Larger sample studies are needed to validate these findings and should be expanded nationally. Risk perceptions and knowledge could be used to evaluate fentanyl response training among first responders.

Health disparities in gentrified communities: The ongoing fight for health equality and social justice of minority residents in Harlem

Historically marginalized communities of color in New York City, such as Harlem, continue to experience rapid social changes as a result of gentrification. This process leads to adverse health outcomes for the community, including increased rates of diabetes, asthma, cardiovascular disease, and obesity. Such health outcomes suggest that gentrification is indeed a social determinant of health and must be addressed as a public health issue. Community zoning often results in the displacement of longtime residents or limited access to imperative resources and services. The affected neighborhood experiences a shift in characteristics, leading to increasingly poor health outcomes for residents that often are not provided for within standard health promotion and disease prevention services. Efforts to combat these resulting inequities would benefit from an interdisciplinary approach, one that includes a partnership with residents and local activist groups, such as Right to the City and Take Action NYC. With at least 15 New York City communities currently being gentrified, public health officials must seek to protect and provide for those who still reside in these communities but cannot afford to live comfortable, healthy lives. Using neighborhood observations and an adapted PhotoVoice approach, we will identify the risk and protective factors related to these visible health inequities, assess concerns and perspectives of current Harlem residents, discuss previous and current efforts made by activists and other community entities in the fight for health equity and social justice in Harlem, and identify next steps for public health officials that link social justice and health equity.
Nicholas Taklalsingh

Hemoglobin Level and Left Ventricular Structural and Physiologic Findings in Hemoglobin SC Disease with Diastolic Dysfunction

Background: Anemia is associated with changes in left ventricular (LV) morphologic and physiologic changes, including eccentric hypertrophy and systolic dysfunction. In sickle cell anemia (HbSS), there is prominent diastolic dysfunction accompanying LV dilation. Less is known about diastolic dysfunction in hemoglobin SC disease (HbSC), and the predictive value of age, Hgb, and underlying structural and physiologic parameters.

Methods: A retrospective cross-sectional study was performed in adult patients with HbSC. Clinical and hematologic data was obtained based on date of echocardiography. Stepwise linear regression analysis was used to assess associations between age, Hgb and Hgb subtype level, and LA and LV size and physiologic parameters and LV diastolic dysfunction.

Results: Among patients with HbSC (n=82), age and hematologic parameters were correlated with Mitral Valve (MV) E/A ratio (R^2 24.9%) and Tricuspid regurgitation maximum velocity (TR max vel) [R^2 12.6%], with age correlated with MV E/A ratio (β-coefficient -0.014, p<0.001) and TR max vel (β-coefficient 1.29, p=0.003). Furthermore, LV and left atrial (LA) structural and physiologic parameters were correlated with LA volume (LAV) index (R^2 93.4%), TR max vel (R^2 16.1%), and MV E/e’ ratio (R^2 38.0%), with LA diameter correlated with LAV index (β-coefficient 3.378, p=0.001), LV systolic diameter correlated with TR max vel (β-coefficient 42.9, p=0.038) and MV E/e’ ratio (β-coefficient -63.98, p=0.018).

Conclusions: Patients with HbSC disease display age associated diastolic dysfunction, with changes in diastolic function associated with chambers in left-heart chamber size. This data indicates the importance of concrete echocardiographic screening guidelines in HbSC disease for longitudinal cardiac surveillance.

Aleksandra Walasek

Next-generation Sequencing of Bacille Calmette-Guerin (BCG) Unresponsive Tumors Identifies Actionable Alterations for Potential Targeted Therapy in Non-Muscle Invasive Bladder Cancer

Intravesical BCG remains standard of care for patients with intermediate- and high-risk non-muscle invasive bladder cancer (NMIBC). Although most patients initially respond to therapy, there is a group of patients who will experience recurrence and subsequent progression to invasive disease. There are limited treatment options for patients with BCG-unresponsive bladder cancer and alternative therapeutic strategies are needed. Next-generation sequencing helps identify and prioritize therapeutic opportunities for clinical trial of novel targeted agents.

DNA from BCG treated, chemotherapy naive, secondary MIBC tumors and matched normal DNA underwent targeted exome capture sequencing or whole exome sequencing. Potentially actionable genomic alterations were defined according to OncoKB (OncoKB.com).

The cohort was comprised of 77 secondary MIBC specimens, each from a unique patient. RTK/MAPK pathway alterations, most commonly FGFR3 (18%) and ERBB2 (15%), were seen in 42% of patients. PIK3CA mutations, seen in 21%, often co-occurred with RTK/MAPK alterations potentially representing a resistance mechanism to FGFR or ERBB2 directed monotherapy. CDKN2A loss, hypothesized to be a driver of progression in FGFR3 mutated tumors, occurred in 10% of the samples. Alterations in cell cycle regulators were seen in 65% of specimens, of which 40% also had an intact RB gene and could potentially be vulnerable to CDK4/6 inhibitors. Inactivating mutations in CREBBP or EP300 occurred in 17% of specimens that might confer sensitivity to HDAC inhibitors. Truncating mutations in KDM6A and ARID1A were seen in 19% and 33% of samples respectively. These might be sensitizing to EZH2 inhibitors.

Genomic profiling identified several actionable alterations which offer potential therapeutic strategies for management of BCG-unresponsive disease. Targeted therapy for NMIBC patients warrants further investigation as further advances are made in development of more selective systemic inhibitors.
Evaluation of Preoperative Prostate Magnetic Resonance Imaging for Cancer Control and Neurovascular Tissue Preservation During Robotic Radical Prostatectomy

Introduction: Prostate multiparametric magnetic resonance imaging (mpMRI) can precisely depict prostate cancer (PCa) location and adverse pathologic features. Surgeons can utilize this information to maximize sparing of the neurovascular bundles (NVBs) during radical prostatectomy (RP) while avoiding a positive surgical margin (PSM). We detail the technique of using preoperative mpMRI to quantify its effect regarding nerve-sparing and rates of PSMs.

Methods: A prospectively maintained database was queried for robotic-assisted RPs (RARPs) with preoperative mpMRI between 2007-2017. Imaging margin risk factors (iMRF) were defined on mpMRI as frank extraprostatic extension (EPE), possible EPE, and capsular irregularity (capsular bulge, lesion-capsule contact, or lesion adjacency to the neurovascular bundles). Surgical adjustments to nerve-sparing technique were made based on these findings.

Results: Five hundred thirty-two patients comprising 1041 prostate sides were included for analysis. Overall, PSM rate was found in 80/1041 (7.7%) sides of the prostate. iMRF were seen in 313/1041 (30.1%) prostate sides, for which adjustments were made in 244/313 (78.0%) of these. In the 69/244 (22.0%) cases where full nerve-sparing was performed despite iMRF, PSM rate was 20/69 (29%) compared to 33/244 (13.5%), p = 0.002. MRI-guided surgical adjustments decreased PSM risk by 68% and 15% in pT3 and pT2 cases, respectively. On multivariable analysis, logPSA (OR 4.06, [95% CI 2.40-12.3], p < 0.001) and iMRF (OR 1.78, [95% CI 1.01-3.16], p = 0.047) were significantly associated with PSM while nerve-sparing adjustment was significantly associated with decreased risk of PSM (OR 0.38 [95% CI 0.22-0.66], p = 0.001).

Conclusions: MRI effectively detects risks for PSM and guides surgical adjustments to decrease PSM rates. As prostate MRI is more frequently acquired for PCa screening and biopsy, this may have additional value for RP planning and potentially improve outcomes.

Overactive Bladder Phenotypes: Development and Preliminary Data

Aim: The purpose of this study is to develop overactive bladder (OAB) phenotypes that can be used to develop OAB diagnostic and treatment pathways.

Methods: An expert panel was convened to develop an overactive bladder (OAB) phenotype classification system. The panel considered disease driven, mathematical modeling and clustering methodology but decided on using physiologic variables derived from a bladder diary, max uroflow (Qmax) and post-void residual urine (PVR) to construct the phenotype system. Three main phenotypes emerged based on the 24-hour voided volume (24HV)–normal, polyuria, and oliguria–which were divided by bladder capacity into normal, large, and small and then subdivided by max voided volume (MVV), Qmax and PVR. This is a retrospective, multicenter, observational study of patients from 6 clinical urology and urogynecology sites. We queried a database for patients with persistent lower urinary tract symptoms (LUTS) who completed the LUTS questionnaire and a 24-hour bladder diary (24HBD) on a mobile app, website, or paper. Those with an OAB symptom sub-score (OABSS) ≥ 8 were included and phenotyped.

Results: Variables selected for inclusion: 24HV, MVV, Qmax, and PVR. Subjects were divided into three phenotypes based on the 24HVâ€“polyuria (24HV > 2.5 L), normal (24 HV = 1.0 â€“ 2.5 L), and oliguria (24HV < 1.0 L). Five hundred thirty-three patients (348 men and 185 women), completed the LUTS questionnaire and 24HBD, and 399 (75%) patients had a diagnosis of OAB (261 men and 138 women). The primary phenotypes had the following incidences: polyuria (25%), normal (63%), and oliguria (11%). The prevalence of each of the 18 phenotypes is presented in Figure 1.

Conclusion: Classification of OAB variants into phenotypes based on 24HV, MVV, Qmax, and PVR provides the substrate for further research into the etiology of OAB and more precise diagnostic and treatment algorithms.
Informational Flyers in Patient and Physician Areas Failed to Increase CRC Screening Rates but Improved Rates of Physician Documentation

Background: Excluding skin cancers, Colorectal Cancer (CRC) is the third most common cancer in men and women. The American Cancer Society estimated there were 97,220 new cases of colon cancer and 43,030 new cases of rectal cancer in 2018. A 2016 survey in NYC showed that only 68% of patients aged 50-75 underwent CRC screening.

Objectives: 1) Increase the rate of screening to above the NYC rate of 68% by promoting awareness throughout the clinic. 2) Increase discussion and documentation of CRC screening.

Methods: 63 charts were reviewed for appropriate CRC screening. In those without documentation of screening, charts were reviewed to determine potential barriers to screening. A 30-day intervention involving flyers placed in both patient and physician areas of Suite B was conducted. The aim was to remind both the patient and providers to discuss CRC screening.

Results: Screening rates were 61% both pre- and post-intervention. The number of charts showing documentation of discussion regarding screening in those who have not been screened increased from 14% to 33% post intervention.

Discussion: The increase in discussion documentation accompanied by the decrease in tests ordered but not done might show that tests were being ordered without adequate discussion and that patients were deciding, after the order was written, to not do the test. This demonstrates that with the intervention, and more discussions, those who did not want screening were more accurately identified. Perhaps with longer follow up more patients might have had CRC screening performed.

Conclusion: 1) CRC screening rates are below the NYC screening rates, and the primary goal of increasing the screening rate in our clinic was not achieved. 2) The intervention achieved the secondary objective of increasing discussion and documentation of CRC screening. 3) Further investigation with longer follow up would help determine if provider-patient discussions around CRC screening increases screening.
Which patients are not receiving PCV13 or PPSV 23 vaccinations in concordance with CDC recommendations?

Purpose: Variations in CDC recommendations for pneumococcal vaccine based on age and medical conditions make it difficult for providers to determine if either pneumococcal conjugate (PCV13) or the polysaccharide vaccine (PPSV23) is indicated. The purpose of this study was to evaluate the concordance of PCV13 and PPSV23 vaccination administration with the CDC recommendations in adult patients based on age, available medical history and underlying medical conditions in a family medicine clinic.

Methods: After receiving IRB approval, a retrospective chart review was conducted on adult patients who received either PCV13 and/or PPSV23 between January 1st 2017 and December 31st 2017 at a family medicine clinic. Data was compiled in tables; the percentage was calculated and the confidence interval was determined for the prevalence rate.

Results: Three of the 251 (1.2%) PCV13 and PPSV23 vaccinations administered to patients were found to be in discordance with the CDC recommendations based on age, documented medical history and underlying medical conditions. A 95% Agresti-Coull CI [0.24%, 3.62%] was seen.

Conclusion: Majority of the patients in the family medicine clinic received the pneumococcal vaccinations in concordance with CDC recommendations.

Identifying Opportunities for Patient Education About Hypertension

Background: 4.9mil New Yorkers have hypertension (HTN), an 11% increase in the last decade. HTN is a modifiable risk factor for multiple conditions with substantial social and financial burdens. Identifying deficiencies in understanding of HTN can help focus patient education efforts.

Methods: Prospective, cross-sectional, multi-center cohort study included hypertensive adult patients at University Hospital Brooklyn (UHB) and Richmond University Medical Center (RUMC). Demographics and HTN knowledge (BP goals, risk factors, complications, lifestyle modifications) were obtained via 5th-grade reading level questionnaire. Two-tailed t-tests compared HTN literacy at UHB vs RUMC.

Results: Of the 43 subjects, 22 (51.2%) were Black and 26 (60.5%) female. Ethnicity and sex significantly differed between the sites: 19 (95%) UHB pts were Black vs 3 (13%) at RUMC (p<0.0001). At UHB, 16 (80%) were female vs 10 (43.5%) at RUMC (p=0.014). Mean age was 63.4+/−12.9 yrs and similar between the sites. HTN complications were the only significant knowledge difference in the two sites. Significantly more RUMC pts knew heart disease was a complication than at UHB (p=0.0241). At both sites, most pts identified stroke, kidney disease, and vascular disease as complications, with the largest knowledge deficiency in kidney disease (11 patients, 25.6%). Twenty-three (53.5%) patients knew only some or none of their HTN medications. Most patients knew diet, lack of exercise, and smoking were risk factors; 36 (83.7%) made lifestyle changes for BP control including 13 (30.2%) using both diet and exercise. Patient-reported BP goals varied between 120/80-150/90; 34 (79.1%) were inconsistent with JNC8 guidelines.

Conclusions: Multiple patient education opportunities were identified. When discussing HTN, raise patient awareness of JNC8 target BP guidelines, advise carrying their medication list, and teach about kidney disease as a HTN complication. At UHB, also teach heart disease as a complication.
Cuong Le

Measuring and Improving Hepatitis C Screening Rates In Suite B Clinic

Hepatitis C (HCV) is the leading cause of liver-related morbidity and mortality in the United States (a). HCV screening is recommended for all patients born between 1945-1965. Our Suite B clinic HCV screening rate was 46%. This study attempts to increase the screening rate by placing a physician awareness poster in the exam rooms. After doing this, our screening rates of eligible patients increased slightly, but not statistically significant.

Nishith Shah

Reducing an Outpatient No Show Rate Using Earlier Reminders

Background: The average outpatient no show ranges from 1%-28% and costs the healthcare industry $150 billion+ annually. No shows also lead to inefficient use of resources. Missed appointment is a strong predictor of future no shows. Research indicates that forgotten appointments is a common reason for no shows. We decided to use earlier reminders to try and decrease forgotten appointments. Purpose: To reduce Suite B no show appointments by 20% over a 4-week intervention period by implementing pre-appointment phone calls 3 to 7 days prior to the appointments in addition to the usual 24-hour appointment call. Methodology: No show rate was calculated for September 2017. Over a 4-week intervention in September 2018, 156 patients from the resident panel were called 3 to 7 days prior to their scheduled visit in addition to the routine 24-hour pre-appointment reminder. Patient data was tracked to determine no show rate during the intervention month of September 2018. Results: Pre-intervention no show rate was 52%. During the intervention, 16% were not reached at all, 41% reached only via voicemail, 32% reached once in person, and 3% had been reach twice. Of 156 patients contacted, 18% rescheduled and the no show rate was 29%. Discussion: The vast majority of patients in the intervention group were able to be reached 3-7 days before the appointment. Through increasing the number of times a patient was contacted, including an earlier reminder calls, the no show rate was reduced nearly half. Many patients used the earlier call as opportunity to reschedule. This probably ultimately reduced the no show rate. Limitations include small numbers over a brief intervention period. Conclusion: Pre-appointment reminder phone calls in addition to a 24-hour reminders can be a cost effective method to combat missed appointments by reminding patients to cancel, reschedule, or confirm the appointment. These results should be confirmed in a larger study with a more diverse population.
Multimodal Reminders Improve Abdominal Aortic Aneurysm Screening Rates

The US Preventive Services Task Force (USPSTF) recommends one-time abdominal aortic aneurysm (AAA) ultrasound screening for men aged 65 to 75 who have ever smoked. Rates of appropriate AAA screening has varied greatly across the United States. In 2015, 1.4% of eligible Medicare enrollees were screened for AAA. In 2012, the Cleveland Clinic reported an AAA ultrasound screening rate of 9.2%; VA Connecticut in 2009 reported a 26% screening rate; and University of Pittsburgh reported a 40.3% screening rate from 2013 to 2014. The objective of this study is to assess the current AAA screening rate at SUNY Downstate Medical Center Suite B Clinic and implement a quality improvement intervention to increase this rate.

Hotspotting ED visits over 1 year for patients in two Family Medicine Clinics

Purpose: Over utilization of the emergency department is a burden on the health care system both financially and physically on medical staff.2 High cost patients are called hot-spotters defined as patients who visit an emergency department (ED) four or more times in a year.1 This study focused on family medicine patients from two clinics in central Brooklyn who were found to have the most ED visits in the practice. The purpose of the study was to explore the factors around their ED presentations and propose possible interventions to decrease avoidable ED visits.

Method: Retrospective analysis of 1885 patients from Suite B and Suite O, two SUNY Downstate Family Medicine clinics, who had 1 or more ED visits from January 2018 to December 2018 using data from the EMR. Focused on the top 35 patients with the most ED visits, looking at their last 5 visits. These visits were further characterized by demographics, chief complaint, ED interventions, and need for inpatient admission.

Results: Of all the visits we reviewed, only 13% resulted in admission to the hospital, and 86% were discharged from the ED. Of all the patients discharged from the ED, 35% of them need no interventions. Another 27% of discharges only needed one intervention from IV, medications, imaging, specialist consult, to labs.

Discussion: The data shows that many of our visits to the ED were for non-essential services that could have been managed as an outpatient. This suggests that many of these visits were unnecessary and it would relieve strain on the hospital system to prevent these visits. Based on the data, we propose the following possible interventions to decrease avoidable ED visits: (1) increased patient education of common ED visit reasons, (2) a provider-run phone triage system available to patients, (3) increased walk-in capabilities, and (4) dedicated prenatal nursing staff. Many of these interventions could decrease the patient burden on the ED and save the system from costly expenses.
Chlamydia Screening Rates Among Women 16-24 years at our Family Practice Center

Intro: Chlamydia trachoma’s infection is the most common bacterial sexually transmitted disease in the US affecting > 2 million people. The USPSTF recommends a one time screening in all sexually active women between ages of 16-24 years. According to the CDC the overall screening rate for this age group is 50% and in New York it is 62% from 2105 data. To address barriers primary care offices have: Toprovided chlamydia education specific training and computer prompts for PCP. Educational posters/brochures for patients to inquire about testing.

Objectives: To determine current rate of chlamydia screening among age 16-24 years old women at our clinic. To create an intervention that provides clinician awareness of the need for chlamydia screening. To re-evaluate chlamydia screening rates post interventions.

Methods: The intervention consisted of placement of educational posters for patients and sending a quick reminder to PCP about the guidelines. We reviewed 100 charts between April-July 2018 pre-intervention and 85 charts between October-January 2019 post-intervention of women between the age of 16-24 years at our clinic. We noted whether or not they were sexually active and if chlamydia screening was done.

Results: Pre intervention screening rate was 75% which is higher than the national average rate of 50%. Post intervention screening rate changed insignificantly from 75% to 68%. Documentation of sexual activity status improved in the intended group of women.

Conclusion
Our rate of chlamydia screening is higher than the national average. The intervention did not improve the rate of screening in the studied population. There was an improvement in documentation of sexual activity status of young women that were properly identified as the group who did not require screening.