Fusion

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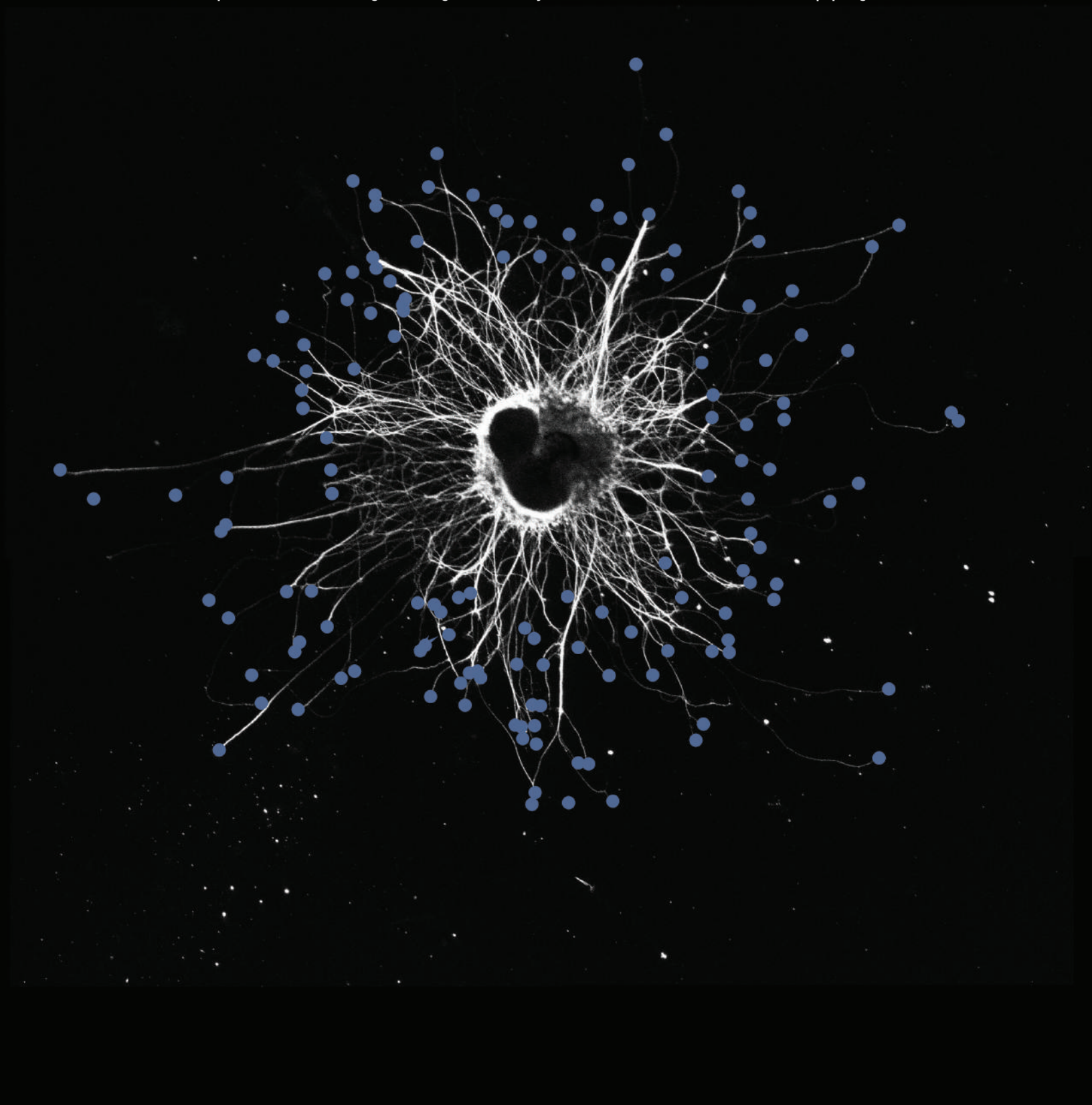

From the Editors

Michael Froehlich, MSII

Jacob Rubin, MSII

With the goal of highlighting the myriad of novel research carried out by the medical students of the George Washington University (GW) School of Medicine and Health Sciences (SMHS), we proudly present the 2017 edition of Fusion. The journal is an entirely student-run publication; everything from the abstracts to the cover artwork was provided by students.

Our goal as this year's co-presidents of the William H. Beaumont Medical Research Honor Society was to build upon the tremendous success of last year's journal. This year's edition was met with a record number of submissions, running the gamut from basic science to clinical public health research. We believe that our growing journal reflects an increasing trend of SMHS student participation in research and an expanding institutional emphasis on research here at GW.

We would like to offer special congratulations to Sharjeel Chaudhry, Brendan Campbell, and Lauren Jacobs, this year's first, second, and third prize winners, respectively, of the William H. Beaumont Medical Honor Society Student Research Award. Your research stood out among a truly impressive body of work and merits the opportunity to present to GW faculty and students at the 22nd Annual SMHS Research Day.

This year's edition of Fusion would not have been possible without the support of numerous individuals. First, we express our heartfelt gratitude to Fusion's faculty advisor, Robert H. Miller, Ph.D., senior associate dean of research and Vivian Gill Distinguished Research Professor. We would also like to thank Sara VanDommelen, research administrator, for her invaluable logistical support. We thank Douglas Nixon, M.D., Ph.D., professor and chair of microbiology, immunology, and tropical medicine and Walter G. Ross Professor of Basic Science Research at SMHS, for contributing this year's faculty letter. We thank the SMHS Office of Communications and Marketing for the design and production of Fusion. Last but not least, we offer a special thank you to our fellow classmates — those who volunteered their time to our Editorial Board,as well as our authors, without whom this journal would not exist.

We hope you will enjoy and learn as much as we did from reading this year's journal.

MICHAEL FROEHLICH, MSII
JACOB RUBIN, MSII
co-presidents of the William H. Beaumont Medical Research Honor Society

Fusion
is a publication of the George Washington University School of Medicine and Health Sciences William H. Beaumont Medical Research Honor Society.

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Explore Medical Research!

When I attended a seminar on the epidemiology of HIV infection and AIDS in Washington, D.C., chaired by Alan Greenberg, M.D. '82, M.P.H., professor and chair of the Department of Epidemiology and Biostatistics at the George Washington University (GW) Milken School of Public Health, I didn't know that it would be a life changing event, and lead me to move across the country from San Francisco and the University of California, San Francisco, to take up the chair of the Department Microbiology, Immunology, and Tropical Medicine (MITM) at GW in October 2013.

Our faculty's research spans basic through translational to clinical research, and is thus an ideal place for a medical student to experience the full spectrum of medical research.

The HIV epidemic in Washington, D.C., is extraordinary both in its magnitude and in the responses elicited to help turn it around. Black men who have sex with men living in the District still have a one in two chance of becoming HIV infected in their lifetime. The prevalence of HIV infection in Hispanic males and black females is around 2 percent — well above epidemic levels. In other words, just from the steps of our nation's government, an infectious disease epidemic of sub-Saharan proportions is occurring, and almost ignored. At the seminar, I saw that some groups in Washington were responding: the Department of Health, the National Institutes of Health (NIH), and GW through its developmental Center For AIDS Research (CFAR). That commitment from these groups, and others, inspired me to move to the East Coast, and to take up the position of chair at MITM.

As both a physician and a scientist, I am often asked what the research part of my job entails. I think of myself as studying "experimental medicine," which the British Medical Research Council refers to as: "Investigation undertaken in humans, relating where appropriate to model systems, to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments." I would add to this that valid animal models are extremely valuable in advancing scientific knowledge, but for my research they need to support what we are doing in human studies. Our studies usually start at the bench, but in some cases then can go into experimental systems, and potentially even into humans. Our NIH funded grant, BELIEVE, one of the Martin Delaney Collaboratories to Cure HIV, under the leadership of Catherine Bollard, M.D., professor of pediatrics and of MITM at SMHS; Greenberg; Brad Jones, Ph.D., assistant professor of MITM; and myself, plans for clinical trials of enhanced immunotherapy to eradicate HIV infection.

The MITM faculty at SMHS have long worked on infectious diseases of poverty, and HIV/AIDS is part of that mission, not only in a domestic context, but also internationally. Our faculty's research spans basic through translational to clinical research, and is thus an ideal place for a medical student to experience the full spectrum of medical research. Basic science research is one of the most exciting activities you can do as a medical student, and the techniques learned for research pay off in expanding your thinking for patient diagnoses. The scientific method helps hone skills you will use with your patients. Essentially basic science can be like a diagnostic analysis: knowing the background of the literature, or the patient; developing a hypothesis, or differential diagnosis; running experiments, or tests; interpreting data, or test results; developing conclusions, or a patient treatment plan; and devising follow up experiments, or a patient follow-up plan.

Our department also has strong programs in translational science. Research, for

example, could involve anything from validating biomarkers for cancer or to addressing parasitic infections.

My Message to the SMHS students is simple, get involved. Apply for a Gill Fellowship; write and visit MITM (or other departments); read about the department's research on the MITM website; come to our academic seminars and interest group meetings.

Discover the excitement of scientific and medical research!

DOUGLAS NIXON, M.D., PH.D., professor and chair of microbiology, immunology, and tropical medicine and Walter G. Ross Professor of Basic Science Research at SMHS

Protecting the Endothelium from Thromboinflammatory Injury Using Parmodulins

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Stimulation of protease-activated receptor 1 (PAR1) on endothelium by activated protein C (APC) is protective in animal models of inflammation, and APC has been used clinically in sepsis and wound healing. Clinical use of APC in sepsis, however, was terminated as it was compromised by APC's anticoagulant activity, which is associated with bleeding and limits its dosing in patients.[1] We used a small molecule approach to circumvent this problem. With support from the Molecular Libraries Program, we screened 302,457 compounds to identify small molecules that modulated PAR1-mediated platelet activation. One class of PAR1-targeted compounds, which we termed parmodulins, was found to act at the cytosolic face of PAR1, at the G-protein binding sites. When evaluated in endothelial cell cultures, parmodulin 1 (PM1) and parmodulin 2 (PM2) inhibited apoptosis induced by thrombin, TNF-α, or staurosporine, in a manner similar to APC.2 PAR1 knockdown using siRNA abolished these protective effects, demonstrating that parmodulins elicit a cytoprotective pathway by acting through PAR1.

To assess the mechanism of action of parmodulin cytoprotection, we first evaluated proximal signaling mechanisms. Parmodulins stimulated phosphorylation of PI3-kinase and Akt in endothelium. Inhibition of Gβγ blocked parmodulin-induced phosphorylation of Akt, indicating that parmodulins act at the cytosolic face of PAR1 by releasing Gβγ. Transcriptional profiling of over 30,000 genes and specific evaluation of NF-κB transcriptional activation showed that exposure to PM2 blocked TNF-α-induced transcriptional activation. In addition to interfering with inflammatory signaling, parmodulins stimulated the upregulation of cytoprotective proteins such as stanniocalcin-1.

Since our premise was that parmodulins could achieve cytoprotective effects without anticoagulant effects, we compared dose curves of APC versus PM2 in both apoptosis assays and standard clotting assays. APC prolonged the aPTT at concentrations lower than those required to achieve cytoprotection of the endothelium. The low APC concentration used in our study was similar to plasma concentrations measured in clinical studies. Hence, these data were consistent with the fact that clinical bleeding was observed at doses of APC used for sepsis. In contrast, despite inhibiting apoptosis as effectively as APC, PM2 had no effect on plasma aPTT at any concentration. Nonetheless, PM2 was able to inhibit lipopolysaccharide (LPS) and tumor necrosis factor-α (TNF-α) induced thrombin generation and FXa activation on endothelium owing to its cytoprotective effect.

PM2 also prevented TNF-α-induced accumulation of platelets on endothelium in bioengineered microvessels. These data demonstrate that PM2 can reduce inflammation-induced endothelial pro-thrombotic phenotype even without directly inhibiting coagulation factors. To assess the endothelial protective effects of PM2 in vivo, we evaluated leukocyte rolling in cremaster venules of mice. Infusion of PM2 significantly reduced surgery-induced leukocyte rolling flux compared to vehicle-treated mice. We also monitored soluble E-selectin levels in LPS-induced inflammation because these selectins are critically involved in leukocyte rolling. Treatment of mice with PM2 significantly reduced the LPS-induced release of soluble E-selectin. Previously, we demonstrated that PM2 blocked platelet accumulation in a mouse laser injury model of thrombus formation. We now show that infusion of PM2 also significantly reduces fibrin accumulation to 25 percent of control ($p<0.001$) at the site of laser injury.

Together, our data indicate that PM2 exerts endothelial-mediated anti-inflammatory, anti-coagulant and anti-thrombotic effects in vitro and in vivo. These results demonstrate the utility of modulating PAR1 at the cytosolic face and could represent an alternative approach to APC in the treatment of thromboinflammatory disorders like sepsis.

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Few High-Risk Patients Eligible for Hepatitis C Virus Screening Received Appropriate Testing: A Community-Based Safety-Net Hospital Experience

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	OR	95% CI	P-Value
Male (vs. female)	1.61	0.86–3.01	0.13
1945–65 Birth cohort	0.34	0.10–1.19	0.09
Non-Hispanic white	1.00	Reference	–
Black	2.59	1.21–5.54	0.01
Asian	5.80	2.26–14.91	< 0.001
Hispanic	10.93	4.41–27.10	< 0.001

TABLE: Multivariate Logistic Regression Predicting Acceptance of HCV Testing

BACKGROUND: Successful eradication of chronic hepatitis C virus (HCV) relies on effective screening programs for early detection and linkage to care. However, awareness of HCV screening guidelines may be lacking, especially among urban safety-net populations with a high prevalence of socioeconomically disadvantaged non-English speaking minorities.

AIM: To evaluate rates of HCV screening and HCV awareness among patients at high risk for chronic HCV at a diverse safety-net hospital

METHODS: A prospective cohort study of consecutive adults undergoing outpatient endoscopy from July 2015-March 2016 evaluated HCV screening rates among high-risk patients (based on U.S. Preventative Services Task Force guidelines), with focus on birth cohort (1945–65) and risk-based (history of drug use, incarceration, blood transfusion prior to 1992) factors. Awareness of prior HCV results and rates of accepting HCV testing were evaluated with chi-square testing and multivariate logistic regression.

RESULTS: Among 869 patients, 65.5% (n=569) were high risk for chronic HCV (51.3% male, 57.8% 1945-1965 birth cohort, 4.5% history of drug use, 6.2% history of incarceration, 5.8% blood transfusion, 9.8% HIV). Among this cohort, 30.6% received prior HCV testing, of which 36% were aware of test results. HCV-positive patients were more likely than HCV negative patients to be aware of results (90% vs. 27.7%, p<0.001). Among high-risk patients offered HCV testing, 83.9% accepted. Compared to non-Hispanic whites (64%), blacks (80.6%), Asians (89.6%), and Hispanics (93.7%) were more likely to accept testing, p<0.001. Non-English speaking patients were more likely to accept testing (91% vs. 77.5%, p<0.001). Patients born in 1945-1965 were less likely to accept testing (82.6% vs. 91.9%, p=0.06). On multivariate regression, blacks, Asians, and Hispanics were all significantly more likely to accept HCV testing compared to non-Hispanic whites (Table).

CONCLUSION: Among adults presenting for outpatient endoscopy at an urban safety-net hospital, 65.4 percent were high risk for HCV, of which only 30.6 percent received prior testing. Of those who received prior testing, only 36 percent were aware of results. Lower rates of test acceptance among the 1945–65 birth cohort is concerning given higher risks among this group.

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Germline ETV6 Mutations Confer Susceptibility to Acute Lymphoblastic Leukemia and Thrombocytopenia

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Somatic mutations affecting ETV6 often occur in acute lymphoblastic leukemia (ALL), the most common childhood malignancy. Inherited mutations of transcription factors have also recently been associated with susceptibility to acute leukemia. However, the genetic factors that predispose to ALL remain poorly understood. Here, we report two unrelated kindreds with inherited mutations in ETV6, the gene encoding the transcription factor ETS variant 6. These families were characterized by a low platelet count (thrombocytopenia) and ALL. Sequencing a panel of genes identified germline ETV6 mutations associated with leukemia and thrombocytopenia in multiple individuals tested. We identify a novel germline ETV6 p. L349P mutation in a kindred affected by thrombocytopenia and ALL (Kindred 1, Figure 1). A second ETV6 p. N385fs mutation was identified in an unrelated kindred characterized by thrombocytopenia, ALL, and secondary myelodysplasia/acute myeloid leukemia (Kindred 2, Figure 1). Leukemic cells from the proband in the second kindred showed deletion of wild type ETV6 with retention of the ETV6 p. N385fs. Enforced expression of the ETV6 mutants revealed normal transcript and protein levels, but impaired nuclear localization. Accordingly, these mutants exhibited significantly reduced ability to regulate the transcription of ETV6 target genes. Our findings highlight a novel role for ETV6 in leukemia predisposition.

ETV6 encodes an ETS family transcription factor that is frequently rearranged or fused with other genes in human leukemias of myeloid or lymphoid origin.[1] Also known as the TEL oncogene, ETV6 is a sequence-specific transcriptional repressor, regulated by auto-inhibition and self-association.[2,3] Descriptions of ETV6 largely focus on the ETV6/RUNX1 fusion, which is a product of a t(12;21) chromosomal translocation, the most common genetic abnormality in pediatric ALL.[4] While somatic deletions or mutations in ETV6 are increasingly recognized in ALL, nothing is known regarding the impact of germline ETV6 mutations.[5] Here, we extend the description of the clinical phenotype and functional effects associated with novel germline ETV6 L349P and ETV6 N385fs mutations, both of which reside in the highly conserved ETS DNA binding domain and co-segregate with disease in two unrelated kindreds affected by thrombocytopenia and ALL.

These findings suggest that germline ETV6 mutations cause a new type of heritable leukemia. This discovery makes possible the presymptomatic diagnosis of leukemia susceptibility in families with germline ETV6 mutations and also provides new information on the causes of leukemia.

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Clinical Effects of Synthetic Cannabinoid Exposure in Patients Admitted to the Intensive Care Unit

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Synthetic cannabinoids (SCs), also known as "K2" or "Spice," are the second most common drugs of abuse after marijuana.[3] These synthetic chemicals are typically sprayed on plant material, which is then most commonly smoked or ingested, providing a relaxing and stimulating effect. The adverse effects of SC toxicity are heterogeneous and can include anxiety, agitation, emesis, hallucinations, convulsions, psychosis, tachycardia, and unresponsiveness.[2] Serious systemic effects include stoke, renal failure, myocardial infarction, respiratory failure, and death.[1] In 2015, the American Association of Poison Control reported that SC cases had increased by 562 percent from March to April of that year. In May 2015 alone, more than 40 deaths in the United States were associated with SC use.[1]

SC abuse is a growing and serious public health concern that demands further clinical investigation, increased public education, as well as further legislative and drug enforcement efforts. Previous research has focused on presentation and outcomes of patients who were reported to poison control centers or admitted to the emergency department (ED).[4] Other studies documented significant differences between SCs and traditional marijuana, with agitation, neurotoxicity, and cardiotoxicity more pronounced in patients who used SCs.[5] Despite well-documented severe effects of SC use, literature regarding the hospital course and outcomes after SC intoxication is scarce. Further research is necessary to improve physician understanding of the potential harmful effects of SC use and to identify patients at greatest risk for adverse outcomes. This study characterizes the clinical presentation and hospital course of patients with reported SC exposure requiring Intensive Care Unit (ICU) admission.

A retrospective case series was done of patients admitted to the medical or cardiac ICUs of an urban tertiary care center with reported SC exposure from Jan. 1 to Dec. 31, 2015. Demographic variables, Sequential Organ Failure Assessment (SOFA) scores, clinical parameters documenting the effects, and hospital course were recorded.

Twenty-three patients met inclusion criteria. Median age was 47 (Inter-Quartile Range [IQR], 32-54); 82.6% were male; 78.3% were black. Patients were most commonly tachycardic (56%) and hypertensive (65%) on admission; none were febrile. The initial chest X-ray and electrocardiogram were abnormal in 43.4% and 68.4% of patients respectively. Myocardial infarction occurred in 8.7%, resulting in heart catheterization. Brain imaging was abnormal in 5% of patients. The most common concomitant exposures were marijuana (30.4%) and benzodiazepines (26.1%).

SOFA scores peaked on admission at 6 and decreased over the next three days, rising thereafter for patients requiring continued ICU care. SOFA scores were primarily driven by altered neurologic status and respiratory failure. Over 30% of patients had seizures as a part of presentation, 91% required mechanical ventilation, 18.2% required vasopressors, and 5% needed dialysis. Other invasive procedures included central and arterial lines (8.7%), lumbar puncture (4.3%), and heart catheterization (8.7%). Median hospital and ICU lengths of stay were 2.6 (IQR 1.4-3.5) and 1.6 (IQR 0.9-2.5) days, respectively. The mean hospital charge was $49,140. All patients survived the index hospitalization with one patient dying on a subsequent hospitalization during the study period.

In conclusion, synthetic cannabinoid exposure can result in serious adverse effects and significant organ dysfunction, particularly neurologic and respiratory. While generally nonfatal, successful treatment requires a high degree of complexity and cost.

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In-Person Clinic-Based versus Smartphone Application-Based Plans for Weight Loss among the Overweight and Obese

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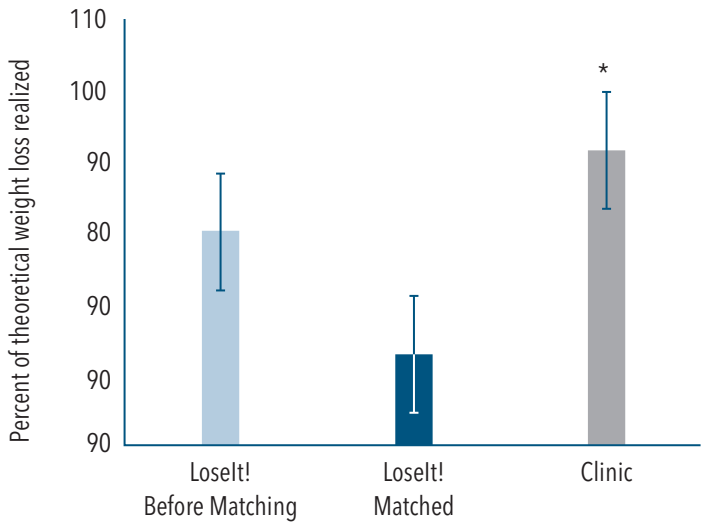

FIGURE: Descriptive Information from Matched Participants Before Analysis

BACKGROUND: The prevalence of obesity in the United States (U.S.) among adult men and women continues to rise. Obesity is a major health problem among the U.S. population, commonly increasing the risk of significant comorbidities such as Type 2 diabetes mellitus, dyslipidemia, and cardiovascular diseases.[1,2] While in-person interventions that address the dietary, exercise, and behavioral aspects of obesity are common, a new wave of weight-loss strategies has emerged with a greater emphasis on technology and internet-based approaches.[3,4,5]

METHODS: This study compared the efficacy of a traditional in-person weight-loss approach utilized by the Johns Hopkins Weight Management Center to a weight-loss treatment via the smartphone application (app), LoseIt! It was hypothesized that the comparison between the Johns Hopkins Weight Management Center protocol and the LoseIt! App program over a 12-week period would show no difference in the percent of actual weight loss compared to theoretical weight loss, i.e. compliance. Using a case-control analysis, 92 Johns Hopkins patients were matched to 3,380 LoseIt! App participants based on gender, age, starting weight, starting BMI, caloric restriction level, and estimated total daily energy expenditure with light activity.

RESULTS: Clinic patients achieved 94.1% of their theoretical weight loss compared to LoseIt! users who achieved 62.8% after matching. In addition, clinic patients achieved 10.5% total weight loss compared to LoseIt! users who lost 6.1% after matching. Overall, clinic patients showed a significantly greater percent

of realized theoretical weight loss or compliance (mean = 28.6, SD = 9.6, p > 0.003) compared to LoseIt! users. Moreover, clinic patients showed a significantly greater percent of total weight loss (mean = 3.2, SD = 0.9, p > 0.001) compared to LoseIt! users.

DISCUSSION: While weight loss programs are ubiquitous, historically, long-term compliance to these programs is often limited. We found that both clinic-based and technology-based weight-loss programs provided a degree of weight-loss success when participants are matched for demographic and biologic characteristics. These findings suggest that application-based weight-loss programs may have a place in weight control. However, as shown here, they may not be as efficacious as a clinic-based intervention. Nonetheless, this technology may be particularly helpful as a cost-effective means for influencing patient dietary and exercise behaviors. Future studies should examine whether smartphone applications like LoseIt! would produce an additive benefit when used in combination with more traditional approaches to weight control.

Characteristics	Clinic N = 92 n (%)	LoseIt! N = 3,380	P value
Gender			0.51
Female	71 (77)	2,505 (74)	
Male	21 (23)	875 (26)	
Age			< 0.001
21–30	8 (9)	727 (21)	
31–40	11 (12)	883 (26)	
41–50	33 (36)	693 (21)	
51–60	33 (36)	693 (21)	
61–70	7 (7)	213 (6)	
Age at first day, mean (SD)	48.0 (10.0)	41.7 (11.8)	< 0.001
Start weight, mean (SD)	240.7 (51.8)	201.6 (44.9)	0.001
First BMI, mean (SD)	38.3 (7.1)	31.9 (6.2)	< 0.001
First BMI, category			0.001
Overweight	8 (9)	1,492 (44)	
Obesity I	28 (30)	1,018 (30)	
Obesity II	21 (23)	512 (15)	
Extreme obesity	35 (38)	358 (11)	
Calorie restriction plan, mean (SD)	1,131 (244)	1,513 (337)	<0.001
Calorie restriction plan (kcal)			<0.001
0–750	0 (0)	8 (0)	
750–1,250	78 (85)	775 (23)	
1,250–1,750	10 (11)	1,747 (24)	
2,250–2,750	0 (0)	34 (1)	
Daily energy expenditure, light activity, mean (SD)	2,454 (414)	2,261 (390)	<0.001
Light activity energy expenditure (kcal)			<0.001
1,500–2,000	10 (11)	1,054 (31)	
2,000–2,500	43 (47)	1,365 (40)	
2,500–3,000	31 (34)	821 (24)	
3,000–3,500	7 (8)	135 (4)	
3,500–4,000	1 (0)	5 (1)	
Percent of theoretical weight loss achieved, mean (SD)	91.4 (68.4)	80.1 (526.8)	0.84
Percent of weight loss, mean (SD)	10.5 (4.5)	6.1 (4.7)	< 0.001

TABLE 1: Descriptive Information from Matched Participants Before Analysis

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Depressive Symptoms and the Health Care Experience of Adolescents with Diabetes

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Guidelines suggest annual screening for depressive symptoms in pediatric diabetes care.[1] Depressive symptoms are associated with poorer glycemic control[2] and may contribute to the decline in diabetes self-care seen in adolescents and young adults (AYA) with Type 1 diabetes (T1D).[1] Depressive symptoms also may influence AYA interaction with their diabetes care provider. Understanding relationships between depressive symptoms and health care interactions will inform optimal diabetes care for this age group.

Our overarching goal was to evaluate depressive symptoms in AYA with T1D; we did this in two ways, using both clinically derived data and data from an ongoing longitudinal study. The Child and Adolescent Diabetes Program at Children's National Health System implemented routine physician-directed depression screening for all youth aged ≥ 13 years. We evaluated this clinic-based screening process as part of overall quality improvement, and analyzed baseline data from the ongoing study to identify relationships between depressive symptoms, interactions with health care providers, and glycemic control.

Number of screens	514
Mean score	4.08
Score range	0–26
Moderate depressive symptoms	11.59%
Severe depressive symptoms	1.27%
Current suicidal ideation	6.72%

TABLE 1: PHQ 9-A Results in Clinic-Based Screening

In clinic-based screening efforts, adolescents completed the Patient Health Questionnaire-9 modified for Adolescents (PHQ 9-A) at a routine clinic visit (Table 1). Through interviews, all providers agreed clinic-based depression screening was valuable and easy to implement. Areas for improvement included screening younger patients, streamlining administrative procedures, and integrating screens with the electronic medical record.

Participants (n = 76) in the longitudinal study completed the Center for Epidemiological Studies Depression Scale (CES-D); scores ≥ 16 are considered at risk for depression. Clinic visits were audio-recorded. Quality of communication was coded using the Roter Interactional Analysis System (RIAS), which generated a measure of patient-centered communication (PCC). Participants rated their interactions with their health care provider during the clinic visit using the Health Care Climate scale (HCC). Hemoglobin A1c (HbA1c) values were extracted from medical records.

Results (Table 2) indicate that 28.9% of this sample were at risk for depression. CES-D scores were directly associated with HbA1c ($r(74) = 0.232$, $p < 0.05$) and PCC ($r(67) = 0.343$, $p < 0.01$). There was no significant association between CES-D score and AYA HCC score. AYA HCC score was negatively correlated with HbA1c ($r(72) = -0.295$, $p < 0.05$). PCC was not significantly associated with HbA1c.

Our data suggest that depressive symptoms are relatively prevalent in AYA with T1D and are associated with glycemic control, reinforcing the importance of routine depression screening in this population.

We have shown that depressive symptoms are associated with HbA1c and PCC in AYA; however, the causality underlying these relationships is not yet understood.

Improved detection of depressive symptoms may reduce diabetes complications; however, incorporating screening procedures into a busy clinic requires cooperation from providers, administrative staff, and the psychology team. As evidenced by provider interviews, to achieve such cooperation, those involved must understand their roles and feel supported, and policies and procedures must be periodically reviewed and revised.

Elevated depressive symptoms were associated with greater PCC, suggesting that providers might have responded to patient mood by encouraging active participation during the clinic visit to both gather information and increase engagement. This finding differs from studies with adults, which have found no difference in PCC based on patient depressive symptoms.

Further study is needed to more fully understand the complex associations among mood and health communication, and how the provider relationship may contribute to overall positive health outcomes. We have shown that depressive symptoms are associated with HbA1c and PCC in AYA; however, the causality underlying these relationships is not yet understood. Elucidating this will inform development of future interventions.

	%		
Participant sex (% female)	53.9		
Insulin pump use	32.1		
Basal bolus regimen	33.3		
Fixed dose insulin therapy	34.6		
White, non-Hispanic	50.0		
Racial minorities	42.1		
No race/ethnicity reported	1.3		
Annual family income ≥ $100,000	56.7		
	Range	Mean	SD
Participant age (years)	16–20	17.77	1.22
Duration of diagnosis (years)	1.22–18.55	8.20	4.41
HbA1c (%)	5.6–14.1	8.20	4.41
CES–D score	0–44	13.11	9.80
Clinic visit length (min)	2.63–48.98	21.28	10.12

TABLE 2: Demographic Information and Study Results

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Lip Service: What Veterans' Illness Narratives Teach Us about the Mental Health Needs of an At-Risk Population

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	Frequency	Percentage of MH	Percentage of Total *
Mental health	42	–	25.5
Anxiety	5	11.9	3.0
Depression	7	16.7	4.2
PTSD	8	19.0	4.8
Substance use	23	54.8	13.9
Suicidal ideation	8	19.0	4.8

TABLE: Frequency of Narratives that Contained Mental Health Themes
* total narratives = 165

Mental health disorders have been identified as some of the most common clinical manifestations American military veterans face, affecting up to 25 percent of veterans at rates that are higher than those of their civilian counterparts.[1] Given the odds of veterans developing a mental illness, it is important for health care professionals to attempt an understanding of how they make sense of their illness experiences. One of the major ways humans make sense of their experiences is through the telling of narratives. Narratives are a crucial tool for making sense of life experiences and for understanding ourselves and others.[2,3,4] It is fortuitous for us then that medicine involves stories.

Using a grounded theory approach, the present study conducted constant comparative analysis, wherein similar and dissimilar data are first identified and then compared in order to generate knowledge about common patterns and themes within human experience. It is important to note that this approach does not involve coding narrative variables as some qualitative methodologies demand, but rather the interpretation of themes in the narratives. The 165 narratives examined in this paper were collected by third-year medical students during their inpatient medicine clerkship at the DC VA Medical Center (described in Chretien et al., 2015).[5]

[V]eterans generally avoided sharing details of their PTSD diagnoses, except when describing their nightmares or instances of moral injury, defined as actions taken by veterans in the line of duty that transgress deeply held moral beliefs and expectations.

Researchers selected narratives for inclusion if they contained particular words related to mental health. It is interesting to first note with what frequency veteran patients spontaneously shared their experiences of mental health, especially while on a general medicine unit (see Table). In fact, one recurring theme among mental health narratives was the complicated relationship between physical and mental illness. One patient describes his experience with COPD, CHF, diabetes, and anxiety: "Trying to balance all of these is a challenge … . Meanwhile the anxiety overlays all of it and makes it harder" (049). Another student recognizes this complexity in his patient's narrative: "He tells me that he has suffered from depression the last couple of years, and to me it sounds like both his diabetes and depression are strongly linked" (112).

Results suggest that veterans generally avoided sharing details of their PTSD diagnoses, except when describing their nightmares

or instances of moral injury, defined as actions taken by veterans in the line of duty that transgress deeply held moral beliefs and expectations. Substance use was the most commonly mentioned mental health condition. Many patients attributed their physical illness to their substance use; others attributed their substance use to their illness. Suicidal ideation was endorsed by 4.8 percent of the narrative authors and was most often in the form of passive death wishes. Patients also shared the things that deterred them from abusing drugs and alcohol and from taking their own lives, important potential points of intervention.

Using veterans' personal narratives as the primary data source, this paper has identified common themes regarding mental health among military veterans to better prepare health care professionals to recognize and treat mental illness in this at-risk population. This investigation expands on a body of knowledge gathered qualitatively about the mental health needs of our military veterans. This knowledge, gained by simply allowing patients to share their personal narratives, allows us to better understand and thus serve their health care needs. The importance of narrative medicine, as both a tool for research and therapy, cannot be understated.

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Rates of HIV, Malaria, and TB Affecting Pregnancies in the United States, 1998-2011

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OBJECTIVES: Our objective was to compare the rates at which HIV, malaria, and TB affect pregnancy outcomes in the United States using national data from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS).

METHODS: We explored differences in pregnancy outcomes between patients with HIV, malaria, and TB diagnoses and compared patterns in outcomes over time, focusing on the following two study cycles: 1998–2000 and 2009–11. We also compared the outcomes of these patients to those pregnant without these diagnoses. We identified pregnancy hospitalizations that resulted in delivery, as well as pregnancy outcomes, using the appropriate International Classification of Disease, Ninth Revision (ICD-9), and V codes. Statistical weighting of the data produced samples that were nationally representative. SAS software and chi-square testing was used to determine p-values.

RESULTS: Overall, there were more cases of HIV, followed by TB, then malaria in pregnancy in both time periods. Women with HIV were more likely to be younger (5.2% vs 6.8% age 0-20; $p<0.05$) in the later time period. Cesarean delivery was more likely for HIV pregnant women in the later time period (57.9% vs. 44.3%; $p<0.0001$) but the odds ratio for undergoing cesarean delivery compared to controls was comparable during both time periods (OR 2.86 vs. 2.84). Complications such as other infections in pregnancy (sexually transmitted infections or urinary tract infections) were less likely in the later time period for women with HIV. In the later years, patients with TB were significantly more likely to experience comorbid diabetes, fetal distress, preterm labor, and urinary tract infections than the control group.

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1998–2000										
Complication	HIV (n=3,803)	OR (95% CI)	P	Malaria (n=144)	OR (95% CI)	P	TB (m=727)	OR (95%CI)	P	Control (n=11 967 487)
Cesarean delivery	1,649 (43.7%)	2.84 (2.45, 3.29)	<0.001	41 (29.1%)	1.50 (0.66, 3.41)	0.3	216 (30.9%)	1.63 (1.14, 2.34)	0.01	520 908 (21.5%)
Diabetes (comorbidity)	60 (1.6%)	2.39 (1.35, 4.23)	0.002		–		10 (1.5%)	2.22 (0.55, 8.99)	0.25	16 246 (0.7%)
Fetal distress	32 (0.9%)	0.45 (0.20, 1.02)	0.05		–		15 (2.1%)	1.12 (0.35, 3.56)	0.85	45 566 (1.9%)
Gestational diabetes	111 (2.9%)	0.83 (0.53, 1.28)	0.39	11 (8.0%)	2.38 (0.56, 10.04)	0.2	35 (5.0%)	1.43 (0.67. 3.07)	0.36	85 293 (3.5%)
Hypertension (comorbidity)	60 (1.6%)	3.04 (1.72, 5.39)	<0.0001		–					12 774 (0.5%)
Intrauterine fetal death	69 (1.8%)	3.034 (1.78, 5.15)	<0.0001		–				–	14 810 (0.6%)
Liver disorders of pregnancy	27 (0.7%)	12.71 (5.26, 30.73)	<0.0001		–				–	1,358 (0.1%)
Premature Rupture of Membranes	369 (9.8%)	1.72 (1.35, 2.20)	<0.0001		–		64 (9.0%)	1.61 (0.91, 2.86)	0.01	142 737 (5.9%)
Pre-eclampsia	234 (6.2%)	1.86 (1.38, 2.51)	<0.0001	10 (7.4%)	2.24 (0.53, 9.45)	0.3	26 (3.8%)	1.10 (0.45, 2.70)	0.84	82 609 (3.4%)
Preterm labor	599 (15.9%)	2.61 (2.14, 3.18)	<0.0001	22 (15.5%)	2.52 (0.87, 7.29)	0.1	90 (12.9%)	2.05 (1.24, 3.36)	0	162 435 (6.8%)
Sexually transmitted infections	105 (2.8%)	18.14 (11.60, 28.38)	<0.0001		–				–	3,737 (0.2%)
Urinary tract infection	352 (9.3%)	2.97 (2.31, 3.82)	<0.0001	15 (10.9%)	3.54 (1.06, 11.74)	0	49 (7.0%	2.17 (1.14, 4.41)	0.02	80 179 (3.3%)

TABLE 1A: Pregnancy Complications of Infectious Disease Patients vs. Control Group During Early and Late Time Periods, 1998–2000

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CONCLUSIONS: The adverse outcomes studied here are much more common among patients with infectious disease, especially those with HIV. Although the prevalence of cesarean delivery among women with HIV has gone up over time, the odds ratio compared to controls has not changed from early to late time period. Infectious disease patients under obstetric care require continued comprehensive care in order to prevent adverse outcomes in pregnancy.

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2009–11										
Complication	HIV (n=3,401)	OR (95% CI)	P	Malaria (n=152)	OR (95% CI)	P	TB (m=723)	OR (95%CI)	P	Control (n=12 173 217)
Cesarean delivery	1,959 (57.7%)	2.86 (2.45, 3.32)	<0.001	10 (32.9%)	1.03 (0.48, 2.19)	0.9	231 (32.2%)	0.99(0.70, 1.41)	0.98	797 124 (32.3%)
Diabetes (comorbidity)	79 (2.3%)	2.15 (1.31, 3.54)	0.002		–		23 (3.1%)	2.92 (1.19, 7.21)	0.01	27 054 (1.1%)
Fetal distress	54 (1.6%)	0.76 (0.42, 1.39)	0.38		–		34 (4.7%)	2.34 (1.09, 5.02)	0.02	50 934 (2.1%)
Gestational diabetes	175 (5.2%)	0.86 (0.62, 121)	0.39		–		33 (4.7%)	0.78 (0.36, 1.66)	0.51	146 407 (5.9%)
Hypertension (comorbidity)	90 (2.7%)	4.73 (2.99, 7.47)	<0.001		–				–	14 139 (0.6%)
Intrauterine fetal death	48 (1.4%)	2.47 (1.32, 4.62)	0.004		–				–	14 421 (0.6%)
Liver disorders of pregnancy	43 (1.3%)	9.27 (4.78, 17.96)	<0.0001		–				–	3,389 (0.1%)
Premature rupture of membranes	239 (7.1%)	1.42 (1.05, 1.91)	0.02		–		24 (3.4%)	0.65 (0.27, 1.60)	0.35	125 217 (5.1%)
Pre-eclampsia	218 (6.4%)	1.54 (1.14, 2.09)	0.005	14 (9.3%)	2.29 (0.70, 7.55)	0.2	19 (2.6%)	0.615 (0.22, 1.65)	0.32	105 201 (4.3%)
Preterm labor	549 (16.2%)	2.55 (2.08, 3.13)	<0.0001		–		86 (11.9%)	1.79 (1.08, 2.98)	0.02	173 551 (7.0%)
Sexually transmitted infections	86 (2.5%)	14.90 (9.19, 24.17)	<0.0001		–			–		4,299 (0.2%)
Urinary tract infection	212 (6.3%)	4.72 (3.45, 6.45)	<0.0001		–		14 (5.5%)	4.13 (2.02, 8.43)	<0.0001	34 351 (1.4%)

TABLE 1B: Pregnancy Complications of Infectious Disease Patients vs. Control Group During Early and Late Time Periods, 2009–11

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Radiation Therapy Improves Survival in Elderly Patients with Locally Advanced Non-Small Cell Lung Cancer:A Population-Based Analysis

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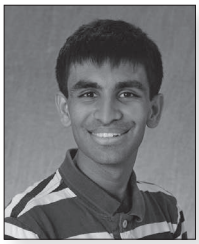

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Age	RT given?	Estimate	95% Confidence Interval Lower Bound	Upper Bound
60-64y	No	6.000	5.442	6.558
	Yes	12.000	11.333	12.667
	Overall	9.000	8.577	9.423
65-69y	No	5.000	4.544	5.456
	Yes	11.000	10.396	11.604
	Overall	8.000	7.604	8.396
70-74y	No	4.000	3.662	4.338
	Yes	10.000	9.450	10.550
	Overall	6.000	5.678	6.322
75-79y	No	3.000	2.711	3.289
	Yes	9.000	8.476	9.524
			5.705	6.295
80-84y	No	2.000	1.782	2.218
	Yes	8.000	7.421	8.579
	Overall	4.000	3.709	4.291
85+y	No	2.000	1.848	2.152
	Yes	7.000	6.258	7.742
	Overall	3.000	2.788	3.212
Overall		6.000	5.858	6.142

TABLE 1: Median OS, RT vs No Treatment, Stratified by Age

PURPOSE/OBJECTIVES: Stage 3B non-small cell lung cancer (NSCLC) is very advanced and is traditionally considered a surgically unresectable disease. This is especially true for elderly patients (60-plus years of age), whose various comorbidities are contraindicative for surgery, leaving them with chemoradiation therapy in an attempt to contain disease and improve survival. The present literature has a dearth of research showing whether this aggressive therapy results in an improvement in overall or cause-specific survival, as compared with purely supportive care (no treatment). We hypothesize that stage 3B NSCLC patients of 60-plus years of age treated with radiation will have better overall survival (OS) and cause-specific survival (CSS) than those left untreated.

METHODS: We selected 29,790 patients of 60-plus years of age, diagnosed with stage 3B NSCLC between 2002 and 2012, given either radiation therapy (RT) or no treatment from the Survival, Epidemiology and End Results Program (SEER) database. As SEER does not release chemotherapy data due to uncertainty regarding data completeness, such data were not included in our analysis. We conducted multivariable (Cox-proportional hazard) analysis, adjusting for age, race, sex, year of diagnosis, and tumor site, and univariable (log-rank) analysis to evaluate the impact of RT on survival.

RESULTS: Forty-two and a half percent of patients were given RT, while the remaining 57.5% were not treated. Patient median age range was 70 – 74 years. The racial composition of the study population was 80.4% white, 11.9% Black, 7.5% other race, .2% unknown race. Forty-four percent of patients were female, 56% were male. Distribution of tumor site within the population was 23.5% lower, 34.8% middle, and 47.2% upper lung, as well as 6.7% within the main bronchus, 1.4% with overlapping lesion of the lung, and 17.8% NOS. Univariable analysis showed RT was associated with an improvement in median and five-year survival compared to no treatment. Median OS was 10 vs three months, and CSS was 11 vs four months in patients given RT vs those untreated (P<.0001). Five-year OS

was 7.8% vs. 2.4% of patients, and CSS was 11.2% vs. 3.8% in patients given RT vs. those untreated (P<.0001). Multivariable analysis showed better OS for those given RT with Hazard Ratio (HR) = 0.605 (95% CI = .59,.621, P<.0001), and better CSS with HR = 0.606 (95% CI = .59,.623, P<.0001). Both median OS and CSS worsened with increased age, and RT improved survival in all age groups.

CONCLUSION: The results of our univariable and multivariable analyses suggest improvement in both OS and CSS for stage 3B NSCLC patients 60-plus years of age, given RT, as compared to no treatment. Approximately equal HRs for OS and CSS (.605 and 0.606, respectively) suggest the impact of confounding factors was insignificant. Our analysis was limited by absence of data on chemotherapy and comorbidities (SEER does not record). Further research ought to be done in the form of an RCT to confirm our findings.

Medical Resource Utilization of Outpatient Care for Children with Neurofibromatosis Type 1

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Neurofibromatosis Type 1 (NF1) is an autosomal dominant tumor predisposition syndrome occurring in 1:3,000 births.[1] Children with NF1 frequently develop manifestations affecting their central nervous system (CNS), musculoskeletal (MSK) system, peripheral nervous system, and cognitive/behavioral functions. Many of these manifestations persist throughout life, requiring multiple medical and surgical interventions, and have a significant impact on quality of life.[2]

The medical resource utilization and economic burden of caring for children with NF1 is unknown. Prior NF1 research has focused on specific manifestations that have inherent selection bias and do not accurately reflect the incidence and resource utilization of these morbidities. In order to identify which disease manifestations are in the most need of improved clinical algorithms and novel therapeutics, the frequency and type of resources utilized (i.e. diagnostic imaging and specialty visits) must be determined.

The current study sought to identify which manifestations of NF1 utilize the most health care resources and validate the accuracy of using International Classification of Diseases, Ninth Revision (ICD-9) diagnostic codes to identify patients with a clinical diagnosis of NF1.

The electronic health record (EHR) at The Children's Hospital of Philadelphia (CHOP) was queried to identify patients seen between January 2011 and December 2015 whose visit contained the ICD-9 code 237.71. Subjects were excluded if the clinical or genetic diagnosis could not be confirmed. For eligible subjects, the frequency of disease manifestations, MRI scans, and specialty visits over the five-year study period were recorded. The positive predictive value (PPV) of identifying subjects using the ICD-9 code was calculated.

Nine-hundred-eleven subjects with NF1 were included (ages 0.7 to 69.5 years, median = 12.9; 51% female). Fifty-four patients could not be confirmed and were excluded. The most common manifestations were cognitive/behavioral (42%), followed by CNS abnormalities (37%), plexiform neurofibromas (32%), MSK (21%), and other (19%).

Understanding the economic costs of caring for children with NF1 will help identify opportunities to improve resource utilization and clinical care as well as encourage academic and industry institutes to partner in therapeutic development for this devastating disease.

A total of 13,643 outpatient provider visits occurred, with ophthalmology (18%) and oncology (23%) being the most frequent. Subjects underwent a total of 4,527 MRI scans; 63% required sedation. Brain MRIs were the most common (N = 2,161). Treatment with prescription medications occurred in 13% of subjects for cognitive and behavioral disorders.

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The 237.71 ICD-9 code accurately identified subjects with a confirmed diagnosis of NF1 (PPV = 94.4%) if the code was present once in the subject's chart. The PPV increased to 98.2% if at least two subject visits included the code.

To our knowledge, this is first study to describe the extent of medical resource utilization, based on disease manifestation, in children with NF1. CNS manifestations required the highest frequency of MRI acquisitions and specialty visits. The ICD-9 code 237.71 accurately identified subjects with NF1.

Understanding the economic costs of caring for children with NF1 will help identify opportunities to improve resource utilization and clinical care as well as encourage academic and industry institutes to partner in therapeutic development for this devastating disease.

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Patients Preference to Participate in Shared Decision-Making for Performing a CT Scan in the Emergency Department

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BACKGROUND: CT scans are widely used in U.S. emergency departments and represent a major source of carcinogenic radiation.[1] Shared Decision Making (SDM) is the principle of including the patient in the decision process regarding diagnostic and therapeutic options. SDM has been used successfully in decisions such as hospital admissions for chest pain and surgery for appendicitis.[2,3] It is unknown if shared decision-making is beneficial in the decision to order a CT scan in the emergency department (ED). Our objective was to assess the desire of ED patients to participate in the decision process regarding CT scan use and describe differences in patients who want to participate versus those who do not want to participate.

METHODS: Patients who were receiving a CT scan in a tertiary care urban ED were approached from June to August 2016 and asked to participate in the study. If they verbally consented, subjects were interviewed in the ED by a research assistant blinded to the objectives of the study after a CT scan had been ordered but prior to ED disposition.

RESULTS: Of the 102 subjects who were enrolled, 58% were female, the median age was 46.5, and 48% received an abdominal CT scan. Forty-eight percent of all patients desired to "participate fully in the decision to perform CT scan," compared to 44% who "did not want to participate in the decision to perform CT." Of those who wanted to participate fully, there was no difference in median age, sex, type of CT, discussion of risks by physician, or explanation of alternatives by physician. Patients who wanted full participation were more likely to have concerns about CT scans (23% versus 11%, p=0.02) but also felt more involved in the decision process (31% versus 20%, p=0.04.)

CONCLUSION: Approximately 50 percent of ED patients want to participate in the decision to perform a CT scan and among those patients, they are more likely to have concerns about CT scans. There was no increase in discussion of risks or alternatives for patients who wanted to participate in the decision.

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Clinical Impact of Panel Testing in a Hereditary Cancer Program

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BACKGROUND: Since the Supreme Court ruling in 2013 against Myriad's gene patent, along with widespread adoption of next generation sequencing, panel testing for hereditary cancer syndromes has expanded rapidly. Its practice has drawn criticism due to concerns about the lack of clinical impact of testing results.

METHODS: A retrospective review was conducted of all patients presenting to the Ruth Paul Hereditary Cancer Program at the George Washington University for genetic counseling and testing between Jan. 2, 2015 and April 13, 2016. Outcomes of testing and clinical impacts of test results were recorded. Clinical management changes were based on current National Comprehensive Cancer Network (NCCN) Guidelines.

RESULTS: Five hundred and twenty-nine patients underwent genetic counseling for either a family or personal history of cancer or a known familial mutation. Of those counseled, 81% (n=426) elected to undergo genetic testing ranging from single site (SS) analysis to 49-gene panels. Test selection was at the discretion of the certified genetic counselor. Of the tests, 4% (n=18) had SS, 0.5% (n=2) had single gene (SG), 13% (n=54) had testing limited to BRCA, and 83% (n=352) had panel testing. Of those tested, 18% (n=75, two individuals had more than one mutation) were found to have a deleterious or likely pathogenic mutation, and 50% of those individuals (n=37) had undergone panel testing (versus SS, SG, or BRCA-limited testing). Only one-third (32%, n=12) of the panel-tested individuals were found to have BRCA mutations, and one of those patients was found to have both a BRCA and CHEK2 mutation. Twenty-three individuals were diagnosed with non-BRCA mutations that would have been missed by BRCA testing alone, representing 31% of those testing positive for a mutation (n=75) and 62% of those testing positive who had undergone panel testing (n=37). True negatives, those testing negative for known familial mutation, encompassed 8% (n=35) of those tested. A variant of uncertain significant (VUS) was found in 28% (n=121) of those tested, and both a VUS and deleterious mutation were found in 2% (n=8) of those tested. One-quarter (26%, n=109) of patients who underwent genetic testing had a change in management; all those who were found to have a mutation, except for one, had an increase in surveillance and/or prophylactic measures (Table), while all true negatives had a decrease from what would have been planned had testing not occurred. All individuals with a VUS or a mutation in a moderate penetrance gene were encouraged to participate in a prospective registry.

CONCLUSION: Panel testing for hereditary cancer syndromes can provide important information for guideline-driven clinical management. Participation in prospective registries is essential for further development of clinical guidelines for individuals with variants of uncertain significance.

Clinical exam	64
Breast imaging	56
TVUS	48
TVUS with CA-125	46
Colonoscopy	19
Endoscopic ultrasound	4
Thyroid ultrasound	2
Renal imaging	3
Endometrial sampling	6
EGD with duodenoscopy	9
Urinalysis	6
Neurology referral	8
Dermatology referral	49
Chemoprevention	17
Prophylactic surgery	46
Reproductive endocrinology	11

TABLE: Change in Management Modalities Based on Genetic Panel Results (N refers to number of patients that subsequently underwent a change in management or surveillance strategies based on a positive genetic mutation result from a specific genetic panel)

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A Novel Computerized Tomography Software Accurately Determines Mass and Adipose Tissue in Humans: A Tool of Predicting Incidence of Diabetes and Hypertension

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Central adipose tissue is appreciated as a risk factor for cardio-metabolic disorders.[1] The purpose of this study was to determine the efficacy of a new volumetric 3-D computerized tomography (CT) software in determining mass and adipose tissue of human subjects compared to currently accepted methods of measuring adipose tissue, including the gold standard, hydrostatic weighing (HW, also called underwater weighing), and the recently innovated air displacement plethysmography (ADP, also called BOD POD).[2] We implemented this software on 1,225 patients to determine the predicting power that central abdominal adipose tissue would have on significant cardio-metabolic diseases, namely hypertension, heart disease, high cholesterol, and diabetes.

Using NovaPACS® software, we implemented two commonly accepted algorithms of converting CT Hounsfield numbers to tissue densities, namely the Schneider

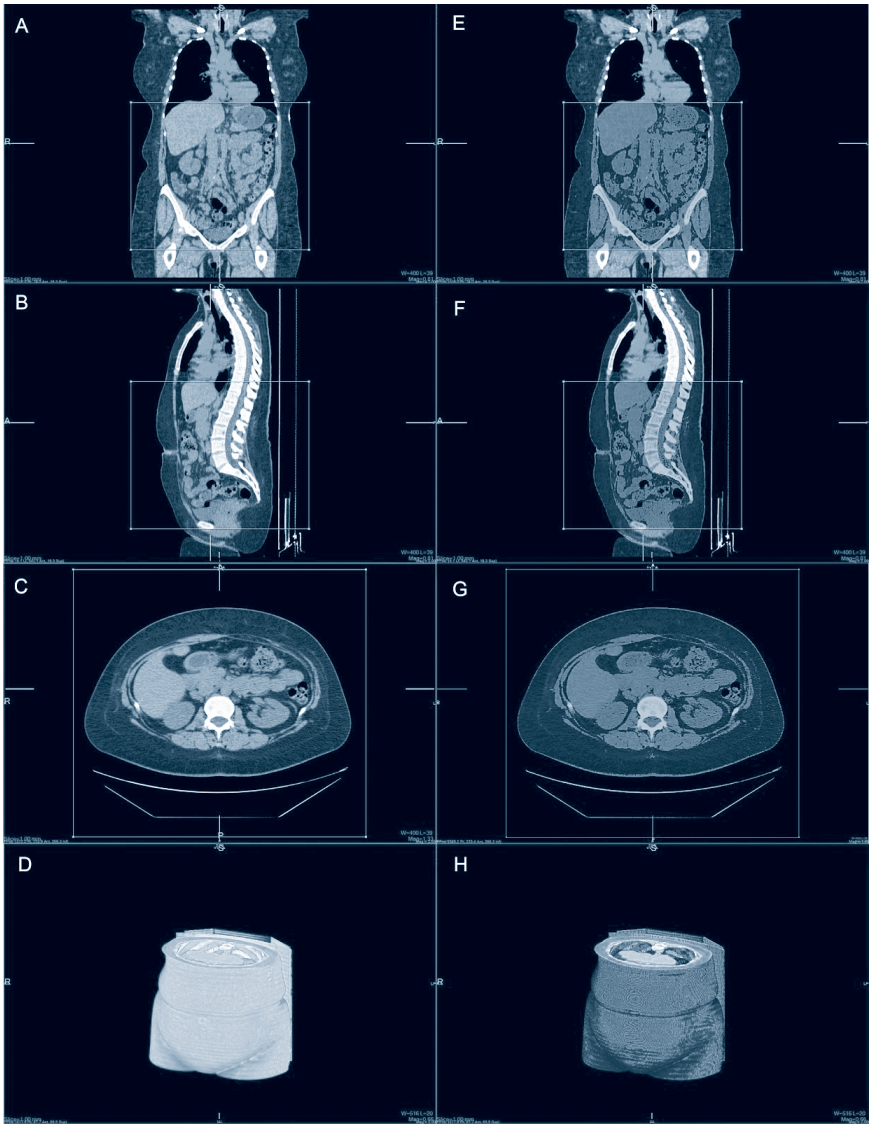

FIGURE: A Typical 2-D Snapshot of the 3-D Rendering from a CT Scan Using Novapacs® with Abdominal Fat Selected from the Top of the Liver to the Pubic Symphysis

On the left, normal coronal(A), sagittal(B), axial(C), and 3-D rendering(D) images are displayed. Coronal(E), sagittal(F), axial(G), and 3-D rendering(H) images are depicted.

	BMI			%cBF			Calcium Score		
	Slope estimate*	Standard error*	P-value†	Slope estimate*	Standard error*	P-value†	Slope estimate*	Standard error*	P-value†
Hypertension	2.14	0.36	<0.0001	3.06	0.64	<0.0001	−118.9	30.73	0.0001
Heart disease	−0.21	0.81	0.7911	−0.32	1.43	0.8232	−444.1	68.34	< 0.0001
High cholesterol	−0.32	0.35	0.3600	−0.61	0.63	0.3342	−115.3	29.93	0.0001
Diabetes	3.73	0.53	<0.0001	4.09	0.95	<0.0001	−57.0	45.26	0.2085
Former smoker	0.8	0.36	0.0250	1.47	0.64	0.0215	−72.2	30.34	0.0175

TABLE: Body Mass Index, Percent Central Body Fat, and Calcium Scores According to Selected Variables Taken from 1,225 Patients

*Adjusting for age, sex, and race. †From the F statistic based on type III sums of squares. Fifteen different models are represented in the table.

method and the Beam method.[3] Twenty volunteer subjects (14 men, six women) received head-to-toe CT scans and height and weight measurements. HW and ADP were obtained from 17 and 12 subjects, respectively. When comparing ADP to CT data using the Schneider method and Beam method for total mass, correlations were r = 0.9806 and 0.9804, respectively. Paired t-tests indicated there were no statistically significant biases. Additionally, observed average differences in percent body fat between ADP and the Schneider method and the Beam method were 0.38% and 0.77%, respectively.[4] In other words, in a 200-pound individual, the Schneider method predicted the amount of body fat to be within .76 pounds of ADP measurements.

Using this newly innovated CT software, full body (i.e. neck to thighs) CT scans were obtained from 1,225 female (518) and male (707) subjects, aged 18-88. Percent central body fat (%cBF) was determined by quantifying the adipose tissue volume from the dome of the liver to the pubic symphysis (Figure). Calcium score was determined from the calcium content of coronary arteries. Relationships between %cBF, body mass index (BMI), and several cardio-metabolic disorders were assessed controlling for age, sex, and race. Higher %cBF was significantly greater for those with Type 2 diabetes and hypertension, but not stroke or hypercholesterolemia. BMI and %cBF correlated roughly equally with diabetes and hypertension. Calcium scoring significantly correlated with all measurements of cardiovascular health, including hypertension, hypercholesterolemia, and heart disease (Table).[5]

CT is not likely to be a screening tool for %cBF. However, millions of CT scans are performed on high-risk patients each year for other reasons. These patients can benefit from the additional information obtained by a quantitative, spatial analysis of adipose tissue within their body correlated to key cardio-metabolic diseases. Providing this information to high-risk patients may provide valuable feedback for behavioral change. Furthermore, CT volume quantification provides an essential foundation for more accurate stratification of risk based on the location of fat and could play a role in developing surgical techniques to remove visceral abdominal fat. The application of these CT algorithms has utility in further research to accurately stratify risk factors with peri-organ, visceral, and subcutaneous types of adipose tissue and has the potential for significant clinical application.

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A Case of Atypical Multiple Evanescent White Dot Syndrome and Multifocal Choroiditis in a 22-Year-Old Woman

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CASE REPORT: A 22-year-old previously healthy myopic white female presented with unilateral painless central scotoma, followed by increasing temporal visual deficit. She denied photopsia, dyschromatopsia, floaters, or recent flu-like symptoms. Corrected visual acuity was 20/100 improving to 20/70 with pinhole in the right eye and 20/20 in the left. Confrontation visual fields revealed a central and inferotemporal visual field defect. Amsler grid testing showed central and paracentral relative scotomas and an enlarged blind spot. Intraocular pressure, slit lamp exam, motility were normal, with a relative afferent pupillary defect noted in the right eye. Past ocular history was significant for high myopia in both eyes and chorioretinal scars in the right eye from what was presumed ocular histoplasmosis (POHS).

The fundus exam was significant for chorioretinal scars (Figure 1). One scar is in the papillomacular bundle, and a concentrically oriented group of scars is temporal to the macula. The macula had an orange coloration with a granular appearance. A few faint lighter colored spots were found in the nasal midperiphery, seen in Figure 3. The nasal margin of the optic nerve was slightly indistinct. There was a soft, yellowish spot temporal to the macula.

Spectralis optical coherence tomography (OCT) revealed attenuation of the ellipsoid zone seen in Figure 2. Fluorescein angiography did not show significant abnormality other than the chorioretinal scars, and indocyanine green showed hypofluorescent spots concentrically around the optic nerve, and in the nasal midperiphery seen in Figure 3. Fundus autofluorescence showed hyperautofluorescent lesions temporal to the macula and nasal to the optic nerve (Figure 4).

The differential diagnosis included MEWDS, punctuate inner choroidopathy (PIC), multifocal choroiditis and panuveitis, and AZOOR (acute zonal occult outer retinopathy). A diagnosis of MEWDS and concurrent MFC was made, given the fundus findings and diagnostic tests.

DISCUSSION: We present what is believed to be the first case of an atypical MEWDS with a paucity of white spots, and concurrent scars consistent with MFC. Although the patient did not present with multifocal grey-white lesions characteristic of MEWDS, she did have the characteristic orange-yellow fovea with granularity seen on fundus examination along with attenuation of the ellipsoid zone on OCT. The peripapillary hypoflourescence on ICG and hypoautoflourescent around the optic nerve on fundus autoflourescence are consistent with a diagnosis of MEWDS and follow the clinical characteristics of acute onset central loss of vision and an enlarged blind spot.[1] The previous diagnosis of POHS seemed unlikely due to lack of characteristic peripapillary scarring. The scar located in the papillomacular bundle could be the result of either PIC or MFC; however, the concentrically oriented group of scars temporal to the macula is indicative of MFC since PIC primarily has scars in the papillomacular bundle.[2,3]

We believe the advent of retinal imaging technology such as SD-OCT and ICG has increased the diagnostic efficacy of MEWDS, and FUNDUS photography has improved the diagnostic efficacy of MFC, which allowed the diagnosis of atypical MEWDS with concurrent MFC that has not been described previously.

The consecutive occurrence of MEWDS and MFC has been documented in the literature, and there has also been one case documenting typical MEWDS and MFC concurrently occurring; however, no clear

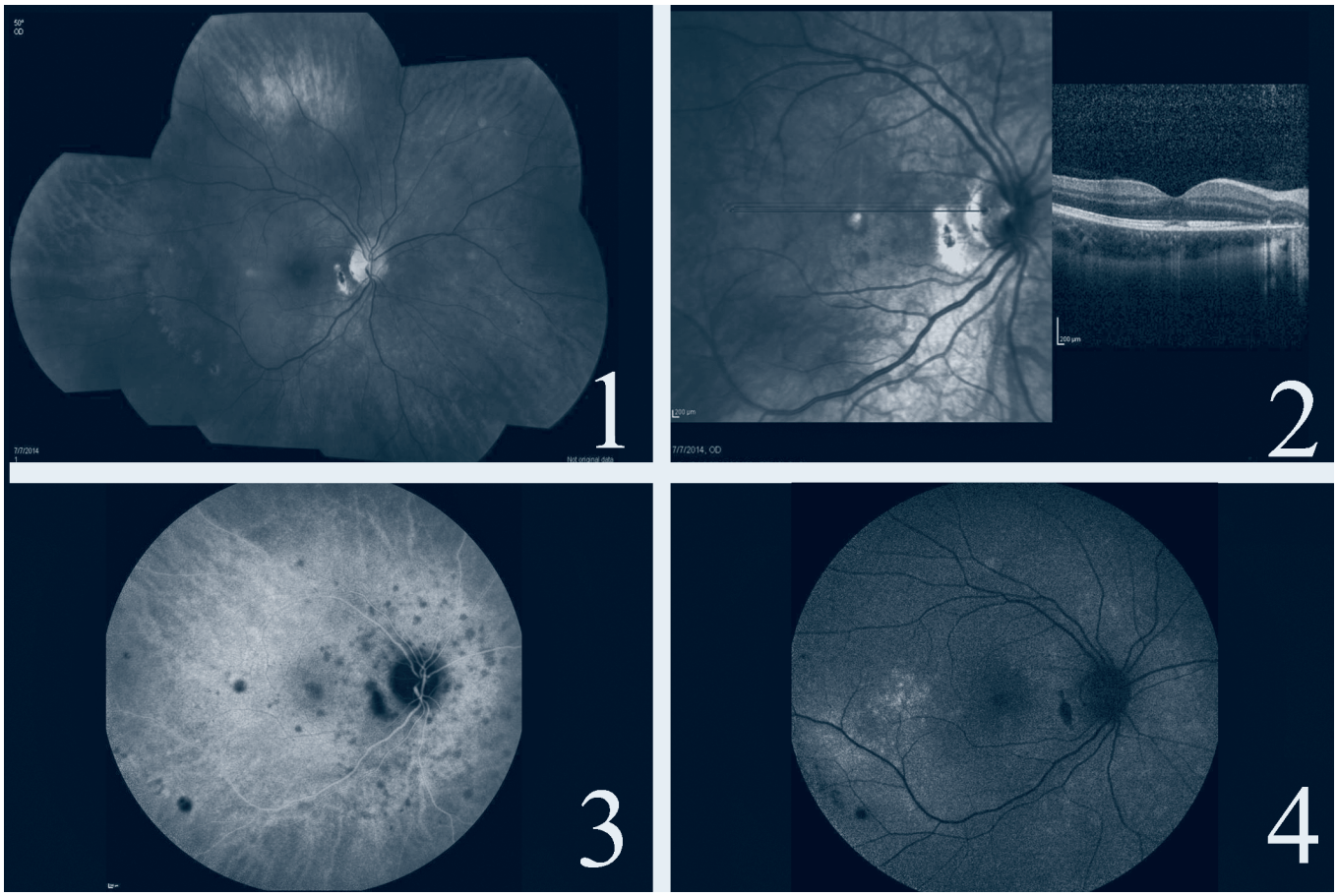

FIGURE: 1. Fundoscopy of the right eye revealing chorioretinal scars. **2** OCT demonstrating attenuation of the ellipsoid zone. **3.** Indocyanine green revealing hypofluorescent spots. **4.** Autofluorescence demonstrating hyperautoflurescent lesions.

link between the two syndromes has been discovered.[4,5] There have been numerous theories proposed encompassing a pathogen or predisposition to a pathogenic mechanism. There has also been proposed sensitization to autoantigens in these patients.[4]

We believe the advent of retinal imaging technology such as SD-OCT and ICG has increased the diagnostic efficacy of MEWDS, and FUNDUS photography has improved the diagnostic efficacy of MFC, which allowed the diagnosis of atypical MEWDS with concurrent MFC that has not been described previously.

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Suprasellar Epidermoid Cyst Originating from the Infundibulum: Case Report and Literature Review

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Epidermoid cysts account for 1-2 percent of all brain tumors and are most commonly found in the cerebellopontine angle and parasellar cisterns.[1] The slow growth of these tumors often results in them remaining asymptomatic until their size is large enough to compress surrounding structures, such as the pituitary stalk or optic chiasm.[2] These cysts are believed to develop during the embryonal period of development, more specifically the third to fifth weeks of gestation, with displacement of dorsal ectodermal cells normally residing in the midline.[3] The incomplete separation of the neural and epidermal ectoderm allows for epiblast inclusion in the neural tube, which typically closes during this gestational period.[3] Most often, these tumors are diagnosed in adults aged 20–40 years old, with incidence peaking in the fourth decade of life.[3] A trans-sphenoidal approach for the removal of these tumors has been shown to reduce morbidity and mortality in these patients due to the better visualization of the neoplasm and surrounding anatomy and minimal (if any) brain retraction.[2] Tumors and cysts of the pituitary stalk and hypothalamic region vary in presentation depending on their location, progression, and extension into the surrounding anatomy, in addition to the age and comorbidities of the patient; all of these factors must be addressed prior to surgery.[4]

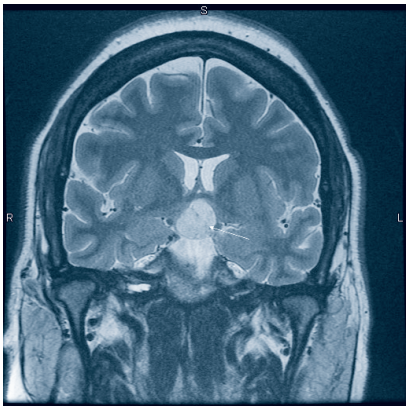

FIGURE 1: Preoperative MRI with Contrast (Coronal View)

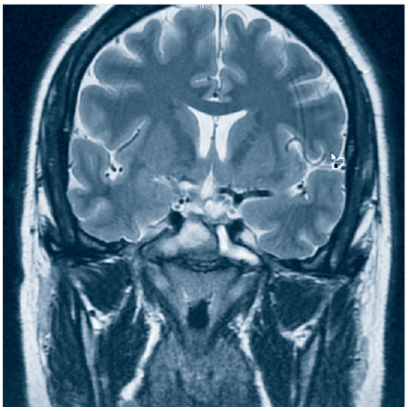

FIGURE 2: Postoperative MRI with Contrast (Coronal View)

Here, we present a rare case of an epidermoid cyst located in the suprasellar region, specifically originating from the infundibulum (Figure 1 and 2). Only one additional case with an epidermoid cyst originating within the pituitary stalk has been previously reported in the literature. The patient in this case presented with headaches, diplopia, and blurred vision without any endocrinopathy. The patient's pre-operative evaluation was significant for pseudotumor cerebri, hyponatremia, obesity, and a history of smoking; post-operative course was significant for neurogenic diabetes insipidus. The only other reported case of an epidermoid cyst occurring within the infundibulum involved a young female patient who presented with a two-year history of significant endocrine symptoms, including amenorrhea, galactorrhea, polyuria, and polydipsia.[3] This patient also reported visual symptoms and a headache, as seen in our patient. Similarities between the two cases include gender, tumor type, and anatomical location; however, our patient was nearly 10 years senior and reported a more acute time course of one to two months. Both patients received subtotal resection of the tumor given its adherence to the stalk and close proximity to the optic chiasm. On pathological examination, both cysts contained keratin debris; however, our patient had a small region of calcification, suggestive of a Rathke cleft remnant.[2] While both patients fall into the age range for these lesions, 20–60 years of age, neither fits the peak incidence of the fourth decade of life.[5] The

similarities and differences between these cases highlight the variety of symptoms and clinical presentations of tumors residing within this region of the brain and the close attention to detail required in diagnosis.

As seen in our patient, tumors involving the pituitary stalk are challenging, given the high risk for postoperative endocrinopathy and management of surrounding structures, including the hypothalamus, optic chiasm, and vessels within the cavernous sinus. While other cases have presented with lesions intruding into the sellar region, epidermoid growth within the stalk itself is rare, and our patient is an excellent example of the neurosurgical management of an epidermoid cyst residing in this specific location.

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Patients Transferred for Upper Extremity Amputation: Participation of Regional Trauma Centers

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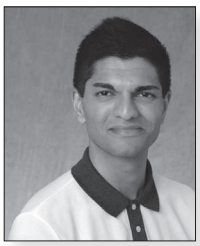

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Level 1 trauma centers are required to provide hand and microsurgery capability at all times.[1] To better understand distant referrals and indirectly study triage patters in our region, we examined patient transfers for upper extremity amputation to our level 1 trauma center. We hypothesize that patients are transferred to our academic, tertiary care center despite the availability of closer, American College of Surgeons (ACS)-designated level 1 trauma centers.[2]

Records were reviewed from 2010 to 2015 to evaluate patients transferred to our level 1 institution for upper extremity amputation. Patients were referred from six states to our institution over this time period (Figure 1). We measured the straight-line distance from each patient's transferring facility to our facility

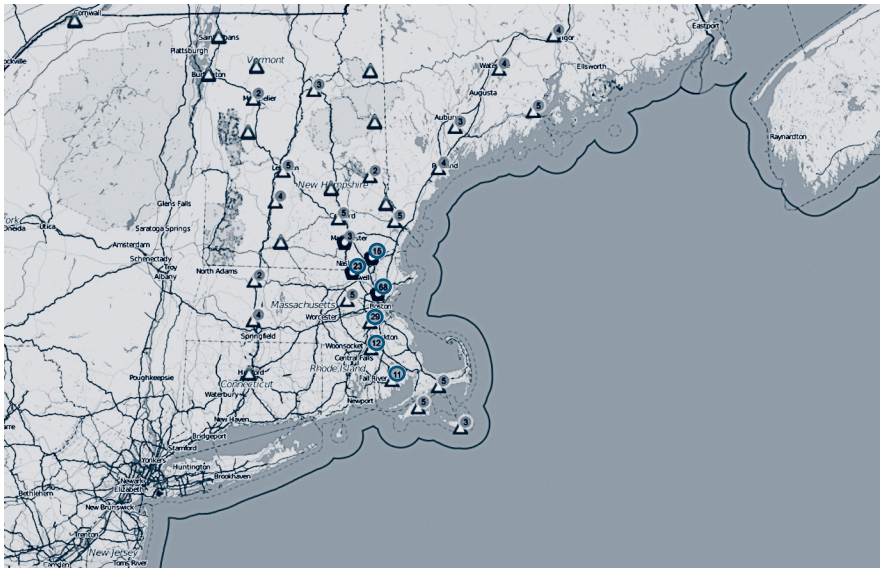

FIGURE 1: Geographic Distribution of Referring Centers (blue circles represent level I trauma facilities)

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Continued from p. 25

and compared this distance to the straight-line distances from the zip code of the transferring facility to the zip code of each level 1 trauma center.

We had data for 250 transferred patients (91% male, 9% female). For 110 patients, our hospital was the nearest level 1 trauma center; however, for the remaining 140 patients, other level 1 trauma facilities were located closer to the referring hospital. Among these 140 patients, the mean distance of the referring facility to the nearest level 1 trauma center was significantly different from the mean distance of the referring facility to our facility (Figure 1A). An average of four level 1 trauma centers were bypassed before patients arrived at our center. Medicaid and "self-pay" patients were more likely to be transferred to our facility.

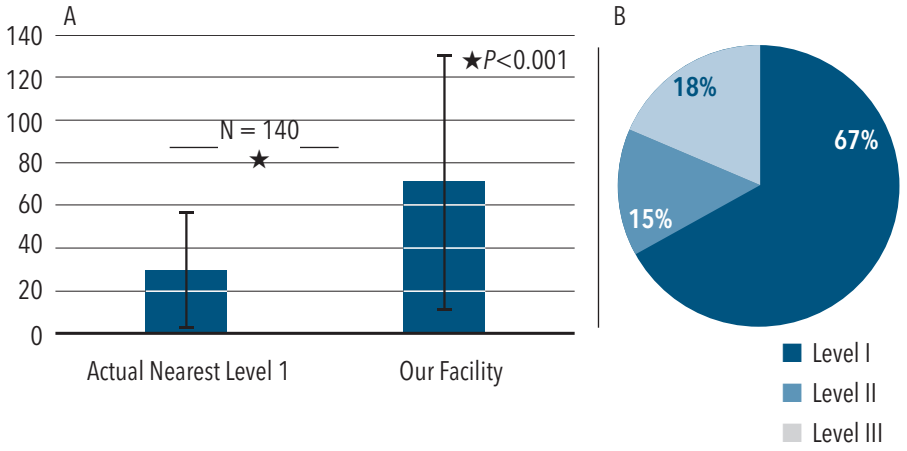

FIGURE 2: Distance of transport from transferring facility to either the nearest level I trauma center, or our facility as more distant level I trauma center **(FIG. 2-A);** trauma designation of transferring facility (n= 27) **(FIG. 2-B).**

This study demonstrated that a substantial number of patients with upper extremity amputation are transferred to our academic, level 1 institution despite the availability of closer level 1 trauma centers.

Twenty-seven of 140 patients (19%) were transferred from a facility with a trauma designation; the other 81% were transferred from a facility without a trauma designation. Out of these 27 patients transferred from a facility with a trauma designation, 18 patients (67%) were transferred from a level 1 trauma center. The remaining patients were transferred from a level 2 trauma center (n= 4, 15%) or a level 3 trauma center (n= 5, 18%) (Figure 1B).

Bivariate analysis showed that insurance status was associated with more distant transfer. After controlling for possible confounders using multivariable logistic regression analysis, we found that patients with Medicaid (OR 6.7; CI 1.5 - 33; standard error (SE) 5.5; P= 0.015) and patients who were self-paying, i.e. "uninsured" (OR 3.3; CI 1.2 - 10; SE 1.8; P= 0.024), were more likely to be transferred to our facility as a more distant level 1 trauma center than patients who had private insurance

Fifty-six percent of patients transferred to our hospital for upper extremity amputation had a level 1 trauma center closer to their injury. This study demonstrated that a substantial number of patients with upper extremity amputation are transferred to our academic, level 1 institution despite the availability of closer level 1 trauma centers. This suggests that microsurgical expertise for replantation is unofficially recognized by referring facilities in surrounding states – even those with level 1 ACS accreditation. Our center has an interest in providing care for these complex patients and in providing quaternary microsurgical coverage for the region. Formal designation of regional microsurgical trauma centers may facilitate patient triage, expeditious referral and transport, and ultimately improvement in outcomes for patients with upper extremity amputations.

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Response of Hidradenitis Suppurativa to Biologic Therapy

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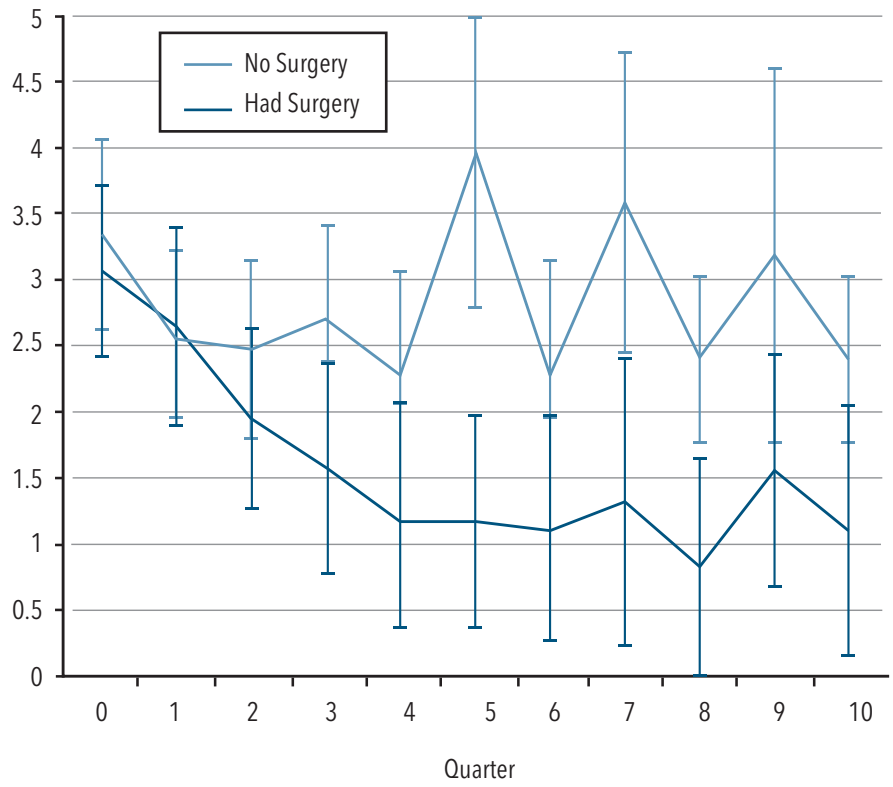

FIGURE: Adjusted AN count by quarter, for patients who ever vs. never had HS surgery. Error bars show 95% CI each quarter

BACKGROUND:
Hidradenitis suppurativa (HS) is a chronic, recurrent, inflammatory disease of the apocrine sweat glands that affects approximately 1–4 percent of the population.[1,2] There is currently no known cure, and molecular drivers of HS are poorly understood. While traditional disease-modifying anti-rheumatic drugs (DMARDS) have been largely ineffective, targeted biologic therapy, including TNF-α inhibitors, have been used with some success.[3] Adjuvant biologic therapy after radical resection has been shown to reduce the risk of recurrence in HS. Until now, longitudinal investigations of clinical outcomes in HS patients undergoing surgical and biologic interventions have been largely retrospective.[4,5] The purpose of this study is to investigate how interventions such as surgery and biologic treatment in HS impact disease activity scores.

METHODS:
This research was conducted through the Wound Etiology and Healing (WE-HEAL) study. At the time of data-lock, 565 patients were enrolled in the WE-HEAL study, and 69 had HS.

HS disease activity was assessed using Active Nodule count (AN count), Hurley Stage, and Hidradenitis Sartorius Score (HSS). Patient variables included baseline disease activity scores, age, gender, race, ethnicity, smoking, disease duration, and baseline comorbidities. Analysis was performed using the SAS Mixed and GLM procedures for multivariate analysis (version 9.3, Cary, NC) with $p<0.05$ considered significant.

RESULTS: PATIENT CHARACTERISTICS
The mean age of the HS subjects was 40.4 years (SD 13.8), 72.5 percent were African American, and 65.2 percent were female. There were no significant differences in demographic characteristics in the patients who underwent surgery or biologic therapy (Table). As expected, patients with a higher baseline HSS score were more likely to have ever been exposed to biologics ($p=0.021$).

RESPONSE TO THERAPY BASED ON HSS SCORE:
After adjusting for the effects of time-varying surgery, time-varying BMI, time-varying opioid dose, time-varying pain score, baseline Hurley

Continued on p. 28

Variable			Surgery			Biologics		
		All Patients (n=69)	Ever (n=33)	Never (n=36)	P	Ever (n=27)	Never (n=42)	P
Age		40.4 (13.8)	38.6 (12.6)	42.0 (14.8)	0.32	39.1 (11.0)	41.2 (15.4)	0.54
Race	AA	50 (72.5%)	23 (69.7%)	27 (75.0%)	0.55	20 (74.1%)	30 (71.4%)	0.40
	Caucasian	18 (26.1%)	9 (27.3%)	9 (25.0%)		6 (22.2%)	12 (28.6%)	
	Asian	1 (1.5%)	1 (2.0%)	0		1 (3.7%)	0 (04%)	
Female Gender		45 (65.2%)	19 (57.6%)	26 (72.2%)	0.20	16 (59.3%)	29 (69.1%)	0.40
Smoker	Current	16 (23.2%)	11 (33.3%)	5 (13.9%)	0.13	6 (22.2%)	10 (23.8%)	0.57
	Former	17 (24.6%)	5 (18.2%)	11 (30.6%)		5 (18.5%)	12 (28.6%)	
	Never	36 (52.2%)	16 (48.5%)	20 (55.6%)		16 (59.3%)	20 (47.6%)	
Disease Duration		9.3 (11.7%)	8.1 (9.1%)	10.7 (14.3%)	0.50	9.0 (7.0%)	9.5 (14.2%)	0.12
Baseline HSS		61.3 (45.2%)	65.6 (41.0%)	57.1 (49.2%)	0.45	77.0 (47.2%)	50.8 (41.1%)	0.021

TABLE: Baseline Demographics of HS patients Stratified by Surgery and Biologic Exposure

Continued from p. 27

Stage, smoking, and hypertension, patient-quarters with biologics present had a mean HSS 12.0 points lower than patient-quarters without biologics (p=0.009).

In this study, we showed that treatment with biologic agents significantly decreases disease activity scores, which is consistent with other clinical studies demonstrating response of moderate to severe HS to TNF-α inhibition.[3]

AN COUNT RESPONSE

In the random effects mixed model, significant predictors of improvement in the AN count included having HS surgery (p=0.0016), disease activity at baseline (Hurley stage 2 (p=0.034) or 3 (p<0.0001)), having biologics prescribed (time varying; p=0.001), time (quarter; p<0.0001), and the surgery x time interaction (p=0.0031).

AN count dropped more for patients undergoing surgery than not undergoing surgery (Figure). After adjusting for time-varying surgery and other covariates, biologic use was associated with a drop of 0.6 AN units compared to no biologic use (p=0.0029).

DISCUSSION:

The cohort of HS patients followed in the WE-HEAL study is representative of the population affected in the United States with a higher prevalence of women and African Americans.[2] In this study, we showed that treatment with biologic agents significantly decreases disease activity scores, which is consistent with other clinical studies demonstrating response of moderate to severe HS to TNF-α inhibition.[3] We demonstrated a similar response in our predominantly African American population and demonstrated that treatment with biologic agents, in combination with surgery, was associated with significant improvement in disease activity scores in this population. The primary limitation of this study is small sample size. However, recruitment of patients with HS into the WE-HEAL study is ongoing. With this data set, we hope to be able to further investigate the interplay of biologic therapy and surgery in HS management.

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Tamsulosin for Urolithiasis: A Review of the Literature and Current Controversies

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In the United States, urolithiasis affects approximately 1 in 11 people, and there is evidence that the prevalence is increasing. A recent treatment strategy for urolithiasis involves using Medical Expulsive Therapy (MET) to increase the likelihood of spontaneous passage of ureteral stones. The two leading drug classes for MET are alpha-1-andrenergic receptor blockers and calcium-channel blockers. Tamsulosin, an alpha-1-adrenocepter blocker, is thought to induce spontaneous stone passage by relaxing ureteral smooth muscle tone in the prostate and bladder neck. In principle, tamsulosin binds to alpha-1a-receptors and alpha-1d-receptors on the ureter smooth muscle, causing dilation of the ureteral lumen, thereby decreasing peripheral resistance from the ureteral wall and subsequently increasing urinary flow.[1] However, tamsulosin has not been proven effective for increasing ureteral stone passage and is not approved by the U.S. Food and Drug Administration for this indication as it was originally designed to treat the symptoms of benign prostatic hyperplasia. There is a relative paucity of data on the efficacy of tamsulosin for urolithiasis, and of the published results, there are conflicting conclusions from the data. Due to the acute nature of symptoms from urolithiasis, emergency medicine physicians are often the first to diagnose and treat this condition. This has led to tamsulosin being frequently prescribed from the emergency department (ED) for off-label use without the support of high-quality evidence. If tamsulosin is proven effective, its use in the treatment of urolithiasis could offer important advantages. The number of procedures, length of hospital stay, and health care costs after the initial ED visit could potentially be reduced. Tamsulosin may also increase patient satisfaction by reducing invasive treatment and decreasing time to stone passage. We conducted a literature review that focuses on the efficacy of tamsulosin. A few data insights are highlighted below.

A meta-analysis of 20 randomized control trials that had a combined 1,593 patients found that the expulsion rate in the tamsulosin group was significantly higher than that of the control group for both distal ureteral stones ($P < 0.00001$) and proximal ureteral stones ($P = 0.02$).[2] This meta-analysis found that tamsulosin decreased average time to expulsion by 3.36 days for proximal stones and 3.66 days for distal stones compared to the control group.[2] However, one randomized control trial with 1,136 patients has shown that tamsulosin is not more effective than a placebo at increasing the likelihood of stone expulsion.[3] This study had 81% spontaneous stone passage in the tamsulosin group compared to 80% spontaneous stone passage in the placebo group.[3] A meta-analysis with a combined 1,283 patients comparing tamsulosin use to placebo in the ED showed that tamsulosin had a higher rate of stone expulsion ($P < 0.001$) and a decreased stone expulsion time ($P = 0.02$).[4] In addition, the study found decreased need for analgesic therapy, hospitalization, and surgery following the initial ED visit.[4] However, a different study, a prospective trial of 100 ED patients who were randomized to either 0.4 mg daily of tamsulosin or placebo for seven days, showed that there was no difference in proportion of stone passage after the seven days between tamsulosin and placebo.[5]

While tamsulosin has shown potential as an effective treatment option for urolithiasis, there is still need for additional investigation on the efficacy of tamsulosin in the acute setting in order to be justified for prescription from the emergency department.

While tamsulosin has shown potential as an effective treatment

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option for urolithiasis, there is still need for additional investigation on the efficacy of tamsulosin in the acute setting in order to be justified for prescription from the emergency department.

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The Impact of Direct Acting Agents on the Hepatitis C Virus Continuum of Care at the Washington DC Veterans Affairs Medical Center

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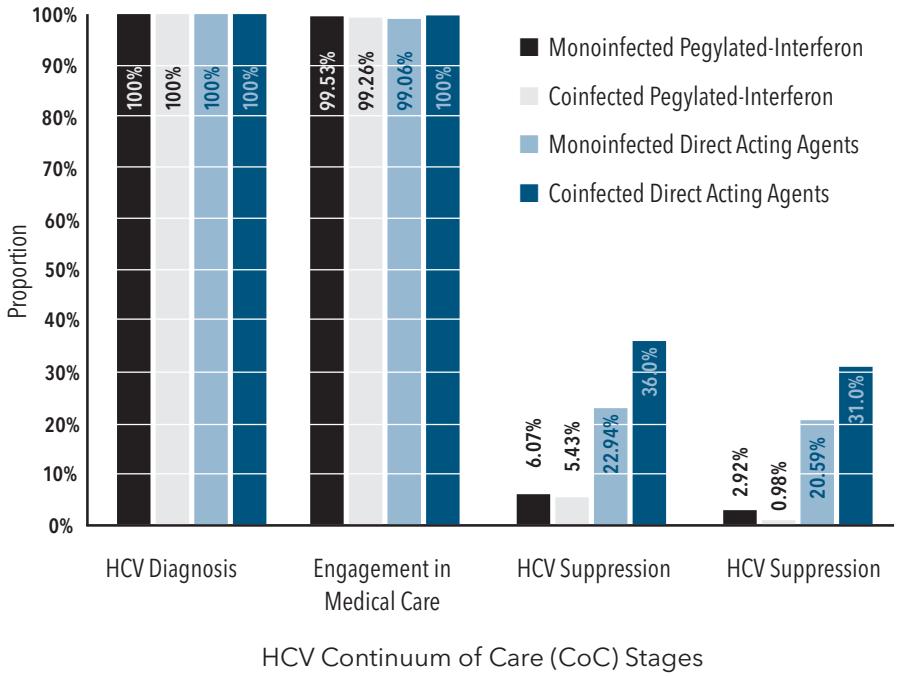

FIGURE: Comparison of Continua of Care for HCV Monoinfected and HCV/HIV Coinfected Individuals during Two Treatment Eras

Recent advancements in the treatment of the Hepatitis C virus (HCV) have resulted in a shift from pegylated interferon-based regimens to the use of direct acting agents (DAAs). Untreated HCV can evolve into cirrhosis and liver decompensation, both of which are three times more common in HCV/HIV coinfected individuals than HCV monoinfected individuals.[1] The goal of HCV treatment is to achieve sustained virologic response (SVR), which is associated with decreased rates of end-stage liver disease (ESLD), hepatocellular carcinoma (HCC), and death.[2] Previously, SVR was assessed 24 weeks following the end of treatment (SVR24); however, an undetectable HCV viral load 12 weeks following treatment (SVR12) is now sufficient for defining treatment success.[3]

Prior to the development of DAAs, pegylated interferon-based regimens would result in 41 percent of monoinfected patients and 27 percent of coinfected patients achieving SVR.[1] DAAs have resulted in SVR in approximately 90 percent of all patients.[3] While safety, tolerance, and efficacy of DAAs are similar for both HCV monoinfection and HCV/HIV coinfection, drug interactions with coinfected patients' HIV

2008–13, Pegylated Interferon	All Patients	HCV/HIV Coinfection	HCV Monoinfection	P Value*
HCV Supression	134 (2.76%)	4 (18.18%)	130 (48.33%)	0.007 [1]*
2014–15, Direct Acting Agents	**All Patients**	**HCV/HIV Coinfection**	**HCV Monoinfection**	**P Value[A]**
HCV Treatment	834 (23.86%)	108 (36.12%)	726 (22.94%)	<0.0001 [2]*
HCV/HIV Coinfection	**All Patients**	**2008–13, Pegylated Interferon**	**2014–15, Direct Acting Agents**	**P Value[B]**
HCV Treatment	130 (18.36%)	22 (5.39%)	108 (36.0%)	<0.0001 [1]*
HCV Supression	97 (13.70%)	4 (0.98%)	93 (31.00%)	<0.0001 [1]*
HCV/HIV Monoinfection	**All Patients**	**2008–13, Pegylated Interferon**	**2014–15, Direct Acting Agents**	**P Value[B]**
HCV Treatment	995 (13.01%)	269 (6.04%)	726 (22.72%)	<0.0001 [1]*
HCV Supression	788 (10.30%)	130 (2.92%)	658 (20.59%)	<0.0001 [1]*

[A] Comparison made between monoinfected and coinfected groups
[B] Comparision made between treatment eras
[1] Two-tailed Fisher's Exact Test
[2] Two-tailed Chi-square with Yate's Correction
* Significantly different proportion

TABLE: Comparison of Proportion of Patients Along HCV Continuum of Care

antiretroviral agents (ARVs) must be considered prior to initiation of HCV treatment.[4]

The Washington DC Veterans Affairs Medical Center (DC-VAMC) provides comprehensive care for veterans in the greater metropolitan area of the District of Columbia. The Infectious Disease Clinic at the DC-VAMC offers HIV care under a multidisciplinary model comprised of physicians, nurse practitioners, psychologists, social workers, and pharmacists. From 2008-13, pegylated interferon-based regimens were used to treat HCV infection. Beginning in 2014, DAAs became the preferred treatment. We describe the HCV Continuum of Care (CoC) at the DC-VAMC for both HCV monoinfected and HIV/HCV coinfected individuals treated between 2008 and 2015.

A retrospective review of the HCV Clinical Case Registry (HCV CCR) at the DC-VAMC was conducted for the pegylated interferon treatment era (2008-13) and the DAA era (2014–15). The patients were analyzed based on a modified HCV CoC: HCV diagnosis, engaged in medical care, prescribed HCV medication, and achievement of a not detectable HCV viral load. Depending on sample size, two-tailed Chi-square with Yate's correction and two-tailed Fisher's Exact Test were used to assess for differences between mono and coinfected patients. The tests were also used to assess for differences within the monoinfected and coinfected groups dependent upon treatment era.

Based on the proportions of patients in the HCV CoC for both treatment eras seen in the Table and the Figure, more monoinfected patients achieved HCV suppression in the pegylated interferon era than coinfected patients (48.32% vs. 18.18%, p= 0.007, Fisher's). While a similar proportion of coinfected and monoinfected patients achieved suppression in the DAA era, more coinfected patients were treated (36.12% vs. 22.94%, p< 0.0001, Chi-square). Compared to the pegylated interferon era, a greater proportion of monoinfected patients were treated (22.93% vs. 6.00%, p< 0.0001, Fisher's) and achieved HCV suppression (90.63% vs. 48.33%, p< 0.0001, Fisher's) through the use of DAAs. Similarly, more HCV/HIV coinfected patients were treated (36% vs 5%, p<0.0001, Fisher's) and had HCV suppression (86% vs 19%, p<0.0001,

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Fisher's) during the DAA era than in pegylated interferon.

Greater proportions of both HCV monoinfected and HCV/HIV coinfected patients were treated and achieved HCV viral suppression during the DAA era at the DC-VAMC. HCV/HIV coinfected patients treated in the DAA era achieved similar suppression rates compared to monoinfected patients.

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Defining Brain Chemical Changes and Areas of the Brain Most Affected by High Ammonia Levels in Children with Urea Cycle Disorders

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BACKGROUND: Urea cycle disorders are among the most common of the inborn errors of metabolism. These disorders affect up to 1/25,000 live births in the United States, and the number of children affected by partial defects may be much higher. Urea cycle disorders can lead to high rates of disability if not treated early. The urea cycle converts nitrogenous waste, a toxic byproduct of protein metabolism, into urea, a safe compound which is excreted in the urine. Children with urea cycle disorders are unable to fully metabolize nitrogenous waste in the liver, resulting in high levels of ammonia in the blood. Hyperammonemia has well-known neurologic sequelae. However, the structural and chemical consequences of high ammonia in the brain of a developing child have not been well-defined. Furthermore, due to compartmentalization, ammonia

Patient	Thalamus	Peri-insuar region	Basal ganglia	Globus pallidus	Frontal lobe	Temporal lobe	Parietal lobe	Occipital lobe	Corpus Callosum	Volume loss	Brain stem
1	–	–	–	–	+	–	–	–	–		
2	–	+	+	+	+	+	+	–	+	+	+
3	–	+	+	+	+	+	+	–	–	–	+
4	–	+	+	+	+	+	+	–	–	+	–
5	–	–	–	+	+	+	+	–	–	–	–
6	–	+	+	+	+	+	+	+	–	–	+
7	–	–	+	+	–	–	–	–	–	–	–
8	–	+	+	+	+	+	+	+	–	–	+

FIGURE 1: Magnetic resonance spectroscopy analysis of chemicals in the brain during symptomatic periods as compared to asymptomatic periods. (♠) denotes an increase of the corresponding chemical in the brain compared to the patient's baseline. (♦) denotes a decrease of the corresponding chemical in the brain as compared to the patient's baseline. (-) denotes no difference in the corresponding chemical between symptomatic and asymptomatic periods.

Patient	NAA	Glutamine	Glutamate	Creatine	Choline	Myoinositol	Lactate	Lipid
1	↓	↑	↑	–	↑	↓	↑	↑
2	↓	↑	↑	–	–	↓	↑	↑
3	↓	↑	↑	–	↑	↓	↑	↑
4	–	–	–	–	↑	–	↑	↑
5	–	–	–	–	↑	–	–	–
6	–	↑	↑	↓	↑	↓	–	–
7	–	–	–	–	–	–	–	–
8	–	–	–	–	–	–	–	–

FIGURE 2: Table showing areas of the brain most affected in children with urea cycle disorders as evaluated by magnetic resonance imaging. (+) denotes that the area in question had structural change, while (–) denotes that the area in question showed no structural change.

levels in the blood do not correlate well with levels of ammonia in the brain. Additionally, patients who experience high brain ammonia levels are not always symptomatic.

OBJECTIVE: To define with magnetic resonance spectroscopy (MRS) how the chemical levels of N-acetylaspartic acid, glutamine, glutamate, creatine, choline, myoinositol, lactate, and lipids vary from the norm in a child experiencing hyperammonemia. An additional objective is to evaluate the brain magnetic resonance images (MRI) of these same patients to identify parts of the brain most affected by high ammonia levels.

[Results from this] retrospective study indicate that there may be a distinct chemical footprint of changes that occur in the brain when ammonia levels are high.

METHODS: This was a retrospective study in which eight patients with various genetic defects in the urea cycle were identified. A neuroradiologist read the MRI and MRS data, and the data were analyzed for similarities.

RESULTS: MRS data (Figure 1) showed that brain levels of myoinositol are decreased in patients with hyperammonemia. Levels of lactate, glutamate, glutamine, and choline are increased. N-acetylaspartic acid may be either decreased or normal. Creatine and lipid levels remain normal. MRI data (Figure 2) showed that areas of the brain affected by high ammonia are the peri-insular region, the globus pallidus, and the frontal, temporal, and parietal lobes. The thalamus, occipital lobe, corpus callosum, and brain stem were unaffected in these patients.

CONCLUSION: The findings in this small retrospective study indicate that there may be a distinct chemical footprint of changes that occur in the brain when ammonia levels are high. This suggests that MRS could be a better tool to evaluate the biochemical consequences of high levels of ammonia in the brain rather than a blood ammonia level. Furthermore, MRI data suggest there are distinct regions of the brain that are more sensitive to the effects of hyperammonemia than others.

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Fracture Risk in Spaceflight and Potential Treatment Options

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Understanding the chronic effects of a microgravity environment on bone is essential, since humans are now considering new long-distance spaceflight missions. Prior to these missions, it is important to acknowledge that the negative effects of long-duration spaceflight on bone may increase the risk of musculoskeletal injuries.[1] As a result, management options for these types of injuries, particularly fractures, should be addressed. The objective of this study was to determine high-risk bone fracture areas after long-duration spaceflight, and identify management protocols for those fractures.

A literature search was conducted for information on current fracture risk predictive models and suggestions for treatment. It is well known that bone mineral density (BMD) decreases during long-duration spaceflight.[1,2] This is likely the result of decreased load on bone in a microgravity environment, which leads to an uncoupling between bone resorption (increased) and bone remodeling (stable or decreased), also causing diminished bone fracture healing.[2] While the risk of fracture in a microgravity environment is believed to be low, the potential risk for fracture increases upon re-entering a gravity environment (such as the Earth, the moon, or Mars).[1,2]

The Bone Fracture Risk Model (BFxRM) is an algorithm developed to determine the probability of fracture at a particular skeletal site in a given loading scenario.[2] As predicted by this model, there is greater fracture risk of the lumbar spine, femoral neck, and wrist, especially with increased mission duration and subsequent physical activity once re-introduced to a gravity environment.[2] While there are many viable suggestions for mitigating bone fracture risk, there are limited proven management options. Exercise is part of a fundamental long-duration spaceflight strategy to mitigate BMD loss, and BMD improvement with exercise has been augmented by the introduction of the advanced resistance exercise device (ARED) on the International Space Station. Additionally, studies have shown that supplementation with bisphosphonates has an additive effect for preventing bone loss.[1]

If a fracture were to occur, promising treatment options to improve bone fracture healing in space (in addition to standard management modalities such as splinting) include the use of low-intensity pulsed ultrasound, electromagnetic field therapy, and intermittent subcutaneous injections of parathyroid hormone.[3,4] In the event of a complex fracture, surgical intervention with a universal external fixation device could be a viable option for management.[5]

In conclusion, the best strategy for reducing musculoskeletal injuries for deep-space missions will be a combination of BMD loss reduction coupled with improvements in management protocols for potential fractures.

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Impact of Expanded Medicaid Coverage on Hospital Length Stay Following Injury

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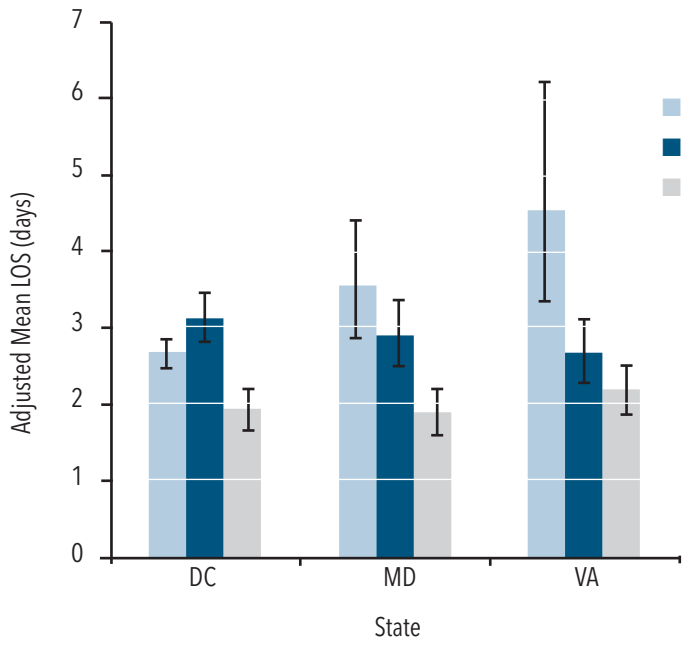

FIGURE: Adjusted Mean LOS by Insurance by State.

Adjusted for age, sex, ISS, AIS, and penetrating injury. Error bars show the 95% confidence interval. LOS = Length of Stay. ISS = Injury Severity Score. AIS = Abbreviated Injury Score.

With passage of the Affordable Care Act (ACA) in 2010, 32 states — including Washington, D.C., and Maryland—expanded their Medicaid insurance coverage. Nineteen states, including Virginia, did not expand their coverage. Within the Medicaid expansion states, specific eligibility requirements vary.[1] For example, non-elderly (under 65), non-disabled adults without dependent children are eligible for Medicaid in D.C. with annual incomes up to 210 percent of the Federal Poverty Level (FPL).[2] In Maryland, these same patients are eligible at annual incomes up to 133 percent of FPL (the ACA's Medicaid Expansion minimum standard).[2] In Virginia, these patients are not eligible for Medicaid at all.[2]

Trauma centers are required to treat all patients regardless of insurance status, yet patients may have different hospital length of stay (LOS) depending on their access to care post-discharge. After controlling for injury severity, insured patients with increased access to post-discharge care, such as rehabilitation and home health services, have been found to have a shorter LOS compared to uninsured patients.[3,4] The purpose of this study is to identify if expanded Medicaid eligibility in D.C. and Maryland correlates with a shorter LOS for trauma patients, as it was shown to do with insured patients in general. A retrospective study of trauma registry patients admitted to the George Washington University Hospital, a Level 1 adult urban trauma center, during a 38-month period (Jan. 1, 2013, to March 6, 2016) was performed. Patients included those on non-commercial insurance, including Medicare and Medicaid, as well as those who were uninsured. Patients with commercial insurance or whose payer information was not identified were excluded. Additionally, patients who were pronounced dead on arrival or who died during their hospitalization were excluded. Primary outcome measures were comparison of type of insurance and LOS by state of residence in Virginia, Maryland, and D.C.

During the study period, 4,883 patients were admitted to the trauma service with 2,728 patients enrolled per our inclusion criteria. Medicaid patients from D.C. had a significantly shorter average LOS (2.64 days) than patients from Maryland (3.53 days, $p = 0.003$) or Virginia (4.56 days, $p = 0.02$) (Figure). This difference persisted after controlling for Abbreviated Injury Score (AIS) for both head and

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pelvis, Injury Severity Score (ISS), gender, age, and penetrating mechanism of injury in our multivariate linear regression model.

The D.C. and Maryland, states that participated in Medicaid expansion, are associated with shorter hospital LOS for trauma patients than the non-expansion state of Virginia. However, as the result of the differing Medicaid coverage eligibility requirements in D.C. and Maryland, discrepancy also exists in LOS between these states. Expanded Medicaid coverage in D.C., which includes undocumented immigrants and individuals at higher federal poverty income thresholds, may result in financial savings opportunities for trauma patients following injury. It is expected that Medicaid expansion is associated with shorter hospital LOS for trauma patients due to increased access to rehabilitation facilities and home health services. However, future work investigating the discharge destination of Medicaid patients under the ACA is needed.

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Outcomes of Clavicle Fractures in the NFL

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Clavicle fractures play a significant role in high-profile athletes' performance. Large-scale studies have reported that clavicle fractures make up 30 percent of all fractures in athletes and are associated with the third longest timeline for return to play among sports-related fractures.[1,2] While studies have evaluated the duration of return to play, impact of surgical versus nonsurgical management, and re-injury rates, there is a lack of studies assessing the long-term impact on athlete performance after returning from this injury.[3,4,5]

Our study aimed to define the time to return to play following clavicle injuries in the National Football League (NFL) and to estimate the quantitative effect on athletic performance.

Data on NFL players who sustained a clavicle fracture were collected from 2000 to 2015. Outcomes data included time to return to play, yearly total yards and touchdowns for offensive players, and yearly total tackles, sacks, and interceptions for defensive players. Using previously accepted methodology, offensive power rating (OPR = [total yards/10] + [total touchdowns x 6]) and defensive power rating (DPR = total tackles + [total sacks x 2] + [total interceptions x 2]) were calculated for the injury season and one season before and after the injury season. Offensive and defensive control groups consisted of all players who completed the 2013 NFL season without an identified clavicle injury.

The study group was comprised of 16 players who sustained a clavicle injury, including 14 offensive, two defensive, and one special teams players. All players returned to the NFL following injury. Athletes returned to competition at a median of 2.6 months following injury and missed a median of seven games. Analysis of pre- and post-injury athletic performance revealed no statistically significant change after return to sport. There was a trend toward lower ratings by position in quarterbacks, running backs, wide receivers, and offensive players overall, but this reached no statistical significance.

Following clavicle fracture, all players were able to return to play in the NFL. While there were some downward trends in offensive power rating post-injury, there was no significant difference in power rating before and after injury.

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"Fungus Amungus" – A Common Disease State That Is Commonly Missed: A Survey Based Study

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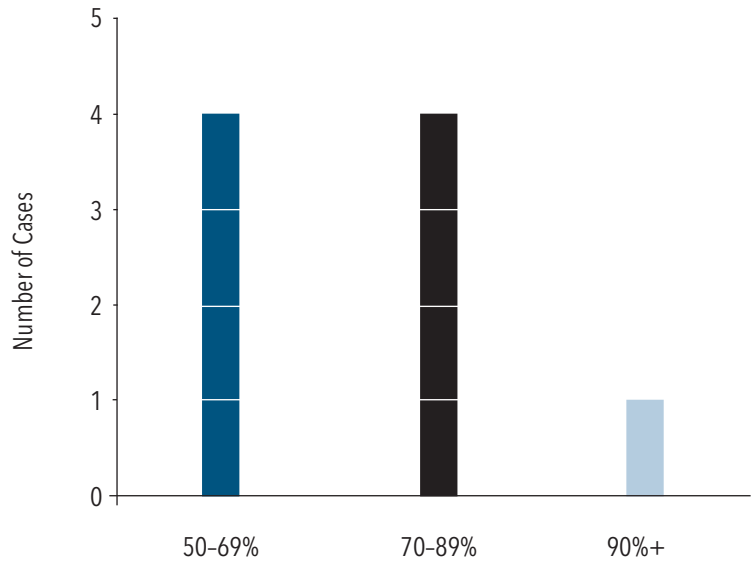

FIGURE: Number of Cases Where Participants Accurately Categorized the Pathology as Either A Dermatomycosis or Not: Organized in Percent Ranges

Dermatophyte infections involving the skin, hair, or nails affect an estimated 25 percent of the world's population1 and accounted for 51 million outpatient visits over a 10-year period (1995-2004) in the United States alone.[2] Dermatomycosis is routinely managed by dermatologists, though given the diversity of clinical presentations, is sometimes misdiagnosed, which can result in inappropriate therapy, worsening of symptoms, and even result in additional skin and soft tissue infections.[3]

An interactive survey of board-certified dermatologists was conducted at the 2016 Orlando Dermatology Aesthetic & Clinical Conference, during a seminar on superficial mycotic infections. The structure of the survey entailed reviewing a presentation of a clinical image followed by responding to a simple yes or no question: is this a fungal infection? Data was gathered anonymously via an audience response system and data tabulated using Microsoft Excel.

The raw data of the survey is presented in the Table. In all, 13 cases were presented, and the results are summarized in the Figure. Although the majority of the cases (8/13) were appropriately categorized by 50+% of the audience, this percentage decreased as accuracy of categorization increased. For example, in only 4 of the 13 cases did audience members accurately categorize the cases >75% accuracy. Moreover, there was only one case for which 90%+ of the audience appropriately categorized the case.

The study limitations included a lack of a measureable response

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rate and a small sample size, which prevent significant conclusions from being made. However, the results do emphasize the protean clinical nature of cutaneous dermatomycoses and the ease with which one may miss the correct diagnosis. Secondary syphilis, annular psoriasis, and pityriasis rosea are among just a few inflammatory skin diseases that can mimic dermatophyte infections as illustrated herein. As such, these data underscore the importance of continued medical education on dermatophyte infections as well as proper education and training on bedside diagnostic techniques, such as potassium hydroxide, during residency and beyond.

		n (%)	
Case	Diagnosis	Yes	No
1	Secondary syphilis	16 (94.1	1 (5.9)
2	Tinea corporis	7 (46.7)	8 (53.3)
3	Erosio interdigitalis blaastomyceticia	12 (70.6)	5 (29.4)
4	Tinea corporis	10 (52.6)	9 (47.4)
5	Tinea faciei	10 (58.8)	7 (41.2)
6	Pityriasis rosea	13 (76.5)	4 (23.5)
7	Tinea corporis	26 (86.7)	4 (13.3)
8	Majocchi's granuloma	3 (13.0)	20 (87.0)
9	Tinea versicolor	18 (72.0)	7 (28.0)
10	Tinea pedis	22 (78.6)	7 (28.0)
11	Erythema annulare centrifugum	10 (33.3)	20 (66.7)
12	Woringer-Kolopp disease (Pagetoid Reticulosis)	12 (46.2)	14 (53.8)
13	Gram negative toe web infection	2 (6.1)	31 (93.9)

TABLE: Participant Responses to Clinical Images

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Differences between Hidradenitis Suppurativa, Chronic Wounds, and Normal Keratinocytes in an In-Vitro Wound Closure Model

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Hidradenitis suppurativa (HS) is a chronic, recurrent, inflammatory disease of apocrine glands. The disease affects approximately 1 percent of the population, and there is currently no known cure. The immune mechanisms of HS are poorly understood. There is an unmet need to elucidate molecular drivers of HS in order to develop novel treatments and improve clinical outcomes for patients. Keratinocytes are cells found in the basal layer of the stratified epithelium that comprises the epidermis. Defective keratinocyte function is thought to play an important role in HS and is considered to be critical in disease prognosis and pathogenesis.[1,2] The purpose of this study was to compare keratinocyte function in HS, chronic wound (CW), and normal (N) skin samples.

Scratch assays are an established method for investigating cellular function in vitro.[3,4] Human epidermal keratinocytes were cultured to

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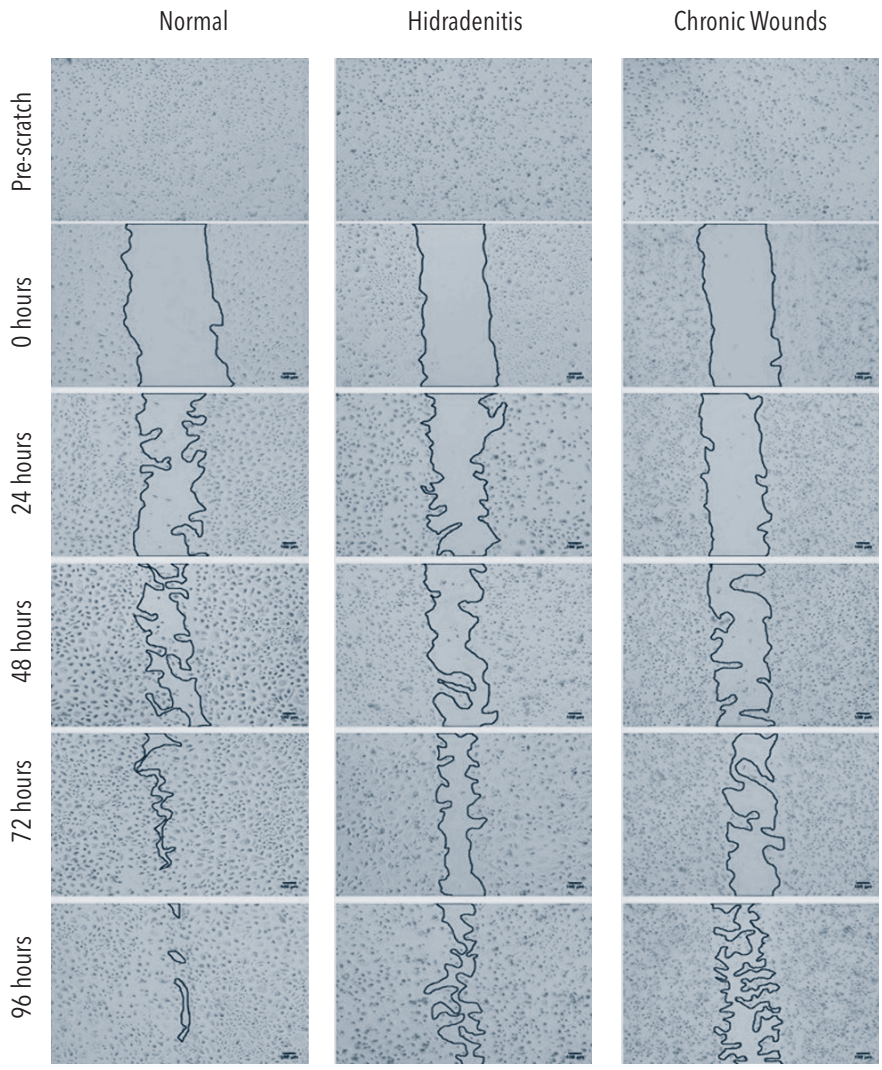

FIGURE 1A: Keratinocytes from normal skin samples demonstrate significantly higher rates of scratch closure than those from chronic wounds or HS skin. Representative images from keratinocyte scratch migration assay showing chronic wound samples have delayed closure compared to normal.

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reach 80 percent confluence and then a scratch was made using 1 ml sterile tip of about 100um in diameter. Individual cultures were photographed at 0, 24, 48, 72, and 96 hours after scratch using an inverted phase contrast microscope. Wound closure was determined as percentage decrease in total scratch surface area over time.

Viable cells at 96 hours after the scratch in each group were determined by fluorescence microscope utilizing a live/dead vital dye staining method. Apoptosis was assessed by flow cytometry for each group at 96-hour time-point after initial scratch using a FITC-annexinV-Propidium Iodide (PI) method5 where apoptotic cells stains annexinV positive and necrotic cells are double positive for annexinV and PI. Multiplex cytokine analysis was used to measure cytokines and growth factors from cell culture supernatant collected at 0, 24, 48, 72, and 96 hours after scratch.

Scratch closure rates were significantly slower in HS and CW compared to normal (Figure 1A). Percent closure was significantly less in chronic wound keratinocytes than in normal keratinocytes at all time points measured (Figure 1B), whereas in the HS keratinocytes, significant differences in closure were seen at the 72 hr. (p=.037) and 96 hr. (p=0.006) time points.

Cell viability was similar at 96 hours post scratch in the normal and HS keratinocytes (Figure 2A). However, cell viability was significantly lower in chronic wound keratinocytes at 96 hours (p=0.0138) (Figure 2b).

Increased apoptosis and necrosis was observed in CW compared to

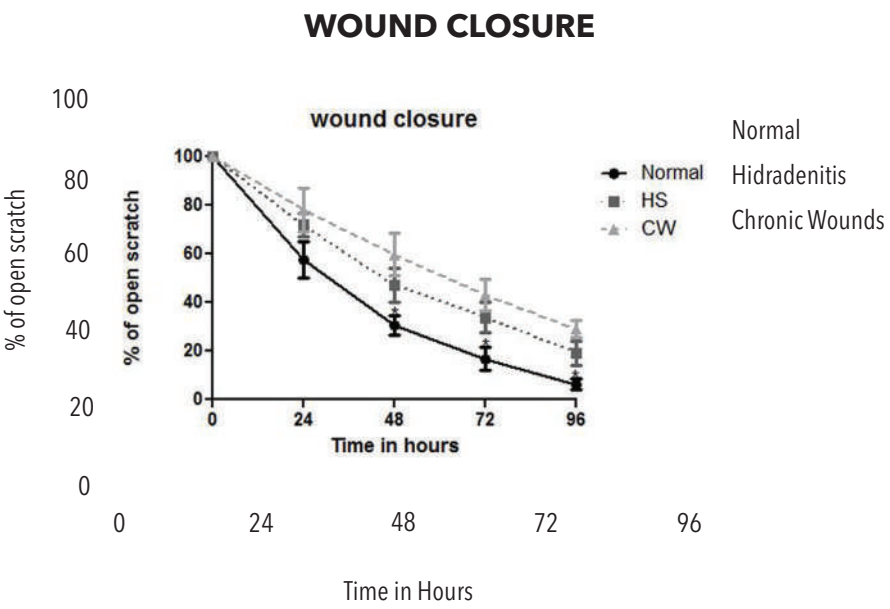

FIGURE1B: The graph shows the percentage of scratch re-epithelialization at different time points. Results are expressed as the mean ± SEM. Closure was significantly less in cultured keratinocytes from chronic wound specimens than from normal keratinocytes at all time points measured (* P<0.05 between normal keratinocytes and chronic wound keratinocytes at 24, 48, 72, and 96 hours). Significant difference was only seen between normal and hidradenitis keratinocytes at the 96 hour time point (~ P<0.05).

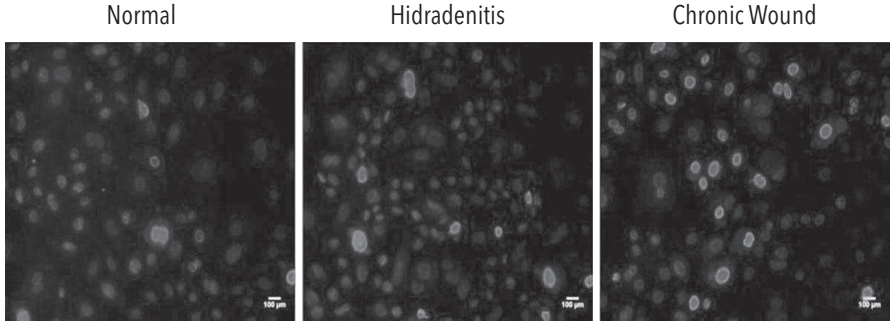

FIGURE 2A: Differences in cell viability and cytokine production among Normal, HS and CW keratinocytes. Fluorescent microscopy showing live (blue) / dead (green) keratinocytes from three representative human samples, which were normal, having chronic wound and hidradenitis patient respectively. Staining was done 96 hours after a scratch was done on a confluent culture surface. Magnification=100X.

normal and HS keratinocytes 96 hours post-scratch (Figure 2C). Flow cytometry for Annexin V/PI demonstrated that CW keratinocytes had a significantly higher rate of apoptosis (annexinV positive) and necrosis (annexinV-PI double positive cells) than normal (p=0.0075) and HS (p=0.028) keratinocytes.

Evaluation of cytokine concentration from scratch assay culture supernatant showed significantly higher IL-1α and VEGF in normal keratinocytes compared to CW. In contrast, IL-22 levels were significantly lower in the HS culture supernatant (Figure 2d) than both CW and normal keratinocytes (p=0.0008). This finding indicates that IL-22 and its downstream pathways merit further investigation as molecules of interest in HS pathogenesis.

Using a keratinocyte scratch assay, we were able to show that keratinocytes harvested from HS, CW, and normal skin exhibit distinct behaviors in response to in vitro wounding. Results indicate that cell viability, key cytokines, and growth factors may contribute to these observed differences in keratinocyte function. Inherent biologic mechanisms at the level of the keratinocyte may contribute to delayed healing in chronic wounds and the pathogenesis of hidradenitis suppurativa.

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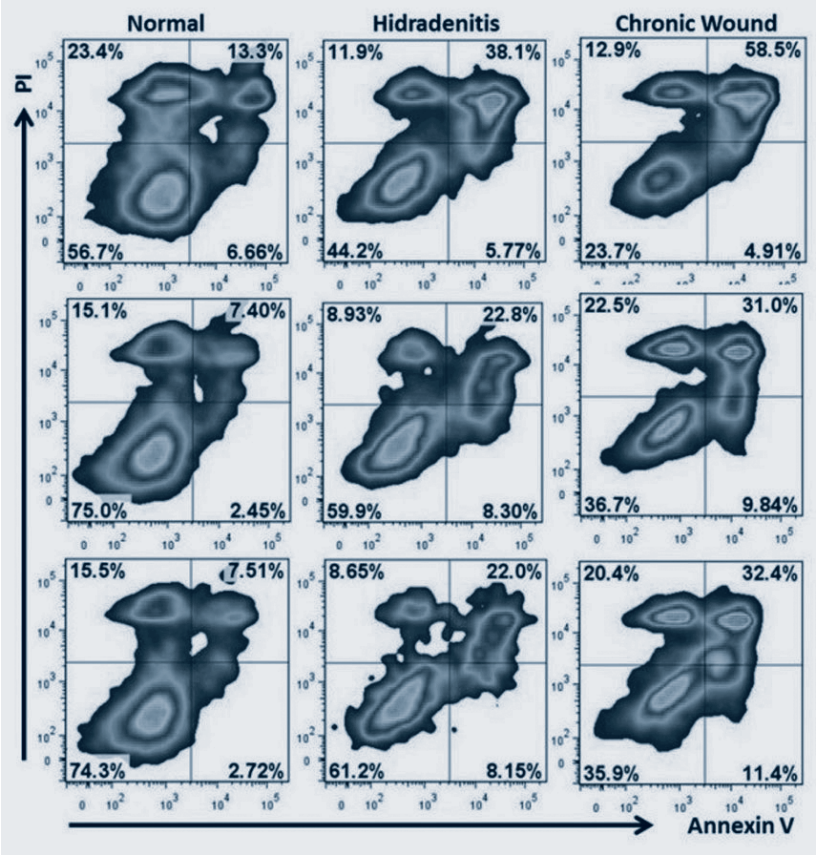

FIGURE 2B: Graph showing % viable cells (keratinocytes) in Normal (N), Hidradenitis (HS) and Chronic wound (CW) samples, 96 hours after scratch. There was a significant decrease in viability among CW compared to Normal and HS.

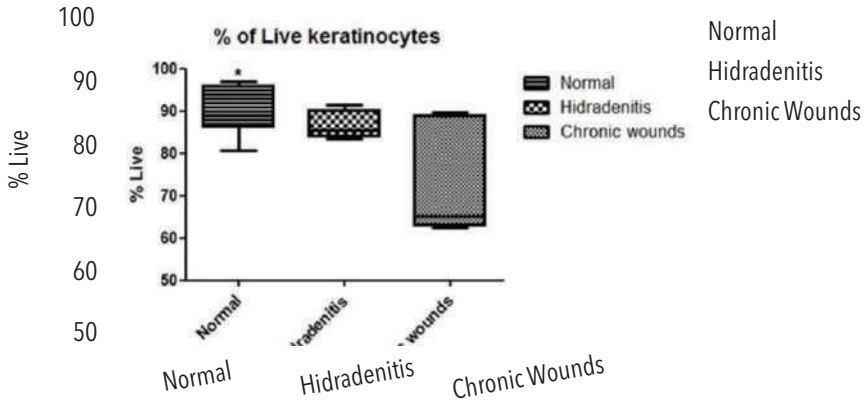

FIGURE 2C: AnnexinV/ PI double negative cells were highest in normal followed by HS group and lowest in CW across all samples.

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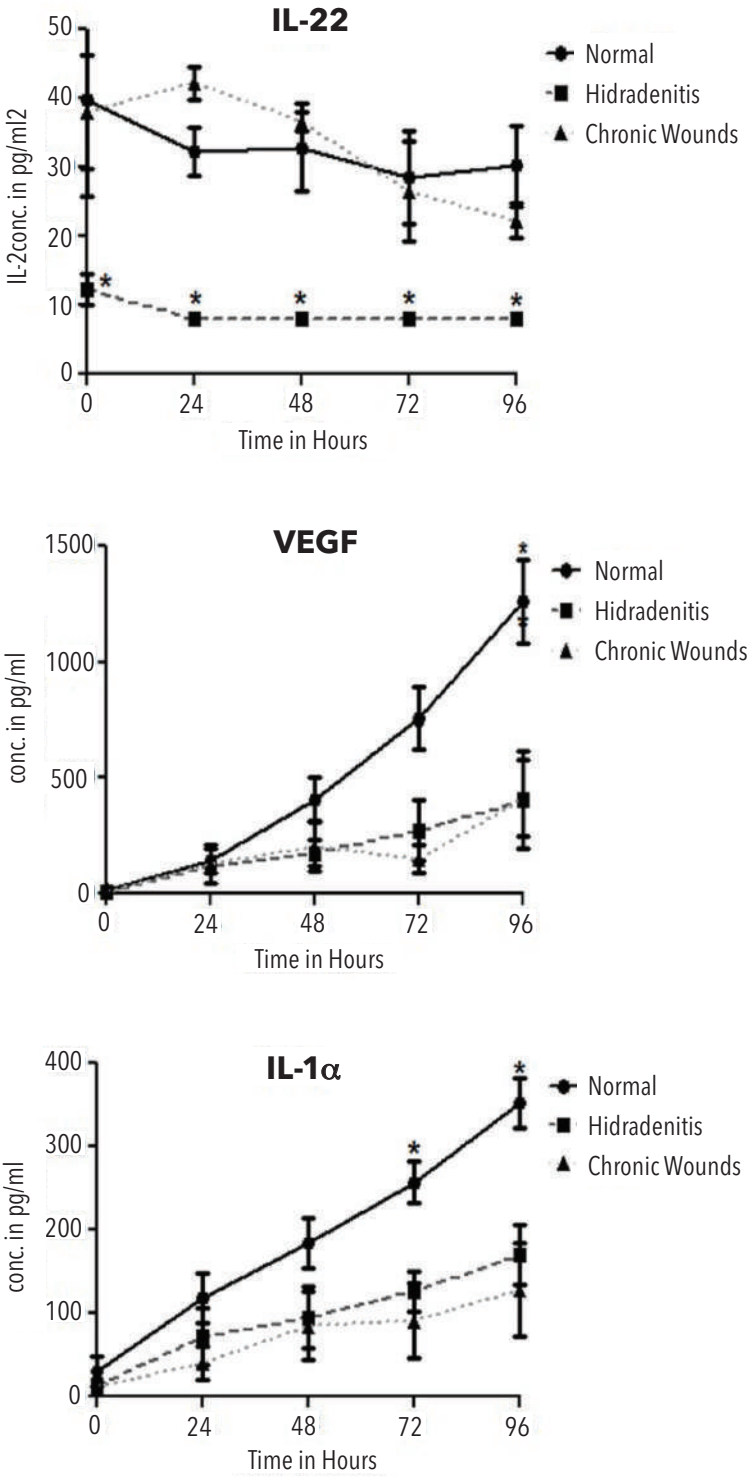

FIGURE 2D: HS keratinocytes had significantly lower production of IL-22 in culture supernatant at all time points whereas, normal keratinocytes had a significant steady increase of VEGF and IL1-α over time compared to other groups.

Unusual Clinical Capnogram Due to Sidetream Sampling Leak: Mechanism by Numerical Analysis

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INTRODUCTION

A leak in the sidestream sampling tube generates a characteristic capnogram (Figure 1A), where PCO_2 on the first plateau is decreased because of dilution with room air (containing no CO_2) into the sampling tube. Then, during the beginning of the next inspiration (last portion of the capnogram plateau), the increased airway opening pressure (Pao) decreases the leak to increase end-tidal PCO_2 ($PetCO_2$) and raise the second plateau. In one patient, we observed the capnogram depicted in Figure 1B, where the waveform is rather narrow and of significant decreased amplitude ($PetCO_2$), which also turned out to be caused by a sidestream sampling tube leak. We hypothesized that the characteristic dual-plateau capnogram with sampling tube leak is not visible with a severe leak because the significant inflow of room air (containing no CO_2) dilutes and decreases the first PCO_2 plateau to near zero. Only the second PCO_2 plateau is visible, when increasing Pao at the beginning of inspiration (last portion of the capnogram plateau) decreases the leak of room air into the sampling tube.

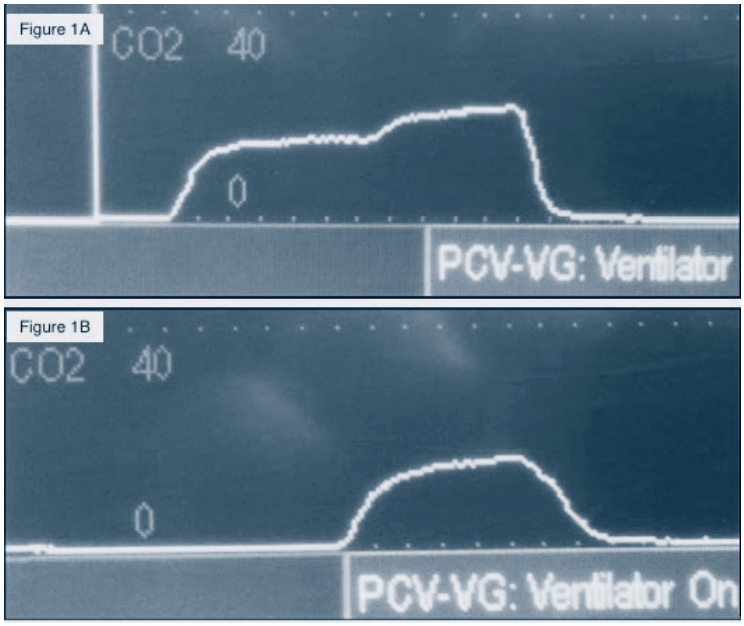

FIGURE 1: A) Capnogram Displaying Mild Leak in Side-Stream Sampling Tube. **B)** Capnogram Displaying Severe Leak in Side-Stream Sampling Tube.

EQUATION

THEN, AT EACH T,
MEASURED PCO2[T] = FLOWST[T] X ACTUAL PCO2[T] / FLOWST[T] + FLOWLEAK[T])

METHODS

To test this hypothesis, we developed a numerical analysis model to simulate mild and severe leaks in the sidestream sampling tube, using digital data from a patient capnogram (PCO_2[t]) and Pao[t]) (Figure 2), where t is time and PCO_2[t] is temporally advanced to account for transit t down the sampling tube. Equations were developed to calculate the flow through the sampling tube (FLOWst[t]) and the leak flow into the sampling tube (FLOWleak[t]), where FLOWleak[t] is decreased by increasing Pao[t].

Data were plotted for one full capnogram (Figure 2). At any t, if Pao[t] + proximal sampling tube P (sidestream sampling suction) was greater than zero (reverse FLOWleak), then FLOWleak[t] was set to zero in the Equation.

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RESULTS

Sampling tube resistance (R = P / FLOW) was 0.15 mmHg/(ml/min) (proximal sampling tube P of -30 mmHg / sampling FLOW rate of 200 ml/min). For the mild sampling tube leak condition, we used Rleak of 0.06 mmHg/(ml/min), generating the dual-plateau capnogram depicted in Figure 2. For the severe capnometer sampling leak condition, we used Rleak of 0.007 mmHg/(ml/min), generating the narrow, low amplitude capnogram also displayed in Figure 2.

DISCUSSION

That the numerical analysis model (Figure 2) qualitatively generated the dual-plateau capnogram during mild sampling tube leak (Figure 1A) and the narrow, low amplitude capnogram during severe sampling tube leak (Figure 1B) supports our proposed mechanisms underlying the $PCO_2[t]$ waveforms when air leaks into the sampling tube. For the severe sampling tube leak, the narrow, low amplitude capnogram is similar to the second plateau of the dual-plateau capnogram observed with a mild sampling tube leak. It is important to recognize Figure 1B as a severe leak into the capnometer sampling tube. Otherwise, the resulting narrow, low amplitude capnogram could be confused with low cardiac output (decreased CO_2 delivery to the lung), depression of tissue metabolic activity (decreased CO_2 production), or excessive alveolar ventilation.

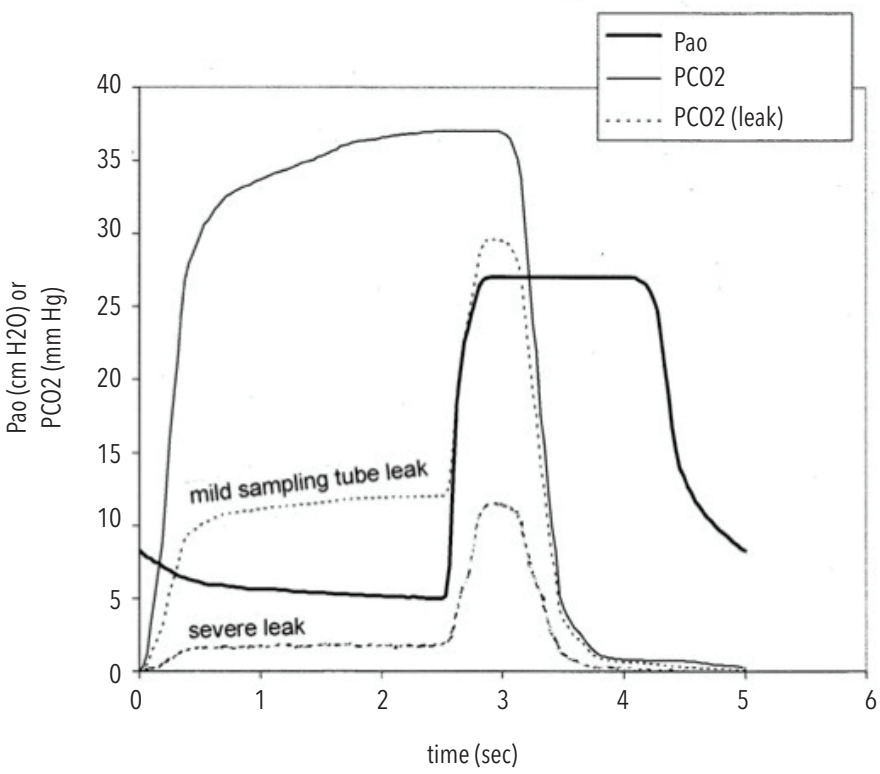

FIGURE 2: Numerical Analysis Model Calculated Graph Displaying Mild and Severe Leaks in Sidestream Sampling Tube with Expected PCO2 and Pao

Modulation of AM251 on Axon Growth in an Explant Model of Mouse Embryonic Retinal Ganglion Cells

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Glaucoma is a leading cause of irreversible blindness worldwide and is characterized by progressive destruction of neuronal connections between retinal ganglion cells (RGCs) and subsequent visual systems in the brain. However, emerging evidence suggests that adult RGCs may be coaxed to behave in a manner similar to that observed during embryonic development, when neural connections are normally formed. Although some mechanisms that govern successful regeneration of damaged neural connections in the adult central nervous system may be unique, there must be significant overlap with certain fundamental aspects of embryonic neuritogenesis, polarization, and axon growth.[1,2,3] Understanding the molecular mechanisms that govern the growth of connections between RGCs and the developing brain may ultimately lead to novel regenerative therapies for patients with glaucoma.

The current priority for investigation is the functional mechanisms of lipid messengers, termed endocannabinoids (eCGs).

The current priority for investigation is the functional mechanisms of lipid messengers, termed endocannabinoids (eCGs). These molecules modulate several types of developmental axon growth mechanisms by activating cannabinoid receptor type 1 (CB1R) and G-protein coupled receptor 55 (GPR55).[4] These receptors, along with other key enzymatic players, are localized to corticofugal growth cones at axon terminals. Activation of these receptors by eCBs, such as 2-arachidonoyl glycerol, promotes normal fasciculation and may be sufficient for stimulating directional growth. Functionally significant components of this system are expressed in RGCs during embryonic development.[5] However, the actions of eCGs on RGCs remain unclear. Elucidating these mechanisms will not only help to advance the understanding of neuronal development, but also advance the understanding of how meaningful connections are formed in order to restore neural function in diseases such as glaucoma.

In this study, retinal explants were obtained from embryonic mice from day 15 and cultured onto poly-D-lysine and laminin-coated glass coverslips in RGC growth medium. Cultures were maintained for 16 hours in the presence or absence of a drug, AM251, and then fixed with paraformaldehyde. AM251 is a high-affinity inverse agonist for the CB1R, which we believe promotes directional axon growth. Fixed retinal explants were then stained using immunocytochemistry with a cocktail of fluorescent antibodies to label various aspects of the RGC, including actin filaments and microtubules, to assess growth cone and axonal development. Explants were then analyzed using multicolor confocal laser microscopy. Collected images were analyzed for quantity and quality of axonal growth.

Stimulation by AM251 significantly increased mouse embryonic RGC axon growth overall (Figure 1). The total number of axon tips were significantly greater for AM251-stimulated RGCs compared to those treated with vehicle alone (110 vs 70 respectively, $p=0.0151$). Moreover, median axon length increased to 330 um vs. 240 um for AM251 stimulation vs. vehicle alone, respectively ($p<0.00005$). Within axon populations, AM251-stimulated RGCs also demonstrated a significantly greater proportion of axons with lengths extending beyond 300 um compared to null controls (0.405 vs. 0.305 respectively, $p<0.0005$).

These results, then, not only confirm the current understanding that embryonic systems likely share fundamental mechanisms of neuritogenesis, but that modulation of growth cone CB1Rs by agents such as AM251 may be effective in promoting axonal development in both the embryonic and adult CNS. Future studies evaluating the effects of AM251, or other eCGs, on adult RGCs could confirm these findings and provide further insights toward the potential for rescuing damaged neurons. This experiment represents a key step in the process of discovering the cure

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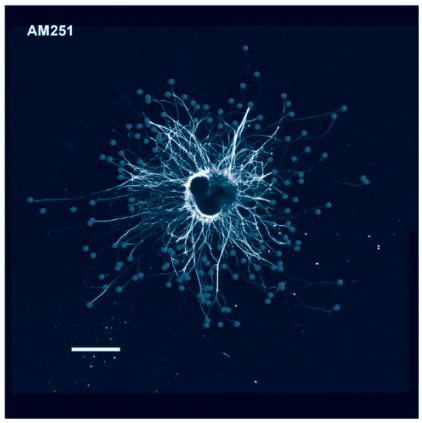
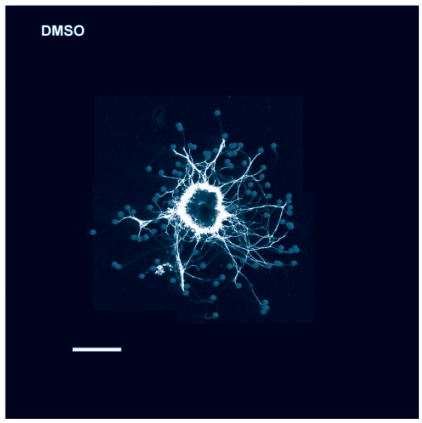
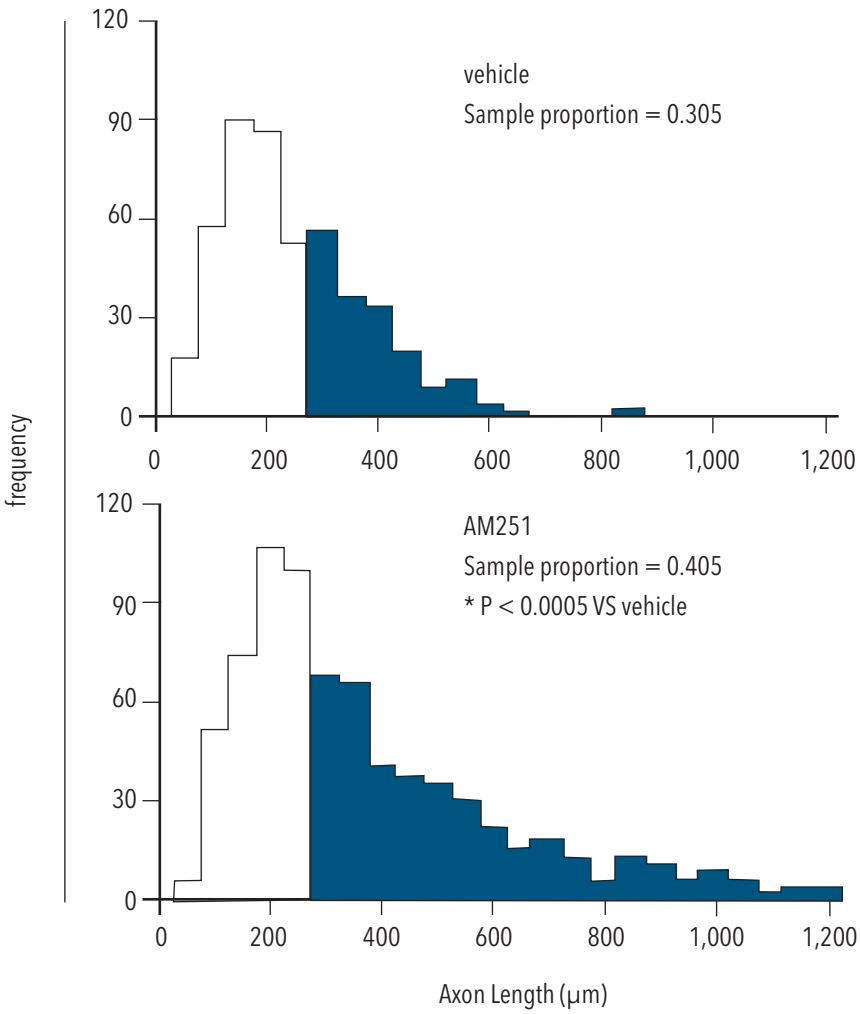
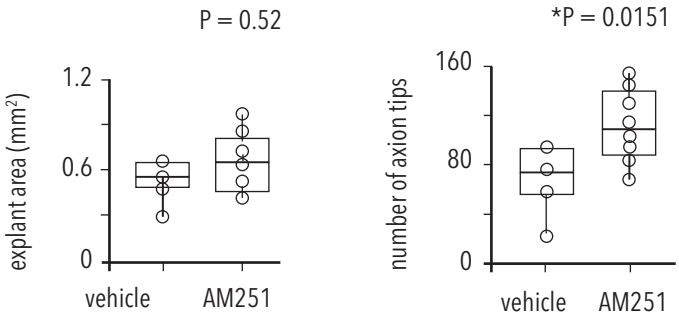
FIGURE 1: Influence of AM251 on Axonal Growth in a Murine Retinal Explant. AM251 increased the average number of axon tips compared to vehicle alone (110 vs 70, p = 0.0151). Stimulation by AM251 also induced growth of significantly longer axons (330 um) vs. DMSO vehicle (240 um, p < 0.00005). The number of total axons greater than 300 um was greater in the AM251 stimulated group (0.405) vs. DMSO treatment (0.305, p < 0.0005). There were no significant differences in retinal explant body size between the two treatment groups.









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for neurodegenerative diseases such as glaucoma.

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Developing a Third-Party HPV-Specific T-Cell Bank for Use as an Immunotherapeutic Strategy for Immune Compromised Patients with HPV-Associated Diseases

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Immune-compromised patients, including those with primary immune deficiencies and recipients of stem cell transplants, are at risk for persistent Human Papillomavirus (HPV) infections and HPV-associated malignancies. Chronic HPV infection is characterized by a weak CD4+ T-cell response and can lead to the development of HPV-associated malignancies.[1] Recent vaccine studies suggest that cytotoxic T-cell responses against HPV antigens correlate with virus control.[2] Adoptive transfer of third HPV-specific T-cells may be efficacious for immune deficient patients with HPV-associated diseases.

HPV-derived E6 and E7 are attractive targets for T-cells as they are immunogenic and play critical roles in malignant transformation. The early oncoproteins HPV16 E6 and E7 are ideal targets for the development of immunotherapy because they are only expressed in infected cells and malignant tumors, and they promote malignant transformation through the inactivation of the tumor suppressor proteins p53 and pRb.[3] A synthetic long peptide (SLP) vaccine against HPV16 E6 and E7 has induced regressions of vulvar intraepithelial neoplasia but is less effective against established cancers, suggesting that the endogenous immune system fails to eradicate bulky HPV-associated cancers even after effective immunotherapies.[2] Recent efforts by Ramos et al. have demonstrated success in expanding HPV16 E6 and E7 specific cytotoxic T-lymphocytes (CTLs) from patients with HPV-associated cervical and oropharyngeal cancers.[4] We hypothesized that strategies for ex-vivo priming and expansion of antigen-inexperienced and anergic T-cells would enable generation of HPV-specific T-cells irrespective of donor source; these cells can then serve as components of an off-the-shelf third-party bank of therapeutic T-cells.

We evaluated the feasibility of generating HPV-specific T-cells from peripheral blood of HPV-primed (n=2) and non-primed healthy donors (n=12) using GMP-compliant methodologies. Antigen presenting cells pulsed with HPV antigens were used to stimulate T-cells in combination with different cytokines.

Preliminary results show we generated T-cells targeting HPV antigens from 8/14 donors. T-cells expanded with a 142 median fold expansion after 23-25 days. The resultant product specifically recognized E6 or E7 proteins by IFN-γ ELISpot (mean 109.7 SFC/1-2x105 cells [range 12.5-334] against HPV compared to mean 6.1 SFC/1-2x105 cells, [range 0-23.5] for irrelevant antigen) and evaluated lines were comprised of 26±0.02% CD8+ and 59±0.08% CD4+ T-cells. Current efforts are focused on developing a third-party T-cell bank and demonstrating functional activity against HPV-expressing targets. Creating a third-party bank would allow us to treat multiple patients using a single manufactured line, thereby reducing the time to treatment, and provide this form of therapy as option to all patients irrespective of donor source.[5]

In summary, expansion of HPV-specific T-cells is feasible from vaccinated and unvaccinated healthy donors, and may be used as an "off-the-shelf" immunotherapy for HPV-associated diseases post-HSCT.

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Diffusion Tensor Imaging Identifies White Matter Dysmaturation in a Hypoxic Porcine Model of Congenital Heart Disease

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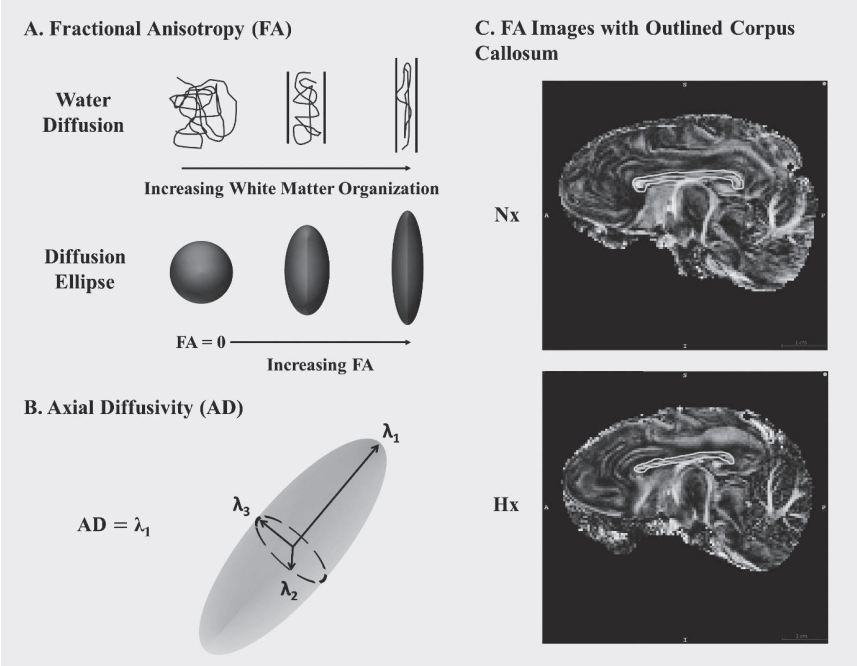

FIGURE: Descriptions of DTI Imaging Metrics (A,B) Images show smaller hypoxic corpus callosum FA values (decreased signal intensity) and volume (C).

Mortality and morbidity in the severe/complex congenital heart disease (CHD) population have been significantly reduced due to advances in neonatal cardiac surgery and hospital care. Despite these successes, CHD patients are at risk for developing long-term neurological deficits. Non-invasive peri-operative neuroimaging has suggested white matter (WM) underdevelopment and/or injury as a possible etiology.[1,2,3] Despite these findings, the developmental mechanisms underpinning WM deficits in CHD remain largely unexplored due to the technical challenges of in utero brain imaging and ethical concerns regarding the use of invasive technologies. To address these shortcomings, a porcine hypoxia model has been developed to recapitulate the WM pathologies associated with pre-operative cerebral hypoxia in CHD. In this preliminary study, diffusion tensor imaging (DTI) was used to assess the extent of WM macroscopic and microstructural dysmaturation due to hypoxia in the porcine model.

DTI is an MRI imaging modality that can provide information about the microstructure of brain tissue by measuring water diffusion. At each voxel in an image, water diffusion is represented in three dimensions by ellipses that show the principle and radial directions of water movement. Fractional anisotropy (FA) is a calculated value that indirectly measures organization of WM by assessing the radial restriction of water diffusion by tissue microstructure (Figure A). Low FA values in WM regions have been correlated with reduced structural integrity and hypomyelination in a variety of neurological diseases. Axial diffusivity (AD) is the principle water diffusion coefficient for a given diffusion ellipse (Figure B). Decreases in AD have been associated with axonal injury.[4]

Female Yorkshire piglets were housed in a hypoxic environment (10.5% FiO_2) between days 3 and 14 after birth in order to model brain development under hypoxic conditions during the late third gestational trimester and early infancy (normoxic control n=2, experimental n=3). At 14 days of age, DTI images were obtained from postmortem brains

		Volume (mm3)	Average FA	Average AD (10-3 mm2/s)
Total Brain	Nx	47,040 ± 1,680	–	–
	Hx	45,030 ± 3,820	–	–
Corpus callosum	Nx	228 ± 2	0.39 ± 0.03	0.22 ± 0.02
	Hx	195 ± 17	0.34 ± 0.02	0.20 ± 0.03
Internal capsule	Nx	234 ± 28	0.59 ± 0.01	0.33 ± 0.01
	Hx	183 ± 41	0.58 ± 0.05	0.29 ± 0.03

TABLE: Comparison of Normoxic (Nx) and Hypoxic (Hx) Cerebral Structure Volume, FA, and AD ± Standard Deviation

using a segmented diffusion echo planar MRI sequence (Figure C). Brain volume, FA, and AD were computed for the corpus callosum and the internal capsule (Table).

Following hypoxia, corpus callosum and internal capsule volumes were 14 percent and 22 percent smaller, respectively, despite a moderate total brain volume difference of 4 percent. In addition, hypoxic corpus callosum FA values were on average 13 percent lower than normoxic controls, whereas FA values for the internal capsule were only 2 percent lower. Hypoxic corpus callosum and internal capsule AD values were 9 percent and 12 percent lower, respectively, compared with normoxic controls.

These preliminary findings provide evidence that cerebral hypoxia results in reduced WM maturation during critical periods of brain development. The reduction in WM volume induced by hypoxia is likely indicative of less myelin content and/or axons. Lower FA values in the corpus callosum and internal capsule after hypoxia suggest disorganization and hypomyelination of these WM structures. Furthermore, hypoxic AD values were lower for both the corpus callosum and internal capsule indicating potential axonal injury.

Dysmaturation of the corpus callosum and internal capsule can diminish neural connections transmitting important motor, sensory, and cognitive information. Studies of CHD patients have shown deficiencies in the aforementioned neural functions.[1,2,3] The findings presented here strengthen the evidence supporting pre-operative hypoxia as an etiology for the long-term neurologic sequelae of CHD. Future studies involving the hypoxic pre-operative porcine model of CHD will aim to correlate DTI findings with WM histological changes.

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GPR83 Function Contributes to Salt Resistance

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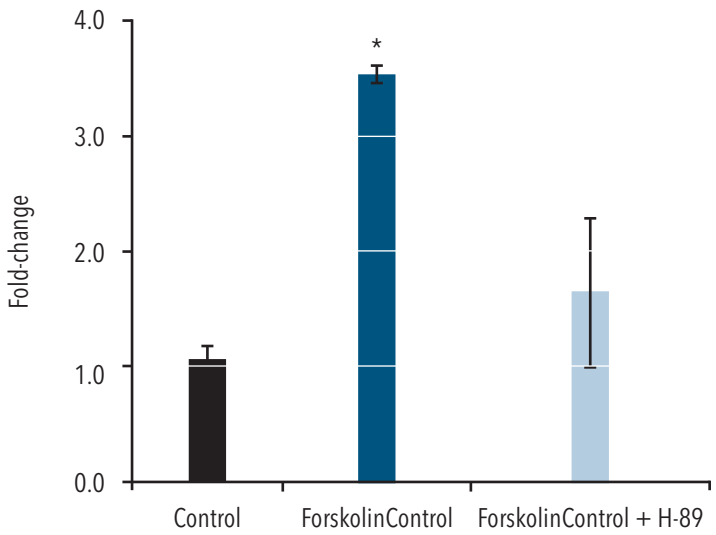

FIGURE 1: PKA Stimulation Increases Gpr83 mRNA Expression. Immortalized human renal proximal tubule cells were incubated with forskolin (10 µM, 30 min) in the presence or absence of the PKA inhibitor H-89 (20 µM, 1 h). Forskolin activates adenylyl cyclase and increases intracellular levels of cAMP, which in turn activates protein kinase A. After incubation, the human renal proximal tubule cells were collected, lysed, and RNA extracted. mRNA expression was quantified by qRT-PCR. N=4/group; P<0.05 vs all others, one-way ANOVA, Holm-Sidak test.

The G protein-coupled receptor (GPCR) 83 (Gpr83) is an orphan receptor belonging to the rhodopsin-like family of GPCRs.[1] Gpr83 was originally identified as a glucocorticoid-induced transcript in a murine T-cell line and referred to as glucocorticoid-induced receptor.[2] Gpr83 is expressed in brain hypothalamic nuclei relevant to energy metabolism control and has a role in the central regulation of energy metabolism.[3] Gpr83 is also expressed in the kidney, but its function is unknown. We found that Gpr83 is expressed in mouse renal proximal and distal convoluted tubules, as well as in human renal proximal tubule cells (hRPTCs). High salt diet increased Gpr83 transcription by 2-fold (P<0.05; n=4/group) in Swiss Jim Lambert (SJL/J) and Bagg Albino (BALB/c) salt-resistant mice, relative to C57 Black (C57Bl/6J) salt-sensitive mice. In C57Bl/6J mice on normal salt diet, the lack of one (Gpr83+/-) or both Gpr83 (Gpr83-/-) alleles resulted in an increase in systolic blood pressure (SBP, ~20 mm Hg (P<0.05; n=4/group, measured under anesthesia) compared with Gpr83+/+ littermates, suggesting that Gpr83 is needed to keep a normal BP. Renal-specific Gpr83 silencing by the renal subcapsular infusion of Gpr83 siRNA (3 µg/day; 7 days) increased SBP in C57Bl/6J mice on a normal salt diet, relative to mice treated with non-silencing siRNA (120±5 vs 98±6 mmHg; P<0.05; n=4/group). In hRPTCs, forskolin (10 µM, 30 min) increased Gpr83 mRNA (3.5±0.06 vs 1.0±0.12-fold; P<0.05; n=4-5/group), the effect of which was blocked by the protein kinase A (PKA) inhibitor H-89 (20 µM, 1 h). In hRPTCs, phorbol myristate acetate (200 ng/mL, 30 min), which activates protein kinase C (PKC), decreased Gpr83 mRNA (0.43±0.2 vs 1.0±0.04-fold, P<0.05; n=4-5/group), an effect that was partially blocked by the PKC inhibitor GF109203x (1µM, 1h). Stimulation of hRPTCs with ZnCl2 (100 µM, 1 h), an activator of Gpr834, increased AKT (2.5±0.5 vs 1.0±0.06-fold; P<0.05; n=4-5/group) and ERK1/2 (1.4±0.1 vs

Gpr83 function may be mediated by the phosphorylation of AKT/ERK1/2 and dephosphorylation of MAPK. Thus, several pathways are involved in the Gpr83-mediated regulation of salt-sensitive hypertension.

1.0±0.08-fold; P<0.05; n=4-5/group) phosphorylation and decreased p-38 mitogen-activated protein kinase (MAPK) phosphorylation (0.1±0.05 vs 1.0±0.1-fold; P<0.05; n=4-5/group). Our results suggest that Gpr83 may protect against the development of salt sensitivity. PKA positively while PKC negatively regulates Gpr83 expression. Gpr83 function may be mediated by the phosphorylation of AKT/ERK1/2 and dephosphorylation of MAPK. Thus, several pathways are involved in the Gpr83-mediated regulation of salt-sensitive hypertension.

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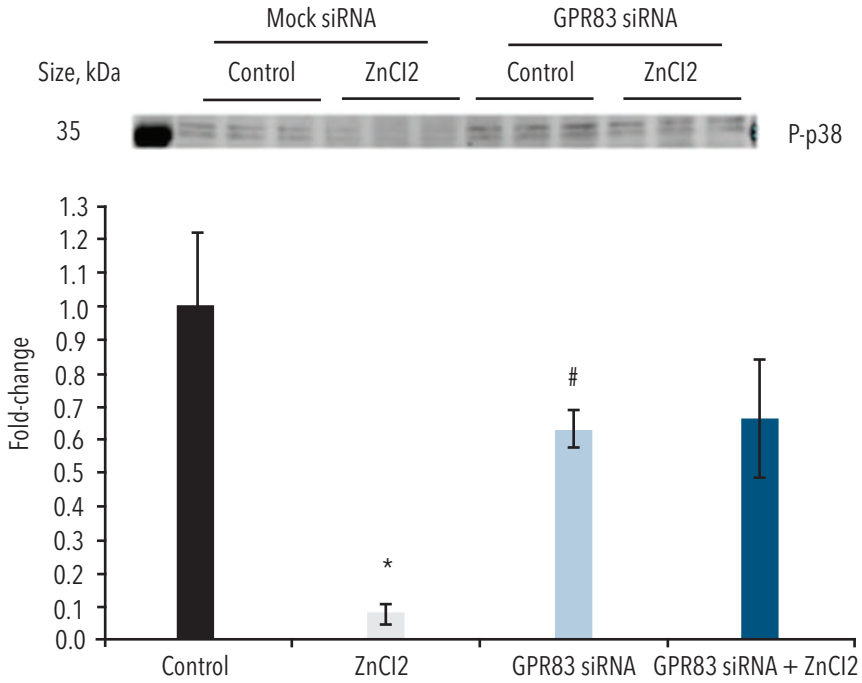

FIGURE 2: Gpr83 Activation Decreases the Phosphorylation of p38 MAPK

Immortalized human renal proximal tubule cells were incubated with vehicle or ZnCl2 (100 μM, 1 h), which stimulates Gpr83 activity. The cells were treated with non-silencing siRNA or Gpr83-siRNA (30nM, 72 h). After incubation, the cells were collected, lysed, and proteins were extracted. Protein expression of phosphorylated p38 MAPK was quantified by western blot. N=4/group; P<0.05 vs all others; #P<0.05 vs cells treated with non-silencing siRNA, one-way ANOVA, Holm-Sidak test.

Medical Student Competency in Wound Care Guidelines

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Chronic wounds are classified as wounds that have failed to heal after three months of appropriate wound care. They affect approximately 6.5 million Americans, with a prevalence of 1 percent and costs estimated at $25 billion per year. However, studies have shown that medical students receive limited wound care training during their medical school career.

The purpose of this study was to investigate medical students' exposure to chronic wound care education through didactic experience and clinical exposure at a single medical school to further assess students' confidence level with respect to chronic wound management in a single medical school.

A survey of 11 questions testing the fundamentals of chronic wound management was developed with the assistance of a trained wound care nurse practitioner based on the Agency for Healthcare Research and Quality (AHRQ) guidelines on chronic wounds (Table). The questionnaire was administered using the Internet-based REDCap survey tool to first-, second-, third-, and fourth-year medical students at the George Washington University School of Medicine and Health Sciences through the class listervs. For the purposes of analysis, students were organized into two groups: pre-clinical (years one and two), and

Question	Answer Options
1. At what time is a wound/ulcer considered chronic?	❍ 2 weeks ❍ 4 weeks ❍ 8 weeks ● 12 weeks
2. The determination of the Ankle Brachial Index (ABI) is crucial in the assessment of a chronic non-healing led ulcer. To initially assess arterial circulation for a chronic non-healing leg or foot ulcer, a patient should have:	❍ Arteriogram ● Pedal pulses palpated ❍ Hand-held Doppler Exam ❍ Non-invasive arterial studies ❍ Ankle Brachial Index measurement
3. What percentage of healing per week represents normal healing?	❍ 0–5% ❍ 5–10% ● 10–15% ❍ 15–20% ❍ 20–25%
4. How frequently should patients with diabetes undergo diabetic foot exams?	❍ Every week ❍ Every month ❍ Every 6 months ● Every year ❍ Every 2 years
5. Clinicians should consider re-evaluation of the ulcer and initiating the use of advanced treatment options if the diabetic foot ulcer or venous leg ulcer has not healed by what percentage in four weeks?	❍ 10% ❍ 20% ❍ 30% ● 40% ❍ 50%
6. What is considered the gold standard for offloading plantar diabetic foot ulcers?	❍ Postoperative shoe ❍ Unna boot ❍ Removable walking boot ● Total contact casting ❍ Half show
7. The standard of care for ulcer management using dressing is:	❍ Saline wet-to-dry ❍ Wound VAC ❍ ACE bandage ● Hydrogel ❍ Xeroform

TABLE: Seven questions from a survey based on current evidence-based AHRQ guidelines assessing the fundamentals of chronic wound management (correct answers in blue).

clinical (years three and four). Data was analyzed using T-test, Fisher's Exact and Chi Square performed using GraphPad Prism 5.0.

Of the 709 medical students who were surveyed, completed questionnaires were received from 60 students, 29 pre-clinical and 31 clinical, with an estimated response rate of 8.5%. Questionnaire performance on chronic wound care guidelines was suboptimal in both groups, preclinical and clinical. The clinical group correctly answered 34.02% of questions and pre-clinical 29.47% (p=0.1551). Medical students reported a mean of 1.38 ± 0.94 hours of didactics on wound healing, tissue injury, or wound management (p=0.0006), with a significant difference between preclinical group (0.97 ± 0.94) and clinical group (1.77 ± 0.76)s. Preclinical and clinical groups had no significant differences in correct response rate on most of the survey questions (Table). However, for the question pertaining to recommended frequency of diabetic foot examination, 9.52% of preclinical students responded correctly compared to 55.56% of clinical students (p=0.0019). Self-reported comfort level of medical students in managing chronic wounds, which was measured on a scale of zero to 10, was not correlated with correct responses on this survey. However, we did note that individuals reporting higher subjective comfort scores had received more wound-related didactic teaching hours (2.38 ±0.74 compared to 1.61±0.84, p=0.02).

Despite prevalence and cost associated with chronic wounds, there is an unmet need for guideline-based chronic wound management training for medical students.

Despite prevalence and cost associated with chronic wounds, there is an unmet need for guideline-based chronic wound management training for medical students. In order to address this deficiency, we recommend re-evaluating the didactic wound care exposure to focus on improving knowledge and comfort level using guideline-based chronic wound management across the medical school curriculum.

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

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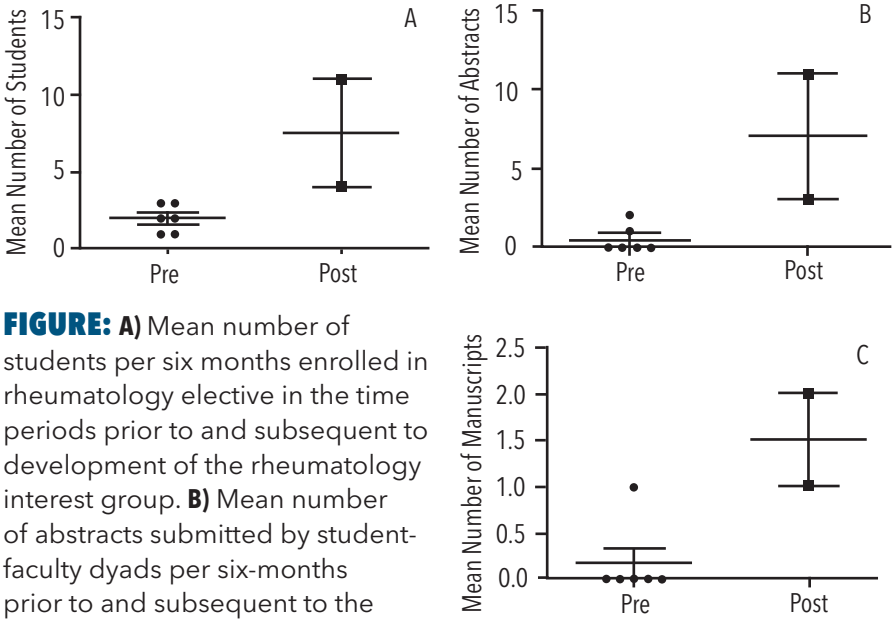

FIGURE: A) Mean number of students per six months enrolled in rheumatology elective in the time periods prior to and subsequent to development of the rheumatology interest group. **B)** Mean number of abstracts submitted by student-faculty dyads per six-months prior to and subsequent to the development of the rheumatology interest group. **C)** Mean number of manuscripts submitted by student-faculty dyads per six-months prior to and subsequent to the development of the rheumatology interest group.

In the coming years, there is expected to be significant increase in demand for rheumatologists; however, the number of trained rheumatologists is declining.[1] Interest in rheumatology often begins during medical school, and many rheumatologists report interactions with a mentor as a driving force behind their decision to select rheumatology as a career.[2,3] The American College of Rheumatology has implemented strategies to try to increase medical student interest in rheumatology, including the Choose Rheumatology program. We sought to investigate the impact of a student-led rheumatology interest group on student uptake of the rheumatology elective and submissions of abstracts and manuscripts.

In April 2015, medical students at the George Washington University (GW) School of Medicine and Health Sciences established a student-led Rheumatology Interest Group. At the inaugural meeting, the Choose Rheumatology team presented on rheumatology careers, faculty gave testimonials, and patients spoke about the impact of their rheumatologist on their lives. Follow-up meetings included a meeting on identifying mentors and research projects and two joint injection workshops.

Data was collected from the two years before initiation of the student interest group (2012-14) and the year following initiation of the group (2015-16) based on three parameters: rheumatology elective enrollment; medical student abstract submissions to GW Research Day; and manuscripts published. The mean number of student-rheumatology interactions per six months in the pre- and post-intervention period were assessed for each parameter. Data was analyzed using GraphPad Prism 5.03.

Student enrollment in the rheumatology elective significantly increased following the development of the Rheumatology Interest Group, with a mean number of students per six months of 2.0 ± 0.36 in the pre-intervention period and 7.5 ± 3.5 in the post-intervention period ($p=0.021$) (Figure 1A).

The number of abstract submissions also significantly increased with 0.5 ± 0.34 submissions in the pre-intervention period compared to 7.0 ± 4.0 in the post-intervention period ($p=0.017$) (Figure 1B).

The number of manuscripts submitted by student faculty dyads has increased since development of the Rheumatology Interest Group from 0.16 ± 0.16 to 1.5 ± 0.5 ($p=0.013$) (Figure 1C).

The Rheumatology Workforce

Study has shown that the supply of rheumatologists entering practice is not expected to meet future demands.[1] To avoid a critical shortage of rheumatologists, efforts must focus on increasing interest in rheumatology among future physicians. Exposure to a field in medical school impacts future career decisions, with 45 percent of students stating that subspecialty exposure in medical school played a significant role in career choices and 27 percent citing a department or teacher as influencing career decisions.[2]

This study demonstrated that a student-led Rheumatology Interest Group, supported by rheumatology faculty, can significantly increase medical student interest in rheumatology during medical school. Participation in the rheumatology elective, and abstract and manuscript submissions all significantly increased after creation of the interest group. This simple, low-cost intervention would be easily replicated at other institutions and could dramatically augment the student interest in rheumatology.

A simple and low-cost intervention of development of a student-led interest group, coupled with a Choose Rheumatology campus visit, provided students with increased exposure to rheumatology and increased access to mentors and research projects. These opportunities generated enthusiasm for the field as evidenced by greater enrollment in the rheumatology clinical elective, and abstract and manuscript submissions.

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Anatomical Knowledge Retention in Changing Curricula

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Traditionally, anatomy is one of the first subjects taught in medical school. Practicing physicians have commented on medical students' poor anatomical knowledge in surgically oriented clerkships. Literature also shows that correlating clinical and anatomical sciences throughout early medical education may improve anatomical knowledge retention. With major medical school curricular changes happening across the nation, more quantitative data confirming this correlation is needed.

The medical curriculum at the George Washington University School of Medicine and Health Sciences recently underwent reorganization, transforming an earlier discipline-based curriculum to that of an integrated system-based one. In order to determine whether reorganization has an effect on anatomical knowledge retention, comparisons of anatomical knowledge between classes in the different curricula were made. Students from the last class of the discipline-based curriculum (2013) and students from the first class of the new, integrated curriculum (2016) completed the same 27-question test before beginning their general surgery and obstetrics and gynecology (OB/GYN) rotations. Scores for specific anatomy categories related to general surgery and OB/GYN were then analyzed and compared between classes.

Comparing the scores from the 2013 and 2016 cohorts, there was an overall decrease in retention from 65.69% to 63.64% (Table). Item analysis per topic revealed a mean decrease in surgical anatomy and OB/GYN anatomy retention of 2.53% and 1.58%, respectively. There was a 21.6% increase in inguinal canal anatomy retention and a 17.33% increase in appendix-related questions. There was also a 12.02% decrease in fallopian

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tube anatomy retention.

In conclusion, when comparing the 2013 to the 2016 data, there were overall decreases in retention for the anatomy as it relates to general surgery and OB/GYN; however, improvements were noted for specific topic areas. These results suggest that the change in retention is apparent and multifactorial. The differences between surgical anatomy retention and OB/GYN anatomy retention scores may be related to the way the subject matter was organized and presented or how the anatomic foundational knowledge was integrated with its clinical relevance. Although integrative learning has been associated with better retention, more studies will have to be conducted to validate this statement. Finally, analyzing the subject matter, curriculum structure, clinical focus, and objectives should be evaluated moving forward.

	Complication by Broad Category	Number of test items	2013 Correct (%)	2016 Correct (%)	Change in Retention 2013–16 (%)
Surgery					
	Inguinal canal	2 MCQs	45.28	66.87	21.5922
	Vasculature	3 MCQs	30.74	35.74	5.0026
	Abdomen	3 MCQs	47.63	48.19	0.5671
	Appendix	4 MCQs	71.53	88.86	17.3297
	MEAN TEST SCORE	13 MCQs	66.98	64.45	-2.53
OB/Gyn					
	Uterine	2 MCQs	45.69	55.73	10.0353
	Vasculature	4 MCQs	49.14	64.31	15.1671
	Peritoneal cavity	1 MCQ	82.76	92.17	9.4114
	Fallopian tube	1 MCQ	63.22	51.20	-12.0184
	Embryology	3 MCQs	47.92	48.79	0.877
	Placenta	1 MCQ	80.14	78.92	-1.217
	MEAN TEST SCORE	14 MCQ	64.40	62.82	- 1.58
Overall Retention for Both Disciplines			2013: 65.69	2016: 63.64	-2.05

TABLE: Scores from 2013 vs. 2016: Retention Comparison

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Showing Your Public Face: Are Residency Applicants Professional on Social Media?

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With the virtually ubiquitous usage of social media, business and medical professionals have become increasingly aware of the presence of, and consequences related to, use of spcial media. The American Congress of Obstetricians and Gynecologists (ACOG) warns its members of the dangers of posting inappropriate information and pictures. They also produced a video titled "Social Media Professionalism in the Medical Community." Studies show that physicians are being "friended" by their patients on social media sites.[1] Employers are increasingly screening their applicants' social media behavior for professionalism, and this is extending to the medical profession as well. As of 2009, 10 percent of residency programs used social media to screen applicants.[2] A 2012 survey found most residency applicants altered their social media profile before the residency match process.[3]

First and last name, medical school, and current photo were provided for each applicant interviewed for the OB/GYN residency position at Brown University. Each applicant was searched on Facebook, Instagram, Twitter, LinkedIn, and Google. When there were multiple accounts with the same name, the medical school and photo were used to differentiate accounts. A quantitative analysis was performed with a final calculation of the number of applicants with publically accessible profiles, private profiles, and any inappropriate content. Inappropriate content was defined as behaving inappropriately in the medical setting, violating patient privacy, boasting of substance use, sexually explicit content, or inappropriate (foul/racist/sexist) language.[4,5]

The accounts of 87 residency applicants were searched for publically available information. None of the applicants met the criteria for inappropriate social network material. Twenty-two out of the 87 applicants had Facebook content a "non-friend" could view. Twitter was not a popular interface, with only seven accounts easily searchable, and among those accounts, some limited content to approved followers. Instagram had the greatest number of private accounts with only four accounts with pictures available to the public. No LinkedIn or Google searches included inappropriate content. During a post-Match Day search in July 2016, results were not significantly different from the original search.

There were no instances of inappropriate content among the candidates' publically available social media postings. One of the difficulties of the search process was that applicants with common names often could not be differentiated, even utilizing their picture and medical school. This suggests that medical students' public persona is professional either because it reflects their behavior, or they are finding ways to keep their private lives disconnected from their professional career. This was sometimes accomplished by using a maiden name, nick-name, or middle name as an account username, which is most easily accomplished on Twitter and Instagram due to the requirement of picking a username. Medical students also did not significantly change their privacy settings immediately following Match Day. Whether students are professional in all aspects of their social media or are merely modifying what is publically available, it was striking that no instance of unprofessional content was visible. This may reflect an increased awareness of social norms through outlets such as ACOG or counseling from mentors. Whether this will translate into decreased episodes of unprofessionalism during residency and practice remains to be seen.

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Fusion

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