Insight

INDIANA UNIVERSITY MEDICAL STUDENT RESEARCH JOURNAL

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Letter from the Dean

August 3, 2018

Dear colleagues,

Our mission, both collectively and individually, is to do all we can to improve the quality of healthcare that we deliver and the health of our citizens.

We each have different ways in which we do that. Some will pursue careers in laboratory research, others in clinical or translational research. Even those who devote most of their time to clinical work, have important contributions to make as they try different approaches, make critical observations and share the results of their successes and failures. We applaud and want to foster all these efforts.

There is no better time to start exploring the possibilities and developing these skills than in medical school. That is why we started the Indiana Medical Student Program for Research and Scholarship (IMPRS) and the Medical Student Research Symposium. We are now pleased to launch the inaugural edition of Insight, a student-led research journal to help share the results of some of the best work of our students and, we hope, inspire others to follow.

Please join me in celebrating research excellence at the School of Medicine by reading and sharing this first issue of *Insight*.

Best regards,

Jay Hess M.D. Ph.D.
Dean, Indiana University School of Medicine

INDIANA UNIVERSITY
SCHOOL OF MEDICINE

Insight

3 August 2018 | Vol 1 | Issue No. 1

In This Issue

From the Editor's Desk

Dear readers,

It is difficult to step out into the world. As medical students, we are pulled into many different directions all at once, whether it be exams, clinical rotations, or personal relationships. There is often little time left in the day to allow our minds to explore.

Insight serves as a medium to showcase and celebrate the research excellence at IUSM. Within the pages of our inaugural issue, you will find works that investigate topics ranging across basic and clinical sciences, from colorectal cancer to domestic violence. Furthermore, we hope to kindle your curiosities with words from renowned physicians including physicians such as Drs. Lawrence Einhorn, Anantha Shekhar, Wade Clapp, Patrick Loehrer, Gary Dunnington, Mark Geraci, and Himanshu Shah. Such diversity of topics speaks to the power of research to touch upon and improve almost every aspect of our lives. Look around, and realize that there are so many questions around us that are deserving of our due diligence and scientific inquiry.

By highlighting the talented works of peers and faculty, our journal serves to inspire and ignite research interest early in medical education. Research is a way of pushing the folds of medicine—to contribute to advances that make a better future possible for patients. We hope that you, as future physicians and physician-scientists, will ask yourself, "What can I contribute today to make for a better tomorrow?" We should strive to carry the load forward, so that those who come after us may build upon our efforts.

We invite you to approach our inaugural issue with an open inquisitive mind and to pass forward the wisdom and knowledge that you will gain through medical school. Finally, we invite you to join the medical community at IUSM in the journey toward becoming physicians who strive to create a better future for our patients through compassionate care, scientific inquiry, and hunger for knowledge.

Sincerely,

Monica Cheng
Editor in chief
Class of 2021

Honglin Xiao
Editor in chief
Class of 2021

Questions? Feel free to contact us at isrsc@iupui.edu

Radiation Oncology

Medical students with their unbridled curiosity can cause many seasoned researchers / physicians to reexamine previously held conclusions. In fact, one could argue that medical students are unsung engines of discovery. For example, in 1896, Emile Grubbe, a 2nd year medical student who did his pre-medical training in Indiana, became fascinated by the recent discovery of "X-rays". Three months after the original publication of this discovery, he opened the first radiation therapy facility in Chicago and was arguably the first to use radiation in the treatment of breast cancer. Thus, a medical student was responsible for identifying a major factor in the fight against breast cancer.

While much has changed since the late 1800's, and investigation is far more regulated, contributions from student doctors can still be important. For this reason, the new journal, Insight, is essential. Insight will allow medical students to continue being engines of discovery, much like our friend, Emile Grubbe.

Rich Zellars, M.D.
William A. Mitchell Professor
Chairman

Commencement Address to Class of 2018

Lawrence H. Einhorn, M.D.

"I want to welcome everyone to the 2018 Indiana University School of Medicine Commencement Ceremony. This is truly a time for celebration as we acknowledge our 300+ medical students and 100+ Masters- and- PhD-level graduates. Our students might take this all in stride, with appropriate humility, if not outright nonchalance. However, I can assure them that their spouses, significant others and parents are beaming with pride.

I had the distinct privilege of meeting with the 2018 class officers. I sought a common thread in this class, but instead, was confronted with a very diverse group as to background and future career aspirations. I was impressed with their individuality, inquisitive nature, and mainly their collective camaraderie. You worked together for the improvement of your classmates during trying times while achieving your own brand of personal satisfaction and individual accomplishment. You will exit the stage with an MD degree, and the school will have benefited from your passion and commitment to excellence. You have left an indelible imprint upon future classes as they too will be challenged by the emotional, physical and mental strain of becoming a physician.

Career changes within the field of medicine are not uncommon during residency. On a personal note, I did my residency here at Indiana University with the goal of joining my father in the practice of general internal medicine in Dayton, Ohio. However, due to an illness, he retired during the first year of my residency. I then did an elective in hematology-oncology and was seduced by the science of the field, the courage of patients battling cancer, and the personal relationships oncologists had with their patients.

As I was preparing these remarks, I pondered what a commencement address would have sounded like 100, 50, or even a mere 25 years ago? Over a century ago, Dr. Roentgen introduced the concept of diagnostic imaging with x-rays. Half a century later, the level of sophistication of imaging took a quantum leap forward with CT scans, MRIs, and PET scans, depicting internal structures with seemingly artistic perfection. An earlier speaker might have asked, "Will wonders never cease?" Our current generation of new graduates will no longer be limited to what can be visualized with the naked eye, thanks to byproducts from Human Genome Project. The current era of molecular medicine and precision genomics allows us to discern germ line mutations to predict future problems, both for patients as well as family members, discover oncogenes associated with cancer that can be therapeutically exploited and solve problems that defied resolution a mere decade ago. And no, wonders will never cease.

These advances are exciting and transformational, but do not alter the immutable doctor-patient relationship at the bedside and in the clinic. As you face your future patients, remember that the human condition is every bit as complex as any genomic report. Do not lose the humanity of being a physician while concentrating on information

in the computer and ignoring the patient who desires human interaction. A computer can read complex genomic data, but is never a substitute for empathy and compassion. Knowledge and later wisdom produces the blueprint for a good doctor, but our patients deserve better from us. We are healers, and what makes a great doctor is compassion as well as passion. A great doctor cares about his or her patients, not merely caring for them.

You will be challenged with future patients with difficult-to-diagnose symptoms and be confronted by illnesses that are incurable despite the tools you have been provided. You can't properly diagnose all medical problems nor cure all disease. It is hubris to think otherwise. It will perhaps be the task of one of you in the future to move the field of medicine forward by scientific inquiry.

Medicine can be a cruel mistress. You need to find a proper balance between work and family that must be individualized. We all too often decide not to cheat upon that mistress to the detriment of our home and family life. This is all too pervasive challenge in the era of patients seeking help via email on weekends and evenings and expecting immediate replies. This type of emotional workload is not sustainable nor should it be expected. This might prove to be the most difficult challenge you will face in the future.

All of our graduates should pat themselves on the back for choosing this noble profession. Never lose your spirit of innovation, passion and thirst for knowledge. You will become good doctors and will make your school proud to call you a graduate. Several of you will become great physicians and scientists and be responsible for future medical breakthroughs. Science will always remain the pursuit of truth without ideology.

The number one movie currently is yet another Marvel Comic Avengers film, Infinity Wars, which ran so long it just seemed like it stretched into infinity. When you were younger, you probably dreamt of having a superpower – perhaps the ability to fly. In medicine, you have the power to heal and save lives. You can be a superhero to your future patients. However, medicine can be a humbling profession and you need to remember to stay grounded in reality while spreading your wings.

I harbor no illusions that you will either remember or follow any of these recommendations. However, I do want to give you one final directive. Join your family and friends later today, celebrate and have a good time. You earned it."

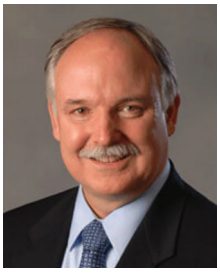
Lawrence H. Einhorn, M.D. is a living legend in the field of medical oncology, having developed a cure for testicular cancer. In 1973, when he arrived at the Indiana University School of Medicine—where he now is a distinguished professor—testicular cancer was the leading cause of cancer death among young men. Dr. Einhorn developed a cisplatin-based chemotherapy that has saved countless patients, including Tour de France champion Lance Armstrong. A former president of the American Society of Clinical Oncology and the first clinical investigator inducted into the National Academy of Sciences, Dr. Einhorn has changed how doctors treat many cancers, and he's a true hero to the thousands of men who are alive today because of his work.

Pediatrics

"It is a great privilege to provide care for patients and work with them and their families. However, it is also a great privilege to work with colleagues and students to drive discovery. Discovery in children's diseases happens predominantly at academic health centers and approximately 65% of all independent research grants in the United States in child health are in 15 Children's Hospitals in the United States. **Student and faculty investigators at IU allow us to be a major component of driving innovation in children's diseases (#8, JAMA Peds 2018).**"

D. Wade Clapp, M.D.
Richard L. Schreiner Professor
Chairman

Oncology



"Most medical students enter medicine to 'make a difference.' There is perhaps no more fulfilling aspiration, except... proving that you did. That is what research is all about."

Patrick J. Loehrer, Sr., M.D.
HH Gregg Professor of Oncology
Director, Indiana University Melvin and Bren Simon Cancer Center

Surgery

"I am inspired by the increasing number of IU medical students seriously engaging in research activity from the beginning of their medical school experience. Research offers not only a gateway to success in medicine but a wonderful opportunity to engage our passion for change into action that will change patient care and patient care delivery in the future as well as the way we educate the future generation of physicians."

Gary L. Dunnington, M.D.
Jay L. Grosfeld Professor of Surgery
Chairman

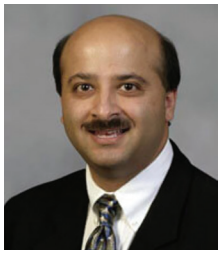
Internal Medicine

"You are the future of Medicine. This seems daunting now, but it is a true statement. Your generation will have more power in knowledge than any previous group. Embrace that challenge as you move throughout your career in Medicine. **Take risks, be inquisitive, and aim to make discoveries leading to better lives for your patients**. Most of all, remember to 'pay it forward' to those who follow in your footsteps."

Mark W. Geraci, M.D.
John B. Hickam Professor of Medicine
Chairman

"The mind is not a vessel to be filled, but a fire to be kindled."
—Plutarch

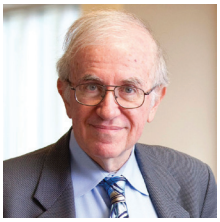
Radiology & Imaging Sciences



"The practice of medicine encompasses more than the mastering of technical skills, developing clinical expertise, accumulating and applying medical knowledge, and passing this on to the next generation of learners. **The major advances in medical care, the breakthroughs and innovations, arise from curiosity. It comes from the desire to improve upon the status quo and overcome current limitations in our ability to heal and care for our patients**. Logic, critical thinking, and reasoning are clearly important, but don't forget to ignite both sides of your brain. Research allows you to kindle and harness your creativity, intuition, and imagination with a goal of improving upon our current knowledge and armamentarium of diagnostic and therapeutic interventions. Research also provides you the opportunity to give back in one of the most fulfilling ways—to harness your passion and creativity to change how patients are cared for in the future."

Himanshu Shah, M.D.
Associate Professor and Eugene C. Klatte Scholar in Radiology
Chairman

Oncology



"Medicine is a truly noble profession. As doctors, we make a difference daily in the lives of our patients. However, research allows us to move the needle forward and not just practice state-of-the-art therapy, but develop innovative treatments that improve quality and quantity of life for our patients."

Lawrence H. Einhorn

Lawrence H. Einhorn, M.D.
Livestrong Foundation Distinguished Professor of Medicine

Neuropsychiatry

"While medical education prepares students to diagnose and treat patients using the standard of care, research experience prepares you to ask the deeper questions, to question the accepted wisdom, and to push the boundaries of knowledge. To be a great doctor, you need to have both. **Be curious, ask questions, push the boundaries.**"

Anantha Shekhar, M.D., Ph.D.
Executive Associate Dean for Research Affairs
Director of Indiana Clinical and Translational Sciences Institute (CTSI)

>> *For Dr. Shekhar's full interview, visit us at* **journals.iupui.edu/index.php/insight/index**

Capturing the Human Essence

Dr. Richard Gunderman is the Chancellor's Professor in the Schools of Medicine, Liberal Arts, and Philanthropy and John A. Campbell Professor of Radiology. He also serves as the faculty advisor for the IUSM Student Research Symposium.

BY HONGLIN XIAO

Honglin Xiao: Tell us about yourself and how you got involved in your field of medicine, research, or your educational background.
Richard Gunderman: I grew up in Indianapolis and went to Wabash college northwest of here. I then did my medical training at the University of Chicago in their Medical Scientist Training Program. I was kind of a test case for them because I was interested in a PhD program which was not in the physical sciences but one that was involved in the humanities and social sciences, the Committee on Social Thought. I believe deeply in the importance of bench and clinical research, but I was concerned at the time and remain concerned that there are important human aspects of our work in biomedical science, clinical medicine, and public health that sometimes do not get the attention they deserve.

X: What was your PhD concentration in?
G: The topic was how our understanding of health can serve as a lens to understand who we are as a people. For example, at one point in some cultures, disease was understood as something of a breach with the divine, a sign that you had offended God, or perhaps a sign that you were at odds with your community. Illness was seen as a kind of punishment. However, another perspective would be that disease results from infectious organisms. These are two very different understandings of health and disease. It is tempting to say one is wrong and one is right, but there is more to it than right and wrong, true or false. There is the matter of how disease fits into a larger culture. We understand how to open clogged arteries, and we are relatively good at eradicating some cancers.

But there are some aspects of health that we may not be so good at, like preventing disease or promoting health or caring for people with chronic conditions. These are just some aspects of care that reflect the lens through which we see health and disease – as a kind of pure biologic problem that must be solved with a purely biologic solution. Say somebody has cirrhosis of the liver due to alcoholism or lung cancer due to smoking. We can say that these diseases are caused by alcoholism and smoking, and yes, it is important to study these biologic mechanisms, but there is a lot more going on. Why did the person start drinking to excess or smoking in the first place? These questions are just as important to investigate as the biological mechanisms. There are social, cultural and spiritual dimensions to disease that must be addressed and that is what my graduate study was focused on.

X: There then seems to be multiple paths in research. For example, you looked at the humanistic side of disease and there are many students and physicians who elect to follow clinical and lab science paths. Do you have any advice for medical students how to get involved in different types of research?
G: We need to make sure that our medical students have time to think. Not just that we should spend every waking hour trying to get the best score on an exam, but that we are spending time thinking about what type of physician we want to be. It could be thoughts on "Am I going to be a surgeon or an internist?" But it could also be "Am I going to be an investigator? Am I going to be a clinician? An educator?" If I wanted to be an investigator, I may be interested in topics outside the biological sciences, such as economics or political science. We need to expose our students to exemplars, advocates for the different career paths available to them. Here is an MD who never sees patients but who is devoted completely to research. Here is another physician who is a clinical investigator who seems many patients a day but does not do bench science. We can place people at different points on different spectra, but we need to enable our students to meet professionals who are there not only to deliver the curriculum. Doing well on STEP 1 is important, but we want you to interact with these people because they represent a career path that you may feel called by in the future.

X: It sounds like you are going against what many medical students hold in their eyes as the most important thing, the STEP scores. How do we change that mindset?
G: During my time as a medical student, we never talked about STEP. It was decades ago, but we knew you had to take it and do well on it. But it was not a priority of the school at all. The school prided itself on the fact that a higher percentage of its graduates pursued academic careers than any other institution. They were dedicated to making sure that over the course of our education, we were encountering different physicians who represent different career paths. Because you are not just assimilating knowledge, not just choosing different specialty options, but you are also choosing a path that will challenge, engage, and reward you for a lifetime. Today, it has been simplified to the point of "career counseling" which makes something big into something little and turns it into something technical. We need to guard against that; our students' imaginations must be nourished. We need to present a full range of possibilities and stimulate our students' imaginations, so they can make a choice about what type of doctor they want to be, which might include the pursuit of knowledge, education, or service.

X: How can IU better achieve this goal and move to making this a reality, to make sure that not only do we do well on STEP and be competitive for residency positions but that our imaginations are also given the chance to grow?
G: I think one way would be to offer regular programming, perhaps extracurricular, where someone comes in and talks about their career. We want their excitement, their enthusiasm to shine through and reach the medical students at such events. We want these presenters beaming with excitement and pride about

RICHARD GUNDERMAN | PHOTO

what type of doctors they are so the students see a wide variety of professional paths. It could be somebody who is tremendously busy seeing patients and who is really excited about that. It could also be somebody who is committed to research. Let our medical students see this excitement. For students, there is a type of research into questions that will get you published and make you a competitive candidate during interviews, but there is also a type of investigation that illuminates what kind of doctor you want to be.

X: To get where you are now in your medical career, there has undoubtedly been key people who have helped you along the way. What should the role of a mentor be for the student to be successful?
G: You need to know that there is somebody who knows you as a person and who cares about you as a person. They may have nothing to do with your intended medical specialty. But they are a physician who knows you and likes you and wants to help you. For them, it is important to help you grow as a person and flourish in your role. Some might like to construct a system that would carry out this function, but ultimately it takes flesh-and-blood human beings with their hearts in the right place for it to be done well. You need a human being who cares about you for this to be successful.

X: Have there been any important mentors in your life or medical career?
G: Yes, at Wabash I had a vague idea that I wanted to do medicine and that I also had an interest in philosophy and religion. Was there any way to do both paths in tandem? A faculty member in the divinity school at my future medical school came as a visiting professor, and for whatever reason he took an interest in me and opened my eyes to possibilities that I did not even know existed. That person is the reason I ended up at the University of Chicago. I was just a hayseed from Indiana, but someone who knew more than I did made a huge difference in my life by opening up the full extent of what is possible.

X: To wrap up — this is going to be distributed at the White Coat Ceremony. There will be a lot of eager minds getting ready to start their careers in medicine. If you had to give one piece of advice what would it be?
G: Don't suppose that just because you are at the beginning of your career in medicine, that you have nothing to contribute. Try to make choices that give you the opportunities to help from the beginning. Supposedly you're not a doctor until you graduate after four years of medical school and until then you don't have the opportunity to help others. In fact, you are capable of contributing from day one. You can listen to people. You can try to care for your classmates. There will be people sitting next you on the first day of class who are lost and alone. You can help connect with them, invite them out and have fun. You can help build a deeper community in medicine and you may be better equipped to do so now than on the day you will graduate. We need this in medicine. We need to care for our patients, but we also need to care for each other.

Dr. Gunderman can be contacted by email at rhgunder@iu.edu

Oral Presentations

INDIANA MEDICAL STUDENT PROGRAM FOR RESEARCH AND SCHOLARSHIP (IMPRS)

The following works represent the student finalists who were selected to give oral presentations to a panel of judges at the 2017 IMPRS summer internship program—a collaboration of Indiana University School of Medicine and Indiana CTSI.

Prevalence of Advanced, Precancerous Colorectal Neoplasia in Black and White Populations: A Systematic Review and Meta-analysis

◆ Thomas F. Imperiale, **Priya R. Abhyankar**, Tim E. Stump, Thomas W. Emmett

Background: Colorectal cancer (CRC) incidence and mortality is higher in Blacks than in Whites. While the reason(s) for these disparities is unclear, some guidelines recommend CRC screening in Blacks starting at age 40-45.
Objective: To compared the prevalence of advanced adenoma (AA) or advanced, precancerous colorectal neoplasms (ACN) between asymptomatic Black and White screen-eligible adults.
Methods: We performed a systematic review and meta-analysis by first searching Ovid MEDLINE, PubMed, Embase, and the Cochrane Library to identify published literature from database inception to June 2017. We included studies measuring prevalence of AA or ACN in average-risk Blacks and Whites undergoing screening colonoscopy. Two authors independently assessed study quality and risk for bias using a modified NIH quality assessment instrument for cross-sectional studies, and independently abstracted descriptive and quantitative data from each study. A random effects meta-analysis was used, providing risk differences and odds ratios.
Results: From 1653 titles, we identified 9 studies that included 299,761 patients. The largest single study included 296,749 (99%) of all observations. Six of 9 studies were of high methodological quality and low-risk for bias. Overall prevalence of AA/ACN was no different between Blacks and Whites (OR=1.03; 95% CI: 0.81-1.30). Proximal AA/ACN prevalence was greater in Blacks than in Whites (OR=1.20; 95% CI: 1.12-1.30). Excluding the largest study resulted in no difference in overall (OR=0.99; CI, 0.73-1.34) or proximal AA/ACN prevalence (OR=1.48; CI: 0.87-2.52). Including only the highest quality studies for which pathology was available (study N = 5, subject N = 8,503) showed no difference in AA/ACN prevalence (OR=1.06; CI, 0.75-1.50) or proximal AA/ACN prevalence (OR=1.44; CI, 0.84-2.49).
Conclusions: Prevalence of AA/ACN is similar in average-risk Black and White screen-eligible persons, findings that support CRC screening beginning at age 50, irrespective of race.

Priya Abhyankar is a third-year medical student currently interested in gastroenterology due to its focus on prevention through colorectal cancer screening. She is also interested in the wide range of pathology from various organ systems. Her greatest takeaway from her experience was realizing the importance of health outcomes research in improving the cost-effectiveness of our healthcare system.

Role of STAT4 in Innate Immune Response of Myeloid Cells

◆ **Maria S. Barrios**, Pegah Mehrpouya-Bahrami, Mark H. Kaplan

Background: Signal Transducer and Activator of Transcription 4 (STAT4), which belongs to STAT protein family, is induced in myeloid cells after exposure bacteria pathogen-associated molecular pattern (PAMP) and IL-12. STAT4 is critical for the activation of genes that are part of the inflammatory response in myeloid cells. Methicillin-resistant Staphylococcus aureus (MRSA) is one of the multi-drug-resistant pathogens that has become a serious nosocomial and community acquired infection in the United States although the innate immune response to MRSA is still not completely defined. Our preliminary data suggests that STAT4 is required for the innate immune response to MRSA early during infection. Our hypothesis is that STAT4-deficient macrophages in mice will have a decreased production of cytokines and chemokine, which are critical for the activation of innate inflammatory response, compare to wild-type macrophages.
Methods: The innate immune response of STAT4-deficient macrophages in mice has been studied in vitro after subsequent exposure to lipopolysaccharide (LPS) and heat killed MRSA. In addition, quantitative PCR (qPCR) and phosphor-STAT4 staining were used to determine the difference cytokines production and phosphorylation of STAT4 between wild type mice and STAT4 conditional knocked out (CKO) in myeloid cells.
Results: Our findings demonstrate that STAT4-deficient macrophages in mice have decreased levels of STAT4 expression and production of cytokines, compared to wild-type macrophages.
Conclusions: Our data fill the existing gaps of the role of STAT4 in myeloid cells and innate immune response, which will allow us to discover alternative treatments against MRSA by manipulating STAT4 pathway in myeloid cells.

Maria Barrios is a third-year medical student interested in neurology. She enjoys learning about the intricacies and mysteries of the human brain, and was inspired to pursue the field after her brother was diagnosed with a neurological disorder at the age of 2.

What is your most important takeaway from your research experience?
Giving myself the opportunity to immerse myself in a lab, not only being exposed to and mastering different lab techniques, but also having a deeper understanding of the steps behind a research project, from beginning to end, were in my opinion, of great value to my development as a future physician and a student of the sciences. This was certainly an intimidating experience at first, since it was my first time designing and presenting a research poster, but it was well worth the effort. I hope my experience will motivate other students who do not have a previous experience with poster and research project presentation to take advantage of this amazing opportunity that IU Medical School has to offer.

Basophils as Mediators in Atopic Dermatitis

◆ **Maria C. Bell**, Lee J. Seymour1, Anita Thyagarajan, Hongming Zhou, Matthew J. Turner

Background: Atopic dermatitis (AD) is an inflammatory skin disease characterized by itching and secondary infections. Basophils accumulate in skin lesions of patients with AD but the role of these cells in disease is not defined. The Bas-TRECK transgene confers basophil-specific expression of human diphtheria toxin (DT) receptor, allowing for DT-mediated basophil depletion. We hypothesized basophil depletion would improve clinical and molecular markers of AD-like disease in Stat6VT mice co-expressing the Bas-TRECK transgene.
Methods: Stat6VT x Bas-TRECK mice were used to model AD and assess the effects of basophil depletion alongside cohorts of WT, Bas-TRECK, and Stat6VT mice. Mice were treated via intraperitoneal injection with DT (50μg/kg) for 11 days. Severity of the AD-like phenotype was determined throughout the treatment course. Skin specimens and spleens were collected to evaluate basophil depletion (via flow cytometry) and the impact of basophil depletion on Il4, Il13 and Ifng transcripts in AD-like lesions using quantitative PCR.
Results: Basophil depletion from Stat6VT x Bas-TRECK mice was associated with reduced clinical scores and molecular (i.e. Il4, Il13 and Ifng transcripts) markers of the AD-like phenotype.
Conclusions: The reduced clinical severity of disease and cytokine transcript levels seen following depletion of basophils in Stat6VT x Bas-TRECK mice suggest that basophils are important for the AD-like phenotype in Stat6VT mice. Although much additional investigation is needed, this preliminary data indicates that basophils could be a therapeutic target for AD.

Maria C. Bell is a third-year medical student who is interested in dermatology. "I love the variety of patient ages and concerns, the detail-oriented nature of procedures, and the way that the skin can provide clues to more extensive systemic disease." For Bell, her summer research experience allowed her to gain a deeper appreciation for the amount of foresight, preparation, and hard work that go into scientific discovery. "Because my undergraduate background was not in science, my summer research was my first real basic science project, and I found it to be both humbling and rewarding."

Association Between Newborn Microbiome and Early Wheeze

◆ **Isabelle A. Dagher**, Sydney E. Ross, Christopher M. Hemmerich, Douglas B. Rusch, Stephanie D. Davis, Kirsten M. Kloepfer

Background: Asthma affects 10% of children and often begins with recurrent wheeze during infancy. Recurrent wheeze is associated with airway dysbiosis (broad community shifts of bacteria) at three months of age, but investigations into airway differences at birth have not been conducted. We hypothesize that airway dysbiosis at birth predicts wheeze during the first year of life, and is linked with decreased airflow measurements at 3 months of age.
Methods: Nasopharyngeal samples from newborns were collected within 48 hours of life. The bacterial V4 region of the 16S-rRNA gene was amplified and sequenced on the Illumina Miseq. Mothur software was utilized for processing and analysis. Sedated infant pulmonary function testing was performed on subjects at three months of age.
Results: Alpha diversity was similar between infants who developed wheeze and infants without wheeze. There is greater dissimilarity within the microbiome in samples from the wheeze group compared to samples from infants without wheeze ($p=0.0001$), with a trend towards greater abundance of Staphylococcus in infants without wheeze ($p=0.06$). At 3 months of age, there is decreased forced vital capacity in children with wheeze vs. no wheeze ($p=0.02$). If antibiotics were administered during labor, changes were seen in the newborn upper airway microbiome at the phyla and genera level (decreased Firmicutes ($p=0.037$) and Lactobacillus ($p=0.04$)).
Conclusions: Early changes are present in the upper airway microbiome of infants who develop wheeze. Prescribing antibiotics during labor alters the newborn microbiome. Identifying the components of the microbiome associated with early respiratory disease could lead to targeted interventions and therapeutics.

Autism and ADHD in NF1: Insights from a Mouse Model

◆ **Hayley P. Drozd**, J.L. Lukkes, A.R.Abreu, E.T. Dustrude, Su-Jung Park, D. Wade Clapp, A.I. Molosh, A. Shekhar

Background: Children with Neurofibromatosis type 1 (NF1) suffer from a significantly higher incidence of ADHD and Autism. Deletion of a single Nf1 allele (Nf1+/-) in mice is a well-established model of NF1 that recapitulates the peripheral tumors phenotype. We have shown that Nf1+/- mice demonstrate autism-like social and communication deficits and that increased activation of the Ras pathway in the basolateral amygdala (BLA) causes social deficits. We hypothesized that Nf1+/- mice will exhibit ADHD-like behaviors.
Methods: To further test the role of BLA, we activated this region in WT mice or inhibited the BLA of Nf1+/- mice through optogenetic stimulation following acquisition of a social memory in the social preference test. Dual immunofluorescence was then used to map pERK activation and GFP expression in the BLA. In a second experiment, we examined impulsive choice in WT and Nf1+/- mice using a delayed discounting task.
Results: Long-term memory of WT mice was disrupted after optogenetic BLA stimulation and pERK expression in the BLA was increased in Experiment 1. In contrast, BLA inhibition of Nf1+/- mice did not rescue social learning deficits. In Experiment 2, Nf1+/- mice choose a higher percentage of smaller rewards when a 10 s and 20 s delay was administered compared to WT mice, suggesting Nf1+/- mice are more impulsive.
Conclusions: These data provide the first genetic mouse model to study ADHD symptoms in NF1 patients and shed further light on the CNS pathways regulating autism-like deficits.

Hayley Drozd is a first-year graduate student in the Medical Scientist Training Program (MSTP). Her current field of interest is developmental pediatrics, a field that serves an avenue for providing holistic care for children and families throughout a child's development. Drozd sees her research experience as a complement to the field, creating opportunities for medical innovation. Research has enabled her to think about medicine from a different perspective, and she says she is thankful for her mentors and lab colleagues who helped her hone her research skills within an environment that nurtures passion for investigating science and improving medicine.

"The summer was foundational to identifying my career path and to laying the ground work for integrating research into my medical career. As a result of my experience in the program, I applied and was accepted to IUSM's MSTP."

Insomnia and Chronic Pain: Insights into Disease Severity and Pharmacological Treatments

◆ **Aubrey Husak**, Dr. Matthew Bair

Background: Sleep disturbances and chronic pain commonly occur together with an estimated prevalence of 40%-80% within the chronic pain population. Furthermore, these conditions appear to have a bi-directional relationship with compounding influence on progression and severity. The goal of this review is to answer 3 questions: 1) How does chronic pain severity and long-term pain duration change for patients with both chronic pain and sleep disturbances?, 2) What are common comorbidities seen in patients with chronic pain and sleep disturbances?, and 3) What are potentially effective pharmacological and non-pharmacological treatment options for both chronic pain and sleep disturbances?

Methods: Ovid Medline and Pubmed were searched using the terms: sleep wake disorder, chronic pain, complex regional pain syndromes, fibromyalgia, treatment outcome, psychotherapy, complementary therapies, and therapeutics. Titles and abstracts were screened. Cohort, case-control, and cross-sectional studies, which assessed the difference in outcomes between individuals with chronic pain and those with comorbid chronic pain and sleep disturbances, were included. Randomized controlled trials were used to assess potentially effective treatment options for both insomnia and chronic pain.

Results: 16 studies were identified for the first question. These studies indicated that patients with both chronic pain and sleep disturbances are more likely to have greater pain severity, longer lasting pain, greater disability, and were less physically active than those without comorbid sleep disturbances. Additionally, 12 studies showed patients with chronic pain and sleep disturbances are more likely to have concurrent depression, catastrophizing, fatigue, anxiety, and suicidal ideation. Forty-three randomized controlled trials were identified that assessed treatment for both chronic pain and sleep disturbances. Pregabalin was the most frequently studied pharmacological treatment option and showed improvement in both pain and sleep. Cognitive behavioral therapy for insomnia showed long-term improvement in sleep for patients with chronic pain.

Conclusions: The results of these studies show the need for concurrent treatment for both sleep disturbances and chronic pain. Individuals with comorbid sleep disturbances and chronic pain have greater symptom severity, longer duration of symptoms, more disability, and additional comorbidities. Treatment may help to decrease symptom severity, duration, disability, and address comorbidities associated with chronic pain. Additionally, both pharmacologic and non-pharmacologic treatment options may be useful in the treatment of concurrent sleep disturbances and chronic pain.

Aubrey Husak is currently interested in internal medicine and enjoys the opportunity to interact with patients on a daily basis. For Husak, she believes research empowers people to find solutions to previously unsolvable questions.

Modulation of Hematopoietic Factors in the Bone Marrow Stem Cell Niche by Prostaglandin E2 Enhances Survival from Lethal Radiation Exposure

◆ **Jessica L. Muldoon,** Plett, P.A., Chua, H.L., Orschell, C.M.

Background: With the increase in nuclear arms, terrorist threats, and nuclear power, there is an increased risk to radiation exposure. Exposure to high dose radiation has acute effects on the body and chronic effects that plague survivors of the acute syndrome for years post-exposure. Acute radiation syndrome (ARS) can be lethal if left untreated due to severe damage to the gastrointestinal and hematopoietic systems. Dimethyl prostaglandin E2 (PGE2) has shown efficacy as a protectant against radiation exposure, significantly increasing survival from ARS and enhancing hematopoietic stem cell (HSC) and hematopoietic progenitor cell (HPC) function compared to control mice. This study aimed to elucidate the mechanism of PGE2's protectant effect and to determine whether PGE2 protects hematopoietic stem cells themselves and/or the supportive microenvironment, thus indirectly enhancing HSC function post-irradiation.
Methods: C57BL/6 mice were treated with 35mg PGE2, then underwent single dose lethal irradiation. At 6h, 24hr, and 9d post radiation and 30min post injection non-irraditated, mouse bone marrow was flushed using a 500 uL of PBS, centrifuged, and supernatants separated. Supernatants were assayed by multiplex analysis (Luminex technology) for factors known to promote HSC and HPC regeneration & function.
Results: Cytokines beneficial to the reconstitution of the hematopoietic system were significantly altered by the administration of PGE2 vs. vehicle.
Conclusions: This study provided information on mechanisms relevant to survival from lethal radiation exposure, protection of the bone marrow, and recovery of hematopoiesis.

Jessica L. Muldoon is a third year medical student who plans to pursue a career in pathology. As an undergraduate student, she majored in clinical lab science and found joy in microscopy work. Medicine is a field that owes itself to the work that is done "behind the scenes"—from pathology results to research findings. As an IMPRS scholar, Muldoon was able to gain experience in the process of research. She learned to formulate proper research questions, collaborate with mentors to design and carry out experiments, analyze data, and finally present her findings at a poster presentation. Not only was Muldoon able to see how research was performed, she gained an appreciation for all the work that goes into research "behind the scenes". Muldoon intends to carry this skillset onward in her career by striving to be a translational clinician, who collaborates with researchers to move the field of medicine forward.

The Effect of N-Acetyl Cysteine on Brain Function in Early-Stage Schizophrenia

◆ **Parth Patel**, Tom Hummer, Michael Francis, Alan Breier

Schizophrenia is a severe and debilitating mental illnesses that typically begins during late adolescence or early adulthood and persists for a lifetime. Existing treatments can subdue the psychotic symptoms but do not slow the progression of the disease, resulting in severe cognitive deficits. Thus, therapeutic treatments that could slow neurobiological changes seen in the progression of the disease, may dampen the degenerative nature of the disease. N-acetyl cysteine (NAC) is a known neuroprotective agent that acts via its antioxidant properties and promotion of glutamate release. We are examining whether NAC impacts brain functioning over the course of a year in the early stages of schizophrenia. Sixty patients with early-stage schizophrenia were randomized to receive NAC or placebo treatment for one year. At baseline, 6 months, and 12 months, subjects performed an n-back test during fMRI to measure brain activity during working memory processes and assess cognitive ability. We will examine whether NAC impacts brain activity during the n-back task in frontoparietal regions involved in working memory. We will also examine behavioral performance on the n-back task, including accuracy and reaction times. We hypothesize that subjects in the NAC group will have greater frontoparietal brain activity and superior performance on the n-back task, relative to the placebo group. We expect changes to increase with time and as cognitive load increases. The goal is to identify whether NAC may be a potential treatment that can alter the trajectory of schizophrenia during its the early stages to minimize lifelong impact.

Parth Patel is a third-year medical student who is interested in radiology. He enjoys the cerebral side of medicine and appreciates that radiology is a growing field that opportunities for him to continue engaging in research. His experience in research has given him a deeper appreciation for how medical advancements are made—the process and all the people involved.

Schizophrenia is a severe, debilitating mental illnesses that typically begins during early adulthood and persists for a lifetime. Existing treatments can treat psychotic symptoms but do not slow the progression of the disease, resulting in severe cognitive deficits. Therapeutic treatments that could slow the neurobiological changes seen in schizophrenia may dampen the degenerative nature of the disease. One potential treatment is N-acetyl cysteine (NAC), a known neuroprotective agent that acts via its antioxidant properties and promotion of glutamate release. We examined whether NAC impacts brain functioning over the course of a year in early stage schizophrenia. Sixty patients with early-stage schizophrenia were randomized to receive NAC or placebo treatment for one year. At baseline, 6 months, and 12 months, subjects performed an n-back test during fMRI to measure brain activity during working memory processes and assess cognitive ability. A matched group of healthy adults received a single baseline scan. At baseline, patients had decreased activation in the superior frontal gyrus and increased activation in the anterior cingulate cortex. Furthermore, patients had poorer performance on the n-back task. NAC did not have a significant effect on performance of the n-back task, but there was a small effect of NAC on activity in the anterior cingulate cortex. The cognitive deficits and decreased frontal lobe activity in patients supports previous research indicating cognitive and neurobiological abnormalities in schizophrenia. Differences in the anterior cingulate cortex has found mixed support in prior research and may indicate the importance of attentional control in cognitive deficits.

Effects of Low Intensity Vibration (LIV) on Murine Trabecular Bone Following Complete Estrogen Deprivation

◆ **Ryan R. Pattyn**, Gabriel M. Pagnotti, Khalid S. Mohammad, Theresa A. Guise

Background: Post-menopausal, estrogen-receptor positive breast cancer patients treated with aromatase inhibitor (AI) experience musculoskeletal deficiencies resulting from complete estrogen (E2) deprivation, making even moderate exercise difficult. Mechanical signals derived from low intensity vibrations (LIV) have been demonstrated to preserve bone in models of systemic bone loss and cancer-induced osteolysis. Therefore, we hypothesized that LIV may mitigate deficits in murine trabecular (Tb) bone microarchitecture resulting from complete E2-deprivation.
Methods: Twenty 4w female C57/BL6 mice were divided into LIV (n=10), which received mechanical signals (90Hz, 0.3g) 1x/d, 20min/d, 5d/w for 28w, and CTL-LIV (CTL: n=10). Complete E2-deprivation was achieved through ovariectomy (OVX) on 9 week old mice plus AI (letrozole,10μg/SC/daily). Ex-vivo micro-computed tomography (μCT), mechanical compression, and dynamic histomorphometry were performed to quantify changes in bone quantity and quality at 28w.
Results: Via μCT, trabecular bone volume fraction (Tb.BV/TV) and connectivity density were significantly greater, 22% ($p<0.05$) and 52% ($p<0.01$), respectively, in LIV-mice when measured in the L5 vertebral body compared to CTL. Vertebral bodies of LIV showed a significantly more uniform distribution of trabeculae ($p<0.01$) in L5 and significantly greater, 11% ($p<0.05$), trabecular thickness in L4 than CTL. Trabecular bone formation rate and mineralizing surface in distal femora were significantly greater, 43% ($p<0.01$) and 31% ($p<0.01$), respectively, in LIV versus CTL. No differences in mechanical properties of the thoracic vertebrae between LIV and CTL resulted from mechanical compression.
Conclusions: Daily LIV administration significantly improved trabecular bone microarchitecture and trabecular bone homeostasis in E2-deprivated mouse model. Our data suggests LIV may maintain trabecular bone mass in the lumbar spine and could enhance bone formation in post-menopausal, E2-receptor positive breast cancer patients undergoing AI treatment.

Ryan Pattyn is a third-year medical student who is undecided in his specialty of interest. Reflecting upon his IMPRS research involvement, Pattyn found that the skills he developed—building a knowledge base, performing tests/procedures, and analyzing data—have applications beyond research to the clinical practice in his clerkships and beyond.

Developing Optimal Type 2 Diabetes Genetic Risk Communication Strategies for Physicians and Patients

◆ **Halley Staples**, Kent Crick, Robert Considine, Jennifer Wessel

Background: Currently, gestational diabetes (GDM) affects 13% of pregnancies; up to 70% of those women and their children will develop type 2 diabetes (T2D). GWAS have been successful at identifying T2D genetic risk variants. Physicians' ability to effectively communicate T2D genetic risk is dependent on their patients' genetic self-efficacy (GSE), genetic knowledge (GK), health literacy (HL), and numeracy.
Methods: The Primordial Prevention Program has the overarching goal of examining the clinical utility of genetic testing for T2D prevention in high-risk families. Parents with a maternal history of GDM were interviewed to assess their preferences and understanding of their children's T2D genetic risk reports. Results from these analyses were used to develop a more detailed survey to assess the correlation of GSE with GK, HL, and numeracy in an independent sample.
Results: Interviews were conducted on 28 mothers and 21 fathers. Participants were 39±8 years old, 41% non-White, and reported high GSE levels (19.3±3.6), which positively correlated with HL (r=0.35, p=0.02) and GK (r=0.28, p=0.05). Adult participants from the follow up survey were 37±14 years old, 84% female, and 32% non-White. Participants' GSE levels were positively correlated with GK (r=0.29, p=1.95x10-6), numeracy (r=0.30, p=9.31x10-7), and HL (r=0.14, p=0.02). In stratified analyses, those with a lower education level scored significantly lower compared to higher educated participants (GSE (8.6±2.8 vs.10.4±3.1, p=2.59 x 10-5), GK (12.9±1.7 vs. 13.7±1.5, p=1.37 x 10-4), numeracy (2.4±1.6 vs. 4.4±1.6, p=1.73 x 10-16), HL (31.5±8.9 vs. 36.5±5.4, p=1.22 x 10-7)).
Conclusions: In our study, parents and a higher educated adult population presented as genetically self-efficacious and had higher HL, numeracy and GK. Physicians' assessment of their patients' GSE, GK, HL, and numeracy will enable effective communication of genetic risk. Physicians should be aware that patients may demonstrate efficacy in their understanding of genetics, even though their understanding may not reflect their actual knowledge.

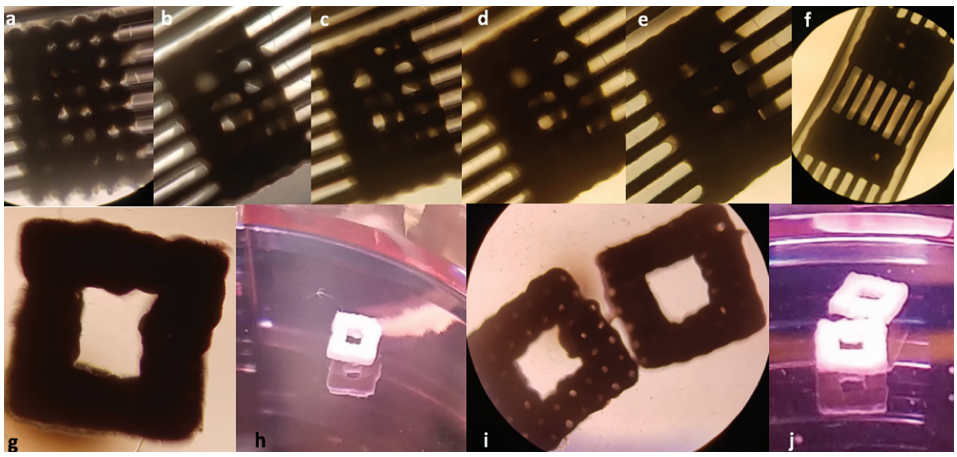
Halley Staples is a third-year medical student who is drawn to OB/GYN for having aspects of both procedural medicine and primary care. Her advice to incoming medical students is to never underestimate the power of research; it has transformed the way society operates and will only continue to do so in the future. Staples has received the Hazel and Tommy Thompson Cardiac Research Scholarship during the IMPRS 2017 Summer Research Symposium

Scaffold-free 3D-Bioprinting (3DBP) of A Porcine Liver Model

◆ **Carlos Vega**, Lester Smith, Ping Li, Kristina Altman, Burcin Ekser

Introduction: Xenotransplantation (XTx) could be the solution to the lack of transplantable organs. Recently, great progress has been made in XTx research and there are currently >26 different genetically-engineered (GE) pigs. The most complex GE pig contains six different gene knock-outs or -ins. However, no researcher knows what would be the best genetic combination for XTx. The production of GE pigs is very expensive and would be quite time consuming for each genetic combination. Capitalizing on a new 3D bioprinting technology, we propose to use GE cells to generate a scaffold-free 3D pig liver tissue constructs, which can be used to study human immunological and coagulative responses in a time and cost-effective way.
Methods: A step-wise model for 3DBP was developed which included (i) determination of optimal size of spheroids, (ii) determination of optimal time of spheroid formation and stability, (iii) designing and printing of the most suitable 3D structure, and (iv) determination of viability of the 3D-bioprinted structure. The optimization of 3DBP was also based on (i) porcine hepatocyte isolation; (ii) cell aggregate (spheroid) diameter, roundness, smoothness, durability, stability, and viability; (iii) the ratio and combination of different cell types; (iv) and the assembly (printing) of tissue constructs using spheroids.
Results: Using a combination of porcine fetal fibroblasts and liver derived cells (LDCs, CD31+) (10:1 ratio), 450-500μm diameter spheroids were generated after 2-3 days of plating and successfully used to print 3 preliminary constructs (Fig.1). These 2 cell-type 3D-bioprinted constructs were later tested for their viability/structure after 1, 2, and 3 weeks of printing (Fig.1). Next, a combination of fibroblasts, hepatocytes, and LDCs (2:1:0.1 ratio) formed spheroids 5 days after plating and were then used to print our first 3 cell-type construct. Most of the spheroids remained intact in this 3 cell-type constructs. After incubation for an additional 5 days, this 3-cell construct fused and formed a stable 3D structure. Histology (H&E staining) shows promising results.
Conclusions: We have successfully printed a scaffold-free 3D Bioprinted Porcine Liver Model containing hepatocytes, liver derived endothelial cells, and fibroblasts. Further cell ratio optimization is required to produce functional spheroids capable of forming a more stable construct in the future. Using CRISPR-Cas9 technology, desired GE pig cells will be printed for future constructs which will allow us to explore the immunogenic and coagulative properties of pig tissues in the human body.

Carlos A. Vega is a third-year medical student whose specialty of interest is general surgery. "I have always found the spectrum that general surgery covers very fascinating. From my prior experiences in the OR I have come to realize that I enjoy working with my hands in a fast-paced environment. Surgeons truly have a direct impact on the health outcomes of a patient, and I find gratification on seeing how patients can quickly recover after an operation." Vegas' research experience has enabled him to see first-hand how advances in medicine unfold. He was involved in groundbreaking research with applications to patients he now sees on a day-to-day basis during rotations, and he believes that research puts the current issues of medicine into perspective.



Scaffold-free 3D-Bioprinted fibroblasts and liver derived cells (CD31+). (a-e) show bioprinted combined wild-type porcine fibroblasts/liver derived cell containing spheroids and their fusion making 3D constructs on micro-needles from day 1 to day 5, respectively. (f) day 5 after 2 bioprinted constructs on micro-needles. (g) microscope picture of scaffold-free 3D-bioprinted constructs moved out of micro-needles. (h) same construct as in picture g with naked-eye. (i) Both 3D constructs as shown in figure f out of micro-needles at the end of day 5. Microholes are also visible. (j) Naked-eye appearance of both 3D constructs as in picture i.

Assessment of Intravitreal Griseofulvin Toxicity in Mouse Models

◆ **Darcy White**, Sheik Pran Babu Sardar Pasha, Timothy W. Corson

Background: Ocular neovascularization is characterized by aberrant blood vessel growth in eyes, inducing irreversible vision loss. Common neovascular eye diseases include wet age-related macular degeneration, proliferative diabetic retinopathy, and retinopathy of prematurity, all major contributors to blindness. Current therapies target vascular endothelial growth factor (VEGF), but 30% of patients are unresponsive to anti-VEGF therapies. This limitation demands the discovery of novel therapeutic targets. Our lab discovered that the enzyme ferrochelatase (FECH) is necessary for angiogenesis, and that the antifungal drug griseofulvin, which inhibits FECH as an off-target effect, blocks neovascularization when injected intravitreally in mouse models. Though griseofulvin has demonstrated safety as an oral medication, its ocular safety has never been tested. Thus, we set out to investigate the toxicity of griseofulvin in mouse eyes, and we hypothesized that griseofulvin would not be toxic when delivered intravitreally.
Methods: Mice were intravitreally injected once with vehicle, 25 or 100 μM griseofulvin. In 7-day and 14-day studies, we assessed retinal damage in vivo using fundoscopy, optical coherence tomography (OCT), and electroretinography (ERG) and used ex vivo immunostaining for stress markers.
Results: Assessment of retinal morphology using OCT, fundoscopy, and fluorescein angiography showed that griseofulvin-injected eyes were identical to control eyes. ERG showed that griseofulvin-injected eyes were equal in retinal function to the control. In immunohistochemistry studies, there was no upregulation of stress markers in griseofulvin-injected eyes. Finally, in paraffin sections, griseofulvin-injected eyes were morphologically indistinguishable from the control.
Conclusions: This lack of ocular toxicity brings griseofulvin closer to becoming an approved treatment for neovascular eye disease.

Darcy White is a third-year medical student who is interested in pediatrics and ophthalmology. On one hand, she loves kids because she is inspired by their resiliency in face of challenge; on the other, she is fascinated by ophthalmology for its complexity of structure and pathology. Through research, White gained a deeper appreciation for the scientists whose countless hours of hard work and dedication to their field have resulted in life-altering and life-saving interventions for patients. Her own research has helped her develop her critical thinking and problem-solving skills, which she can apply as a doctor who employs strategic investigational approaches to patient work-ups. She expresses deep appreciation for her lab for teaching her so much.

Bone-Targeted Pharmacological Inhibition of Notch Signaling Decreases Resorption and Potentiates PTH-induced Bone Gain in Skeletally Mature Mice

◆ **Gerald Jiang Wu**, Jesus Delgado-Calle, Teresita Bellido

Background: Parathyroid hormone (PTH) regulates plasma calcium levels by resorbing bone through indirect actions on osteoclasts. Interestingly, chronic exposure of PTH produces catabolic effects on bone while intermittent injections of PTH (iPTH) produce anabolic effects. PTH has been shown to activate Notch signaling, a critical pathway in cell-to-cell communication, though the exact role that Notch plays in the skeletal actions of PTH remains unclear. To dissect these effects, the Bellido lab created a novel bone-targeted Notch inhibitor (BT-GSI, Bone-Targeted Gamma Secretase Inhibitor), activated when exposed to the microenvironment of resorption sites, thus achieving Notch inhibition only in bone.

Methods: C57BL6 skeletally mature mice were divided into 4 treatment groups: control; BT-GSI; iPTH; and BT-GSI with iPTH. My work focused primarily on quantifying bone formation rate, osteoblast, and osteoclast numbers of the treatment groups using dynamic and static histomorphometry, respectively, of bone sections. I also performed MicroCT analysis of vertebral bone to measure bone microarchitecture and gene expression analysis of bone, brain and gut samples to assess BT-GSI's ability to inhibit Notch signaling in various tissues.

Results: BT-GSI specifically inhibited Notch signaling in bone, but not in other tissues. Short-term inhibition of Notch signaling with BT-GSI increased bone mass of spinal cancellous bone and enhanced PTH-induced bone gain by decreasing bone resorption while preserving PTH-induced increases in bone formation rate.

Conclusions: BT-GSI presents as a promising approach in treating skeletal diseases characterized with bone loss by inhibiting bone resorption and can potentially circumvent the gastrointestinal toxicity associated with systemic inhibition of Notch using unconjugated GSI.

Gerald Wu is a third-year medical student who is undecided in his specialty choice but approaching his rotations with an open mind as he explores his interests. Through his research experience, while Wu learned a great deal about bone biology and metabolism, he found the process of interpreting hard-earned data and translating it into an answer to a scientific question truly rewarding. Interpreting data in order to gain a better understanding of the bigger picture is now a skill he uses every day when seeing patients on his clerkships. He adds that great research requires great mentors and a great lab; for this, he is grateful to Drs. Bellido and Delgado-Calle and the Bellido lab for their guidance and for such an enriching, rewarding and productive summer.

MICHAEL MENEGHINI | PHOTO

To Go Far, Go Together

Dr. Michael Meneghini is the associate professor of orthopedic surgery, fellowship director at the IU Health Hip and Knee Center at Saxony Hospital, and practicing orthopedic surgeon.

BY HONGLIN XIAO

Honglin Xiao: Thank you for taking the time to sit down with us for this Insight Spotlight. To get us started, please tell us a little bit about your educational background and your career thus far.
Michael Meneghini: Well, I grew up in Terre Haute, a native Hoosier, and received my engineering degree from Rose Hulman before heading to IU School of Medicine where I graduated in 1999. I then did my residency at Rush University Medical Center in Chicago followed by a fellowship in lower extremity adult reconstruction at the Mayo Clinic. I started practicing at Saint Vincent Hospital with a group called Joint Replacement Surgeons of Indiana, a highly reputable joint replacement group which I was with for two years before joining the faculty at the University of Connecticut.

While in private practice, I realized that I wanted to be an academic orthopaedic surgeon. I had always wanted to teach and had the opportunity to get the hip and knee program at Connecticut up and running. Then, for personal reasons, I wanted to come back home because I have family here [in Indiana]. I was given a unique opportunity when I came back: IU Health was building a hospital in Fishers and wanted to focus on orthopedic and heart surgery. They asked if I would be willing to become the director of orthopedics. I had to start my practice and build this hospital from scratch. In 2011 we opened the Hip and Knee Center here and within 5 years became the busiest hip and knee center in all of IU health.

X: So, it sounds like you really went full circle. Besides the involvement you have within clinic and the OR, can you speak to the involvement you have here within research?
M: Yeah, it has been a great journey; when I first started we had 3 exam rooms and we didn't even have a bathroom in our small office over on Spring Mill street where our practice started was while waiting for IU Saxony to be built. My office was in one of those exam rooms, so we effectively had 2 exam rooms. Now, our

team consists of 4 surgeons, multiple nurses and assistants and its been great to build this staff here which all help with research.

Our research program here is designed to be a center of excellence for the tripartite mission that embodies IUSM: clinical practice, education, and research. Our fellowship program embodies that educational component. When I came back to IU, we really built up the hip and knee fellowship training program. The first year we had 5 applicants for 1 spot, now we have over 100 applicants for 3 spots. It is probably within the top 10-15 fellowship programs now.

The research component has exploded as well. It started with me and my spreadsheet of surgical cases and collecting certain data points. I had an engineering student, Luke Lovro from New Mexico, who emailed me when I first started and asked if he could do research with me for a year. At that point, I had very little grant money, barely $30,000, and told him I could only pay him a portion of that. He agreed regardless; so this engineering student from New Mexico drove all the way to Indiana and essentially started our research program before he got into medical school.

Now, our research wing includes a research director, a full-time engineer, a data analyst, and multiple medical students. It really has exploded, and we've gone in 8 years from essentially a small program to one of the best hip and knee surgical and research centers in the Midwest. It's been a labor of love; I can tell you my car is the first to get here and the last to leave.

X: Wow, a student was so dedicated that he drove from New Mexico of all places. For those of us right here at IUSM, do you have any advice on how to get started on research?
M: As a medical student, I was very fortunate. My first research project was with Dr. Bill Capello, an orthopedic surgeon here at IU. I was at the IU Northwest campus in Gary and called the anatomy department in Indianapolis and told them I had an engineering background and was interested in knee replacements and asked if there was anyone who worked with implant design. They referred me to Dr. Capello and I still remember the meeting: I told him I wanted to do hip and knee replacements and he pulls an implant off his shelf and says to me, "I designed this". This was in 2000, my first year of medical school. 18 years later, I can point to this implant that's sitting here and say to you that I designed this myself.

Eighteen years ago, I was a first-year medical school and had a mentor who gave me an opportunity to do research. So, my advice for medical students has two parts: the easy one is to find a mentor and be aggressive and get involved in whatever way you can. For me, clinical research is important because as surgeons we must think clinically. It helps us make everyday decisions. The second part may be more challenging. If you want to do academic medicine and research, the sooner you can identify your field of interest, the quicker you can reach your goals and the better off you will be in your pursuits by focusing your efforts and getting ahead. Even if you can't focus on what you want to do right now, pick something and get started from there. Easier said then done but I believe it is crucial to get started sooner rather than later, particularly if you want to be an academic physician or surgeon.

X: You mentioned that Dr. Capello gave you the first building block to start your career in orthopedics. It seems that you are passing it down through the years with all the fellows and medical students you educate here. How did you get started in mentorship and what value do you see in finding an appropriate mentor for medical students?
M: Mentorship cannot be overvalued. It is as big as people say it is. If I look at the times when I have succeeded, I can identify mentors and people who have guided me along the way. This includes my parents first and foremost.

As you get out into the professional world, you can't learn this world from a textbook and you can't learn it from the internet. Much of success comes from relationships and learning from others who have traveled a similar path. Mentorship is so invaluable in that not only can it help you focus on what you want to do, but a good mentor is able to guide you and allow you to be more productive.

Moreover, from a professional development perspective, mentors are great friends and lifelong contacts. If you look at what our medical profession struggles with right now, you see it every day in emails, magazines, what have you. Physician burnout, dissatisfaction with work, dissatisfaction with EMR. I read all these things and realize that despite having such a busy lifestyle with clinic and research, I feel fulfilled because of my great relationships with my mentors.

To this day, I am still in contact with Bill Capello; he was in my clinic yesterday and brought in one of his friends to have me operate on them. Yesterday was an extremely satisfying day for me professionally. Despite all the same stressors of clinic, of all those things, it boils down to me as a first-year medical student and reaching out for an opportunity.

X: It sounds like you have enjoyed a great amount of success because of your mentors. What has been the biggest challenge for you in terms of balancing your time in the OR, in the clinic, and with research?
M: The biggest challenge that comes to mind is managing time with my family and my clinic duties. For someone who is driven like me, it can be difficult to balance clinical practice and family, but it takes communication and perseverance. I have 5 children and it is very hard to manage everything that comes with being a parent with my career. I am blessed to have a spouse who is supportive and who is an amazing mother.

As a physician, it is easy for people to say the spouse doesn't have to sacrifice and all that nonsense. In reality, the spouse sacrifices a lot. They have to be on board with what you do and if you pretend that it won't matter, or sacrifices won't happen, it is very hard to overcome. For example, next week I have to travel to a conference in Florida. I take my wife and my kids with me when I go to these. While it is hard in terms of preparation as I can't prepare my talks on the plane like I would do in the past because I help with the kids, it allows me to enjoy time with my family. To do so however, I have to be more efficient and put in the effort to prepare for a work trip with the family.

Communication is a huge part of this. It is crucial to work life balance, I can't emphasize it enough. There will be times when it is hard, but my wife and I communicate constantly. For example, at the end of the year, I have all the medical students who do research with me come over and have a pizza party and I schedule that based on availability of our family calendar and after I help her get the kids down to bed.

I guess this is just a long-winded answer to say that my wife is equally responsible and deserves equal credit for my success. She allows everything to happen.

Dr. Meneghini can be contacted by email at rmeneghi@iuhealth.org

Indiana University Student Research Symposium

The following works were accepted for presentation at the Indiana University Student Research Symposium, which serves to highlight student research from all levels of experience in order to ignite interest and support for scientific inquiry in the IUSM medical community.

An Unusual Presentation of Undifferentiated Connective Tissue Disease

◆ **JULIE BITTAR**
Contributing authors: Dunfee EH, Wang, CY, Rohr-Kirchgraber T

The hallmark of panniculitis, an inflammation of subcutaneous adipose tissue, is hard, tender skin nodules. Systemic signs such as weight loss and fatigue may be present. More common in women, it begins in the lower legs, may spread to the arms/upper chest, lasting about 6 weeks.

A subset has increased lymphocytes in the panniculus which must be distinguished between benign reactive processes, lymphoma, and other conditions. Accurate classification of the panniculitis is crucial to direct clinical management as treatment options vary from non-medical therapy to immunosuppressive agents to aggressive chemotherapy. An adequate biopsy including skin and deep subcutaneous tissue and collaborative effort between physicians will lead to specific diagnosis.

A 45 year-old female presented with mild fever, arthralgia, and 6 months of persistent painless, non-tender, subcutaneous nodules over the bilateral upper extremities and left anterior chest. These nodules originated as "small red dots" on her left arm that spread and developed into multiple 4-6 cm hyperpigmented, erythematous subcutaneous mobile nodules. PMH: mild intermittent asthma. FHX: lupus and lung cancer. Workup: positive Antinuclear Antibody (ANA), anti-U1 Ribonuclearprotein antibody (anti-U1 RNP) and Anti-streptolysin O (ASO) titers, negative dsDNA antibodies, Rheumatoid Factor (RF) and Angiotensin Converting Enzyme (ACE) titers and normal WBCs. Biopsy: lobular lymphocytic infiltration of subcutaneous fat, c/w Lupus Erythematosus Profundus (LEP). Unlike many of the other panniculitides, LEP is more commonly identified on upper arms, trunk (including breast) and face, but, not meeting the classification criteria for Systemic Lupus Erythematosus (SLE), a diagnosis of unspecified connective tissue disease (UCTD) with lobular lymphocytic panniculitis was made and the patient was started on steroid therapy leading to significant improvement.

In usual conditions like this, it is important for the clinician and the pathologist to collaborate as the effort to provide appropriate care depends on an adequate biopsy and the clinical history.

An Experienced Surgeon Can Meet or Exceed Robotic Accuracy in Manual Unicompartmental Knee Arthroplasty

◆ **ASHLEIGH BUSH**
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Background: Existing studies report more accurate implant placement with robotic systems; however surgeon expertise has not always been taken into account. The purpose of this study was to compare the accuracy of achieving target tibial component position in manually instrumented UKAs performed by an experienced high-volume surgeon to published data on robotic accuracy.
Methods: Seventy-six consecutive manual fixed-bearing UKA's performed by a single surgeon between 2011 and 2016 were radiographically reviewed. Tibial slope and varus alignment were measured on pre and postoperative radiographs by an independent reviewer. Tibiofemoral component collinearity was measured on postoperative anteroposterior views. Manual targets were set within 2° of native tibial slope and 0 to 2° of varus tibial component alignment. Deviations from target were calculated as root mean square (RMS) errors. Findings were compared to high quality studies of robotic-assisted versus conventional UKA.
Results: RMS error for tibial slope in manual UKAs (1.4°) was lower compared to published robotic cohorts (1.6 to 1.9°). RMS error for manual tibial component varus alignment surpassed or was equivalent to published robotic cohorts (1.5° vs. 1.8 to 5°). The percentages of manual UKA patients within targets for tibial slope and tibial component alignment were closer to published robotic data than the manual data to which robots have been compared.
Conclusions: These data demonstrate that an experienced, high-volume surgeon's accuracy in manual UKA can meet or exceed robotic-assisted UKA. While robotic-assisted surgery has been shown to improve accuracy of component placement compared with manual instrumentation, surgeon experience and aptitude have not been examined specifically. This study supports a commonly held notion that the cost associated with robotic-assisted surgery may be most appropriate for lower volume and/or less experienced surgeons who perform UKA.

Thrombolysis During Liver Procurement Prevents Ischemic Cholangiopathy in DCD Liver Transplantation

◆ **ARIANNA CABRALES**
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Background: Ischemic cholangiopathy (IC) is the primary cause of inferior outcomes associated with donation after circulatory death (DCD) liver transplantation, including high rate of graft loss, retransplantation, and recipient mortality. Development of IC in liver transplant recipients appears to be associated with peribiliary arterial plexus microthrombi formation that can occur in DCD donors. Our center has demonstrated success using tissue plasminogen activator (tPA) flush during DCD organ procurement to prevent microthrombi formation and prevent IC. This study investigates the long term impact of tPA flush on graft outcomes and program use of DCD organs.
Methods: All records for liver transplants over a 15 year period at a single center were reviewed and data extracted. DCD organ procurement followed carefully established protocols including a 5-minute wait time after determination of cardiac death prior to initiation of the procurement procedure. The procurement consisted of rapid aortic cannulation, aortic clamping, and decompression through the vena cava. Preservation solution included initial flush with histidine-tryptophan-ketoglutarate solution (HTK), followed by infusion of tPA in 1L NS, then further flush with HTK until the effluent was clear.
Results: There were 57 tPA procurements (48%) and 62 non-tPA procurements (52%). Patients receiving tPA grafts were older and had higher MELD scores. tPA grafts had less cold and warm ischemia time and had better survival at 7- and 90-days ($p=0.09$, $p=0.06$) and at 1-year (95% versus 79%, $p=0.01$). Cox regression showed better long-term survival for tPA grafts (88% versus 45% at 10-years; $p<0.01$).
Conclusions: Our center has shown that optimization of perioperative conditions, including use of an intraoperative thrombolytic flush, significantly lowers the incidence of IC in DCD liver grafts. As a result, the percentage of DCD grafts at our center has increased, including the use of expanded criteria DCD livers, without a worsening of outcomes.

Sex-Specific Outcomes Reported in High-Impact Orthopedic Journals

◆ **KARSEN CORN**
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Background: There are two categories of biological distinctions between men and women. The direct hormonal differences, and the indirect differences that influence bone density, joint laxity, tendon strength, and muscle mass. With these distinctions, it is curious that sex-specific differences in orthopedic injuries and treatments are not more widely discussed. In this study, we compare orthopedic journals and analyze their commitment to publishing rotator cuff and knee osteoarthritis research that reports sex-specific outcomes.
Methods: We reviewed four different high-impact orthopedic journals. These journals included the Journal of Bone and Joint Surgery (JBJS), Clinical Orthopaedics and Related Research (CORR), the American Journal of Sports Medicine (AJSM), and the Journal of Arthroplasty (JOA). JBJS and CORR were both searched for rotator cuff and knee osteoarthritis research. As specialty journals, AJSM was searched for rotator cuff, and JOA was searched for knee osteoarthritis research. The first 100 articles per journal per topic were included. If there was any further analysis of sex beyond the statement of how many men and women were included in each experimental group, a study was designated as successfully reporting sex-specific outcomes.
Results: JBJS publishes significantly more articles reporting sex-specific outcomes with research pertaining to knee osteoarthritis than rotator cuff injuries ($p = 0.00009$). In regards to specialty journals, JOA publishes significantly more articles reporting sex-specific outcomes with knee osteoarthritis than AJSM does with rotator cuff injuries ($p = 0.043833$). No other significant differences were found.
Conclusions: Sex-specific outcomes are more widely reported in topic areas where there is already well-known sex-based differences. It is our opinion that sex-specific outcomes should be analyzed across all fields of orthopedics. It is our recommendation that further research is done in this area to include more journals and topics.

Pelvic Exenteration as a Radical Lifesaving Measure

◆ **FATMOUMATA BAH**
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Vulvar cancer is the 4th most common gynecologic malignancy in the US, with squamous cell carcinoma comprising 75% of cases. For most patients, diagnosis is early while still confined to a primary site and the 5-year survival rate is 72.1%. For advanced cancers that spread to regional organs, there is another option offering hope for cure. Pelvic exenteration is a surgical option for patients with advanced gynecologic cancers that have spread and cannot be resected with smaller procedures, and for patients who have failed to respond to radiation. It involves removal of the uterus, ovaries, uterine tubes, bladder, rectum, vagina and urethras.

A 52-year-old woman presents with a 2-month history of fatigue, vaginal bleeding and discharge. She had recently undergone coronary artery stenting for her CAD. Post stenting, she experienced increasing uterine/vaginal bleeding and discharge and was sent home with Depo-Provera and Diflucan for fungal coverage. Two months later, she presents to the ER with increasing fatigue, painful vaginal bleeding, and was found to have a hemoglobin of 4. Ensuing workup revealed Stage III squamous cell vulvar carcinoma that was refractory to chemotherapy and radiation trials. After careful consideration and evaluation, she opted to undergo pelvic exenteration surgery. Her operation was successful in removing all the cancer and was discharged to a rehabilitation facility for further recovery.

This case illustrates several points. Pelvic exenteration is an ultra-radical surgery that has been proven to have >50% 5-year survival. Though life-saving for many patients, it involves major changes in gastrointestinal, genitourinary, and sexual function as well as body image. Additionally, this patient's delay in diagnosis could have been prevented with proper medical workup at initial presentation. Although it was reasonable for her to be treated with Depo-Provera at the time, any case of unexplained vaginal bleeding necessitates close follow up.

Eating Disorders - A Sign of Survival!

◆ **CHANELLE BENJAMIN**
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Case: 37 yo female with Anorexia Nervosa: restrictive/purging wants to stop the delusional/compulsive thoughts about eating and exercising and restart a healthy meal plan. Intermittently restricting and purging, struggling with weight and body image, compulsively counting calories and exercising except during her 2 pregnancies. Her eating disorder (ED) started at age 17.

A victim of childhood sexual abuse (CSA) by her father at age 4 years, and again as a 17-year-old by her employer. Soon after she began restricting, developed depression, anxiety and began purging. Her weight dropped from 130 to 106lbs until she was forced to get help. She has been in treatment for her disorder many times, both at inpatient and residential facilities and has attempted suicide at one point. To her, restrictive eating and purging allows her to exercise some sense of control over her life and avoid thinking about her CSA.
Conclusion: Approximately 30% of those with an ED have a history of CSA and the ED is used to self-manage the feelings and experiences. The self-harm of the victims of CSA and other traumas is related to body shame which triggers habits geared toward destroying the body of which the victim is so ashamed, resulting in starvation, purging, or binge eating, depending on the manifestation of the ED which serves as a coping mechanism.
Clinical Significance: It is important to recognize, understand and create awareness about the different long-term sequelae of sexual assault which may manifest as some variation of an Eating Disorder. Those at high risk for eating disorders because of trauma include:

- Victims of sexual abuse, particularly those who suffered at a younger age
- Victims or observers of domestic violence
- Those who suffer from PTSD

Patients with self-harm activities, including ED behaviors, should be screened for abuse and treatment for the trauma be included in the management.

If In Doubt, Cut It Out! A Skin Lesion Raises Suspicion For Systemic Disease

◆ **MARIA BELL**
Contributing authors: Waterman CL, McNeil-Masuka JK, Li W, Hess KL, Rohr-Kirchgraber TM

Case: A 27-year-old female presented with a 2-year history of a 1.2 cm enlarging soft pink telangiectatic nodule to the right parietal scalp. A shave removal was performed to rule out basal cell carcinoma or Merkel Cell tumor. Pathology report indicated the lesion was a cutaneous myxoma, raising concern for Carney Complex (CNC). Physical exam demonstrated widespread lentigines in sun-exposed areas, without abnormal pigmentation in the mouth, conjunctivae, or eyelids. No blue nevi were found. The patient's mother and grandmother also display lentigines of the upper body. An echocardiogram demonstrated no evidence of intracardiac myxoma.
Conclusions: Classic CNC consists of lentigines, atrial myxoma, and blue nevi. Cutaneous myxomas are found in less than 50% of CNC patients but strongly suggest a diagnosis of CNC if histologically confirmed. Due to the potential for cardiac and systemic complications of CNC, further investigation of an underlying genetic abnormality is prudent in this case to assess the risk of future complications. If genetic testing is positive for a PRKAR1a mutation, appropriate genetic counseling should be offered for patient and family.
Clinical Significance: CNC is a rare autosomal dominant disorder with 600 reported cases since 1985. Its pleomorphic manifestations range in severity from benign cutaneous lesions to multiple endocrine and nonendocrine tumors. CNC is genetically heterogeneous but is associated with inactivating mutations in the PRKAR1a gene in 70% of cases. Workup should be initiated to rule out cardiac myxoma, the leading cause of mortality in CNC patients. Patients with CNC should be encouraged to pursue annual screening for cardiac myxomas, and for patients with a history of cardiac myxomas, echocardiograms should be obtained biannually due to the risk of recurrence. Dermatology referral for new enlarging lesions may allow for earlier identification of underlying disease processes prior to manifestation of systemic symptoms.

It's Not the Alcohol: Autoimmune Hepatitis in an Alcoholic Woman

◆ **SOFIA BERTOLONI MELI**
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Case: 47 y.o. alcoholic female (1L vodka/day) presented with fatigue, shortness of breath, and intermittent edema. CT demonstrated cirrhotic liver changes, small varices, and ascites. Labs notable for elevated liver enzymes. GI counseled patient to stop drinking, with plan to follow closely. Five months later she presented with shortness of breath and received an inhaler. Two weeks later, with continued shortness of breath, ascites, and edema, CXR showed pleural effusion and 1.2L of fluid was removed. Two months later with worsening ascites, fecal incontinence, abdominal pain, and increased dyspnea, patient was admitted for possible spontaneous bacterial peritonitis with 4.5L of ascitic fluid removed. Liver biopsy lacked Mallory hyaline or megamitochondria characteristic of alcoholic liver disease. Labs showed high titer anti-smooth muscle antibody confirming the diagnosis of autoimmune hepatitis with cirrhosis. She was treated with prednisone and is continuing therapy.
Conclusions: Autoimmune hepatitis is rare, with an incidence of <2 per 100,000 per year according to the CDC. Presentation of autoimmune hepatitis varies, ranging from asymptomatic incidental finding to acute liver failure. It may mimic alcoholic liver disease or viral hepatitis, thus requiring serologic testing for classic antibodies to establish diagnosis. Initial treatment involves glucocorticoids +/- azathioprine, with subsequent management depending on response. According to AASLD guidelines for evaluating liver failure, our patient's autoimmune markers were tested. Diagnosis was made and appropriate treatment was initiated.
Clinical Significance: We present a case of autoimmune hepatitis that was initially assumed to be alcoholic cirrhosis. A comprehensive workup uncovered our patient's underlying condition. This case demonstrates the necessity of clinical guidelines to ensure a broad differential that includes rare conditions that may be hidden under classic risk factors for common disease.

Perfusion and Diffusion Imaging in Distinguishing Pilocytic Versus Pilomyxoid Astrocytomas Above and Below the Tentorium

◆ **MICHAEL GROSWALD**
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Background: Pilomyxoid astrocytoma (PMA) is more aggressive and has a higher likelihood of leptomeningeal dissemination, leading to worse outcome compared to pilocytic astrocytomas (PA). Furthermore, genetic differences have been found between supratentorial versus infratentorial PAs. Perfusion and diffusion imaging was utilized to assess for differences between PMAs and PAs as well as supratentorial versus infratentorial tumors.
Methods: This retrospective, IRB exempt study included consecutive patients from 2011 to 2016 with histologically diagnosed PA or PMA with dynamic susceptibility contrast perfusion and diffusion MR imaging. Solid tumor volumes (VOI) were manually traced on commercially available software (Olea Shere 3.0, Olea medical, La Ciotat, France) using T1+C or T2 imaging registered to computed ADC, rCBV, K2 leakage, and MTT maps. The resulting data were evaluated with paired and unpaired T-tests.
Results: 49 subjects (mean age 6.7, 1–15 years, 24 females) met inclusion criteria. There were 30 infratentorial PAs, 8 supratentorial PAs, 5 infratentorial PMAs, and 6 infratentorial PMAs. No significant differences were found between the means of the VOIs between all supratentorial versus infratentorial tumors, PAs above or below the tentorium, PMAs above or below the tentorium, or between PAs and PMAs for ADC, K2 and MTT. Significant difference for paired t-tests but not unpaired t-tests were seen in rCBV between supratentorial (2.60 ± 0.63 95CI) and infratentorial (2.06 ± 0.18) tumors (p=0.02 vs 0.1) , as well as between supratentorial (2.53 ± 0.68) and infratentorial (2.04 ± 0.19) PAs (P=0.04 vs P=0.14).
Conclusions: PAs and PMAs, as well as supra- and infratentorial locations cannot be distinguished by ADC, K2, or MTT parameters. There is a trend toward a higher perfusion difference in supratentorial tumors versus infratentorial tumors.

Primary Care Providers' Attitudes, Practices, and Knowledge in Treating LGBTQ communities

◆ **EMILY HADLEY**
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Background: Healthcare inequalities within the lesbian, gay, bisexual, transgender, and queer (LGBTQ) community are in part due to a lack of LGBTQ-specific content at all levels of medical training. Cultural competency is a direct product of education and key component in providing quality care. While LGBTQ cultural competency has been found to be lacking within various medical specialties, no studies have compared competency among primary care providers.
Methods: The authors evaluated 127 Indiana providers. LGBTQ cultural competency was assessed using a 37-item self-reporting, anonymous survey battery that quantified providers' attitudes, practices, and knowledge. Survey item means were computed and frequencies were analyzed across medical specialty using Fisher's exact tests. Knowledge item accuracies were compared to the probability of chance correctness using one-sample t-tests and examined across medical specialty using one-way analysis of variance (ANOVAs).
Results: Overall, 78% of respondents agreed that they were comfortable treating LGBTQ patients, and 80% agreed that there should be more education in health professional schools on LGBTQ health and mandatory educational events at IUSM (69%). Yet many providers did not feel well informed on specific LGBTQ health needs (70%), on clinical management of LGBTQ care (74%), nor on referring patients with LGBTQ issues (78%). Overall accuracy on LGBTQ knowledge questions was 51% (8 of 12 items had accuracies less than 50%). There were significant differences in attitudes, practices, and knowledge across medical specialty.
Conclusions: The academic medical community is in an ideal position to improve attitudes and knowledge about LGBTQ care. However, this study revealed a lack of cultural competency among Indiana providers and significant disparities in providers' attitudes, clinical practices, and funds of knowledge. This study disclosed those specific differences and emphasized the need for greater LGBTQ-specific education to increase providers' comfortability and competency in the needs, management, and referrals within LGBTQ healthcare.

New Onset Central Diabetes Insipidus in Children Undergoing Posterior Spinal Fusion

◆ **KYLE HARDACKER**
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Background: Our scoliosis surgery protocol uses TIVA with infusions of remifentanil, propofol, ketamine and tranexamic acid (TXA) (loading dose 10 mg/kg, maintenance at 1 mg/kg/hour, later increased to 5 mg/kg/hour). Since increasing TXA dosing there have been several cases of intraoperative central diabetes insipidus (CDI) marked by sudden development of polyuria. We did not recall any cases of CDI prior to TXA use or at the lower dose of 1mg/kg/hour.
Methods: Retrospective chart review
Results: A total of 9 cases out of 599 cases over a 3 year period from 3 different surgeons developed CDI intraoperatively. The 9 patients had a mean urine output of 1.1 ml/kg/hour prior to TXA infusion. Urine output increased to 4.2 ml/kg/hour within 1–3.5 hours of the start of TXA infusion. Concomitantly, plasma sodium increased from 137 ± 3.2 mEq/L to 142 ± 3.5 mEq/L. All responded to vasopressin infusion with TXA continuation or cessation of TXA alone. No cases of postoperative CDI were seen. Group 1 (TXA at 1 mg/kg/hr) had 0/363 cases. Group 2 (TXA at 2–5mg/kg/hr) had 9/236 cases. A Fisher's exact test for comparing the Group 1 Rate (0%) vs. Group 2 Rate (3.8%) had a significant p-value of <0.001.
Conclusions: This is the first reported series of intraoperative CDI development in pediatric deformity correction surgery utilizing TXA infusion. The evidence suggests a dose-dependent association between TXA and CDI. There is enough evidence to perform an observational study on a large series of patients undergoing scoliosis surgery at the higher TXA dosage. This study would measure sequential serum and urine sodium levels, plasma and urine osmolality, urine output, and vasopressin levels. Should such a study confirm our hypothesis that TXA causes CDI further studies measuring the effect of different doses of TXA or a comparative study with epsilon-aminocaproic acid are warranted.

The Effects of Transitioning to a Pass-Fail Grading System on Student Volunteer Activity at a Student-Run Free Clinic

◆ **JASON HOARD**
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Background: In 2016, the Indiana University School of Medicine transitioned to a pass-fail grading system for first year students in the Class of 2020. The purpose of this study was to compare the volunteer activity of IUSM medical students at the IU Student Outreach Clinic while these students were enrolled in preclinical courses with tiered (Honors, High Pass, Pass, Fail) vs. pass-fail grading systems, and to assess the impact of the pass-fail curriculum on volunteer participation.
Methods: Medical student volunteer data was collected in a cross-sectional manner in 2017 from the IU Student Outreach Clinic volunteer website for the Classes of 2018, 2019 and 2020. The number of medical student volunteers per class was determined by the number of active volunteer accounts on the website (≥ 1 clinic volunteer encounters). The total number of volunteers, as well as the average number of volunteer encounters per student per year, were compared between the three classes.
Results: 51.6% of the Class of 2020 volunteered at the clinic at least once during their first year of medical school, compared to 38.7% of the Class of 2019. There was a 118.4% increase in the average number of volunteer encounters for the Class of 2020 compared to the Class of 2019.
Conclusions: The change in grading system for preclinical courses from tiered to pass-fail had a positive impact on volunteer participation among first and second year medical students. Under a pass-fail grading system, more first and second year students volunteered at the Student Outreach Clinic, and those students volunteered more frequently.

Neurologic Impairments from Pediatric Low-Grade Glioma by Tumor Location and Timing of Diagnosis

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Purpose: To better characterize the neurologic outcomes of low-grade gliomas (LGGs) according to tumor location and duration of presenting symptoms in children.
Methods: We retrospectively reviewed neurologic impairments in 246 pediatric patients with LGGs (88 with optic pathway and midline tumors, 56 with posterior fossa tumors, 52 with cerebral hemisphere tumors, 35 with brainstem tumors and 15 with spinal cord tumors) who were treated at St. Jude Children's Research Hospital between 1995 and 2005. We compared neurologic impairments (defined by Common Terminology Criteria for Adverse Events, version 4.03) by tumor location and prediagnosis symptom interval (PSI) (≥3 months or <3 months) at first and last patient visits.
Results: The median age of diagnosis was 7.1 years; median PSI was 2.1 months; and median time to last follow-up was 11.6 years. LGGs in the cerebral hemispheres resulted in significantly fewer neurologic impairments, compared with that of other locations at baseline (P<0.001) and at last follow-up (P<0.001). In all patients, PSIs greater than 3 months resulted in a significantly higher incidence of ataxia and dysmetria at last follow-up (41.6%, P=0.003). Greater PSI was also significantly associated with worsening lower extremity motor weakness from cerebral hemisphere tumors; dysmetria from optic pathway and midline tumors; eye and visual dysfunction from posterior fossa tumors; and ear and vestibular disturbances from brainstem tumors (P≤0.05).
Conclusions: Neurologic impairment in pediatric LGGs varies by tumor location, and PSIs greater than 3 months affect some functionally important neurologic outcomes.

Hepatitis C Prevalence among Injection Drug Overdoses Identified in ESSENCE - Indiana, 2017

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Objective: To investigate the prevalence of Hepatitis C virus (HCV) infection among injection drug users (IDU) presenting to Indiana emergency departments (ED). To determine the prevalence of incarceration history and hepatitis A and B vaccination among HCV positive patients.
Methods: From July 1 to December 12, 2017, injection drug overdoses were identified using the Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE). Medical record numbers were used to access patient name, date of birth, and address, which were matched to HCV cases in the Indiana National Electronic Disease Surveillance System (I-NEDSS) and the Indiana Department of Corrections Offender Database. Demographic, geographic, vaccination, and incarceration information were collected and compared with HCV status.
Results: A total of 1,587 ESSENCE alerts for injection drug overdose were reported. Poisoning by heroin was the most frequent discharge diagnosis/chief complaint. After accounting for duplicate patients and missing addresses, 1,084 unique individuals were identified; 34% were HCV positive (n=360). Those who were HCV positive tended to be older (35 years vs. 33 years), white (84.7% vs 70.1%), and had a history of incarceration (40.3% vs. 21.1%) compared to IDUs who visited an ED with no history of HCV infection. Of those positive for HCV, 97.2% were chronic cases (n=347), 17.6% had a history of hepatitis B vaccination (n=63), and 5.2% had a history of hepatitis A vaccination (n=18).
Conclusions: More than one-third of injection drug overdoses who visited a participating ED during this time period were HCV positive. Because we cannot account for IDUs who have never been tested, the prevalence of HCV in this study is likely an underestimation. Increasing screening among IDUs will improve our knowledge of the true disease prevalence in this population. Exploring characteristics that differ with HCV status can identify areas of intervention for IDUs and help guide policies and services.

Patient Reported Outcomes Following Revision Total Hip Arthroplasty (THA) Compared to a Matched Cohort of Primary THA Patients

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Purpose: Patient reported outcomes following revision and primary THA have not been empirically compared. Patients requiring revisions may have more functional disability, emotional frustration with failed surgery and limited access to care. This study purpose was to determine if patients undergoing revision THA were more satisfied than primary THA.
Methods: Ninety-six consecutive aseptic revision THAs were retrospectively reviewed. 17 revisions were excluded due to inadequate followup (n=5) or inability to match (n=12). The remaining revision THAs were matched on sex, age, body mass index (BMI), and American Society of Anesthesiologists (ASA) Classification to 79 primary THAs.
Results: Fifty-percent of the revision cohort was female, mean age was 64 years and mean BMI was 30 kg/m2. There were no differences in demographics between groups (p ≥ 0.661). More revision patients had concomitant spine disease or back pain (21.5% vs. 7.6%, p=0.023), depression (29.1% vs. 15.2%, p=0.054), and preoperative opiod use (43% vs. 20.2%, p=0.003).
Mean UCLA activity level was 3.6 versus 4.2 preoperatively (p=0.060) and 5.0 versus 5.7 at minimum one-year follow-up (p=0.046) for revisions and primaries, respectively. Mean HOOS Jr. disability scores were 42 and 49 preoperatively (p=0.553) and improved to 78 and 87 at minimum one-year (p=0.013), respectively. Improvement in activity level (p=0.536) and hip disability scores (p=0.240) did not differ between groups. 84% of revision and 91% of primary patients reported they were satisfied with THA (p=0.433). Among patients with spine disease or back pain, fewer revision (77%) than primary (100%) patients reported high satisfaction.
Conclusions: While activity levels and hip disability scores were higher in primary patients, the interval improvement did not differ between revision and primary THA patients and revision patients were not more satisfied with THA than primaries. This data also suggests concomitant spine disease and back pain may mitigate satisfaction in revision THA patients.

The Effect of Tourniquet Use and CO_2 Preparation on Cement Penetration adjacent to the Tibial and Femoral Components in Primary Total Knee Arthroplasty

◆ **ZACH GAPINSKI**
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Background: Tourniquetless total knee arthroplasty (TKA) is experiencing resurgence in popularity to minimize postoperative pain. Further, optimal cement technique and implant fixation remain paramount to long-term cemented TKA success. The purpose of this study was to determine how tourniquet use and novel bone preparation using sterile compressed carbon dioxide (CO_2) gas affects cement penetration in TKA.
Methods: A retrospective review was performed of 303 consecutive primary TKAs of identical design. Cement penetration was evaluated by two independent, blinded raters across zones defined by the Knee Society Radiographic Evaluation System. Cement penetration was compared between three groups: tourniquet only, no tourniquet with CO_2 gas, or tourniquet and CO_2 gas. Radiographs were calibrated and excluded if the TKA components were not collinear with the X-ray collimator. Data were analyzed with p = 0.05 indicating statistical significance.
Results: The three groups did not differ in age, body mass index or gender (p ≥ 0.100). Groups that used CO_2 gas, regardless of tourniquet use, always showed greater mean cement penetration compared to the tourniquet only (T) group. Three of seven radiographic zones (p ≤ 0.039) showed significantly more cement penetration in groups utilizing CO_2 gas.
Conclusions: Bone prepared with CO_2 gas showed significantly greater cement penetration in zones characterized by cancellous bone (p ≤ 0.039). While not statistically significant, the other four zones and overall average cement penetration was higher for at least one group involving the CO_2 gas compared to the tourniquet only group. Improved cement penetration via use of CO_2 gas may lead to less implant loosening and therefore better patient outcomes. Further, CO_2 bone preparation appears to mitigate any potential deleterious effects on cement penetration during tourniquetless TKA as measured by mantle thickness.

Is there Benefit in Keeping Early Discharge Patients Overnight After Total Joint Arthroplasty?

◆ **KENT KRAUS**
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Objective: With increasing interest and availability of outpatient total joint arthroplasty (TJA), whether next-day discharge patients receive beneficial medical interventions the night of surgery is of clinical and economic importance. The purpose of this study is to define the extent and nature of medical interventions being performed the first night after TJA surgery.
Methods: 1136 primary unilateral TJAs performed between 2011 and 2016 at a single institution in a rapid-discharge program, managed by a perioperative medicine specialist, were reviewed. Medical records were examined for diagnostic tests, results, procedures, treatments, and all-cause readmissions. Interventions before 4 pm the day of surgery were excluded to avoid confounding the results since outpatient TJA patients could receive interventions prior to discharge. Recorded interventions included any that varied from the preoperative treatment plan, beyond standard-of-care interventions, and those that could not be completed at home.
Results: 333 patients were discharged postoperative day one. After exclusions, 88% (291) received no medical interventions. Six (1.8%) received diagnostic tests, 8 (2.4%) received procedures, and 28 (8.5%) received treatments. One received a diagnostic test and a treatment, and 3 received a procedure and a treatment. All diagnostic tests were negative, all procedures were in/out catheterizations for urinary retention, and 75% of treatments were intravenous fluids. Readmission rates did not differ based on whether interventions were received.
Conclusions: The majority of patients received no overnight interventions suggesting unnecessary costly hospitalization. The most common issues addressed were urinary retention and IV fluids for hypotension, which if protocols to prevent are developed would facilitate TJA and improve safety in the outpatient setting. This study directs focus and effort in the immediate postoperative care of TJA patients which could improve healthcare quality, patient safety and reduction of healthcare costs through a more rapid discharge home.

Proper Evaluation of the Patient with Vaginitis

◆ **LAUREN KUS**
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Background: Symptoms of vaginitis, discharge, irritation, odor, and inflammation are among the most frequent causes of patient visits to gynecologists, primary care providers, and urgent care centers. Trichomonas, bacterial vaginosis, and vulvovaginal candidiasis have been extensively studied, and are usually diagnosed and treated easily. However, these are not the only causes of vaginal irritation. The literature and training regarding the evaluation and diagnosis of vaginal disorders outside of the three most common causes is lacking leaving practitioners ill prepared to care for many patients. This discrepancy puts a tremendous psychological burden on patients left with uncontrolled or recurrent symptoms.
Objective: To provide trainees and practicing providers with a diagnostic algorithm aimed to improve the likelihood of accurate diagnosis of incident and chronic vaginitis.
Methods: Based on a review of the currently published literature combined with clinical experience in a subspecialty chronic vaginitis clinical care center at Indiana University, we describe a more comprehensive diagnostic algorithm. The clinical presentation of patients with symptoms of vaginitis appears to fall into one of two diagnostic pathways: Inflammatory or non-inflammatory vaginitis. In women with inflammatory signs, in addition to trichomonas, providers should consider gonorrhea and chlamydia, group A strep, estrogen deficiency, multi-mucosal erosive disease, and inflammatory vaginitis (desquamative or idiopathic). Candidiasis may be inflammatory or non-inflammatory, and may present as a mixed infection of both candida and bacterial vaginosis. BV is a non-inflammatory cause of vaginitis, but providers should identify acute versus chronic BV in order to select an appropriate treatment regimen.
Conclusion: The evaluation of patients with vaginitis is complex, and the correct diagnosis is essential to making accurate treatment decisions. We present a systematic algorithm for the diagnostic pathway of vaginitis that can be easily implemented by any outpatient care provider to ensure proper management.

Ventriculoperitoneal Shunt Fracture After Traumatic Motor Vehicle Collision

◆ **ADAM LEIBOLD**
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Background: Ventriculoperitoneal (VP) shunts are highly effective in relieving a patient's hydrocephalus, but they are also notoriously susceptible to complications, leading to the need for shunt revision. The clinical features of shunt malfunction are important to recognize quickly so that a revision may be performed in a timely manner. If a shunt malfunction is suspected it should be investigated using a plain X-ray of the shunt system (lateral skull, AP chest, AP abdomen), known as a "shunt series," and a CT scan of the head looking for enlargement of the ventricles. Here we describe a unique case in which a trauma fractured the diaphragm within the shunt's valve system, requiring subsequent revision.
Methods: Patient data was collected through a review of the patient's chart in Indiana University Health's electronic medical record system.
Results: Our patient is a 26-year-old male who had a VP shunt placed in 1991 at the age of 3 months for post-infectious hydrocephalus due to meningitis. Per EMS, the patient was struck by a vehicle traveling around 30-35 MPH, and his head struck the windshield of the car. On arrival the initial survey showed a left posterior scalp laceration. Initial imaging revealed only a small subarachnoid hemorrhage. Two days later the patient's mental status declined, and a repeat head CT showed hydrocephalus and shunt displacement. The patient was then taken to the OR for a shunt revision and a fractured diaphragm in the shunt's valve system was found. After replacement of the valve the patient had an unremarkable hospital course and was discharged three days later.
Conclusions: Our case demonstrates the importance of assessing the integrity of the entire shunt system after a trauma. This includes an evaluation not only of the shunt tubing, the most frequently fractured component, but also of the valve system itself.

The Roles of Sarcopenia and Early Protein Delivery in Critically Injured Patients Recovery

◆ **MOZHU LI**
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Background: Sarcopenia, the age related loss of skeletal muscle volume, and inadequate early protein delivery are identified to be associated with increased complications and length of stay in critically injured patients. Our purpose is to understand the role Sarcopenia plays in association with early protein delivery and mitigation of complications.
Methods: We conducted a retrospective study, reviewing data from 160 trauma patients admitted to the ICU at IU Methodist Hospital, Indianapolis IN. The CT images from these patients were analyzed using the SliceOMatic Ò V4.3 software to measure body composition, including muscle and fat volume, which were later used to calculate skeletal muscle index (SMI) and to define the sarcopenic status of patients. Relationships between SMI and age, sex, Injury Severity Score (ISS), morbidity, mortality and nutrition delivery parameters were analyzed.
Results: After trajectory models were applied, patients were found to follow one of five protein deficit recovery patterns. There was a statistically significant reduction in overall complications between Group 2, who closed their protein debt by hospital day four, and the other four Groups, who failed to close their protein debt with in four days (p=0.009). There was no statistical difference in mean SMI among these groups (p=0.6168).
Conclusions: Early closure of protein debt, rather than increased baseline SMI, plays an essential role to mitigate complications in critically injured patients.

Atypical Clinical Presentation of a Seborrheic Keratosis in the Primary Care Setting

◆ **AMANDA HORNBACH**
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Case: Patient is a 68-year-old female presenting to scheduled clinic visit with a five week history of a single rapidly enlarging skin lesion on the left posterior arm. Patient reports that the initial lesion had been stable "at dime size" over many years, only beginning to enlarge, change color, and change texture over a five-week period. In addition, the lesion had become intermittently pruritic and painful. Physical exam revealed a non-tender raised 2.0X1.5 cm nodule-like lesion with variegated color and texture. Surgical excision with subsequent pathology revealed an irritated and inflamed seborrheic keratosis with warty features. Microscopic description of pathology revealed bland epidermal acanthosis with horn cysts, as well as papillomatosis with focal spires of parakeratosis and suggestion of koilocytosis. No further intervention was required at that time.
Conclusions: Seborrheic keratosis is a common dermatologic diagnosis. These lesions typically present as multiple brownish slow-growing "stuck-on" lesions to the chest, back, and face. Several distinct histological patterns are recognized for seborrheic keratoses, and the sharing of features across types is considered to be common. Common histological features include cell mass of mixed basal and squamous origin, with keratin-filled invaginations and small "horn" cysts. Rarely, lesions present with pre-cancerous or cancerous features amid those of the seborrheic keratosis; these can reflect contiguous growth of separate lesions or changes within the keratotic lesion itself. This rare event is more likely in clinical presentations where the keratosis appears irritated.
Clinical Significance: Skin cancers are the most common type of cancer for women and men, both in the United States and worldwide. While many skin cancers exhibit benign or indolent courses, some seemingly innocuous lesions can mask more serious pathology, delaying imperative diagnosis and treatment. Careful exclusion of a more serious lesion, especially in the clinical setting of change within a stable lesion, may be necessary.

Clinical Impact of Strength and Class of Pre-transplant Donor Specific Antibody on Kidney Transplant Recipients Receiving Steroid-Free Maintenance immunosuppression Regimen

◆ **OLIVIA KAMMEGNE-SIMO**
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Background: The class and strength of pre-transplant DSA has been described as playing a role in determining future risk of acute rejection (AR) and kidney allograft failure in few studies. These studies were mostly done on patients placed on steroid-based immunosuppression regimen.
Methods: A retrospective chart review of patients who received a kidney transplant between January 1, 2005 and June 31, 2015 with minimal one year follow-up. Patients with history of positive crossmatch or multi-organ transplant were excluded. Patients received anti-thymocyte antibodies with pulse steroid induction (Early five days withdraw) except zero-mismatches who received basiliximab. Patients were placed on steroid-free two drugs immunosuppression regimen. Donor specific antibodies were checked using single antigen beads (One Lambda Inc).
Results: 1978 patient's kidney alone patients were included in the study over a 10.5 years period. Mean follow-up was 4.52 +/2.79 years. 101 patients (4.7%) had pre-transplant DSA (DSA+, MFI> 500) at time of transplant with negative flow cytometry crossmatch. There was an overall increased risk for AR in DSA+ vs DSA− patients (29.7% vs. 18.3%, p=0 0002). Likewise, there was an increased rate of AR in patients with DSA MFI>2000 or class 2 DSA when compared with DSA− patients (38% vs. 15.4% p<0.0001 and 37.5% p=0.0003). Cumulative death censored graft survival was similar with DSA+ vs. DSA− (p=0.13), DSA Strength (MFI>2000 vs. 2000 vs. No DSA, p=0.319) and DSA Class (p=0.007).
Conclusions: Presence of pre-transplant DSA with characteristic of class 2 and MFI strength of >2000 are associated with increased risk of one year acute rejection in kidney transplant patients receiving steroid-free maintenance immunosuppression regimen. However, the higher risk of rejection in this patient cohort did not translate to worse graft outcome in the intermediate term and thus should not be a barrier in the use of steroid-free maintenance immunosuppression or to transplant.

Effects of Music Intervention on Inflammatory Markers in Critically Ill and Post-Operative Patients: A Systematic Review of the Literature

◆ **MICHELLE KITSIS**
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Background: Music listening has been shown to reduce anxiety, stress, and improve patient tolerance of procedures. Music may also have beneficial effects on inflammatory biomarkers in mechanically ventilated and post-operative patients, with subsequent benefits on delirium (by reducing neuro-inflammation).
Objectives: We conducted a systematic review to evaluate the effects of music, and the quality of evidence for these effects, on: 1) inflammatory biomarkers in mechanically ventilated patients; 2) inflammatory biomarkers in post-operative patients; and, 3) delirium incidence or management.
Methods: A comprehensive search (from inception until March 2017) of the literature was performed by a medical librarian. Fifteen studies were selected for inclusion.
Results: In 7 studies, there was a significant decrease in cortisol levels. Interleukin-6 and epinephrine levels were decreased, but a variety of other biomarkers were unchanged.
Conclusions: Music intervention decreased cortisol levels, but other biomarkers were unchanged. Further research on music effects on inflammatory biomarkers, stress and delirium management are needed.

Maternal Thrombocytopenia Associated with Neonatal Alloimmune HPA-5b Antibodies

◆ **KATHERINE KRAUSE**
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Case: A 33-year-old G4P2012 female presented to her OB clinic at 28 weeks gestation with maternal thrombocytopenia to 134,000/microL. Incidental testing revealed maternal antibody against HPA-5b, which is concerning for potential neonatal alloimmune thrombocytopenia (NAIT). The father was found to express HPA-5a/HPA-5b and HPA-1a/HPA-1a platelet antigens. Amniocentesis at 38 weeks revealed the fetus expressed HPA-5a/HPA-5b. However, the child was healthy with a normal platelet count (232,000/microL) at birth. The patient is currently G5P3013 at 33 weeks gestation. The fetus expresses HPA-1a; therefore, the patient has the potential to develop antibodies against fetal HPA-1a. The fetus does not express HPA-5b.
Conclusions: NAIT is a potentially devastating disease that may present with extensive purpura or intracranial hemorrhage. NAIT is a low fetal platelet count due to the destruction of fetal platelets by maternal antibodies. Fetal platelets express a paternal antigen that is foreign to the mother, which stimulates the formation of maternally derived IgG antiplatelet antibodies that cross the placenta. Based on current recommendations, intrapartum treatment with corticosteroids or intravenous immunoglobulin is reserved for mothers with a previous infant with thrombocytopenia, or a previous fetus or neonate with intracranial hemorrhage. After considering the possible adverse effects, this patient is being closely monitored.
Clinical Significance: In deciding whether to perform routine screening, physicians must consider whether the screening test is a sensitive and specific test, the burden caused by the disease, and whether effective treatment is available. Because the screening tests for NAIT are not cost-effective and definitive treatment for NAIT has yet to be determined, NAIT is not currently among the diseases for which prenatal screening is performed. There is a need for a more cost-effective screening test and definitive management for NAIT to prevent the devastating consequences of this disease.

Improved Metabolic and Psychiatric Outcomes with Discontinuation of Atypical Antipsychotics in Youth Hospitalized in a State Operated Facility

◆ **SAMANTHA PARKHURST**
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Purpose: To assess the impact of antipsychotic tapering and discontinuation on measures of metabolic functioning and psychiatric symptom severity in severely impaired youth hospitalized in a psychiatric state hospital.
Methods: The study examined psychiatric and metabolic measures in 67 hospitalized children and adolescents (mean age 10.5; 56 with discontinued use of antipsychotics, 10 with continued use of antipsychotics, and 1 started on an antipsychotic) from admission to discharge.
Results: Upon admission, 56 youth were tapered off of antipsychotic medications, started on other forms of pharmacotherapy (92.9% were started on medications used to treat attention-deficit/hyperactivity disorder), and received evidence-based behavioral programming and were ultimately discharged from the hospital. The mean duration of treatment was 228 days for the discontinuation group and 204 days for the continuation group. Significant decreases in body mass index [BMI; $t(53)=7.12$, $p=0.0001$] and BMI percentile [$t(53)=6.73$, $p=0.0001$] were found from admission to discharge in the antipsychotic discontinuation group. Changes in BMI, BMI percentile, or systolic blood pressure were not found in the group (n=10) who were maintained on antipsychotics. Both groups experienced a significant increase in their Global Assessment of Functioning score [$t(52)=19.98$, $p=0.0001$ for discontinued; $t(8)=5.092$, $p=0.001$ for maintained]. Psychiatric symptom severity scores significantly improved in many subscales relevant to disruptive behaviors and mood disorders for those who were removed from the medications. For those maintained on the antipsychotics, there were fewer changes in psychiatric symptom scores.
Conclusions: Discontinuation of atypical antipsychotic medications in conjunction with tailoring treatment to presenting diagnoses resulted in metabolic and psychiatric symptom improvement among severely impaired state hospital inpatient youth. These results serve as a feasibility demonstration that discontinuation of antipsychotics does not provoke psychiatric destabilization, particularly among disruptive behavior disordered youth.

Simultaneous Labyrinthectomy & Cochlear Implantation for Treatment of Advanced Meniere's Disease

◆ **HENNA PATEL**
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Case: A 48-year-old female presented with severe vertigo, tinnitus, aural fullness, and hearing loss in the right ear. Her one-hour long vertiginous episodes began in 2015 and were associated with nausea and vomiting. At initial evaluation, she demonstrated moderate-to-severe right-sided hearing loss with 40% word understanding. An MRI of the internal auditory canal was performed and was ultimately negative for retro-cochlear lesions. She was diagnosed with Meniere's disease, and was trialed on hydrochlorothiazide/triamterine and a low salt diet. In March 2017, the patient's condition deteriorated; she experienced worsening right-sided hearing loss and debilitating vertigo. She now demonstrated profound deafness (7% correct AZBio sentences) in her right ear, and normal caloric vestibular responses on the left. She elected to undergo right labyrinthectomy with cochlear implantation in July 2017. Postoperative follow-up at 3 months revealed complete resolution of her vertigo and the ability to hear soft whispered spondee words in the implanted ear.
Conclusions: Simultaneous labyrinthectomy and cochlear implantation for Meniere's disease is a relatively novel surgical technique in the management of advanced Meniere's disease. In this case, this technique resulted in resolution of vertigo, improvement of consonant-nucleus-consonant (CNC) monosyllabic words, AZBio sentences, sound localization, and decreased tinnitus.
Clinical Significance: Meniere's disease, or endolymphatic hydrops, is a potentially devastating inner ear disease that affects as many as 150 per 100,000 people in the United States. It is a clinically-diagnosed disease that is marked by hearing loss, episodic vertigo, tinnitus, and aural fullness. In cases of advanced disease with severe hearing loss, concurrent labyrinthectomy with cochlear implantation can cure dizziness and improve hearing.

Bilateral Spontaneous CSF Leaks: Recognition and Repair

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Case: A 60 year-old obese (BMI = 34 kg/m2) female with obstructive sleep apnea presented with chronic bilateral otorrhea. 2 years prior, she had bilateral myringotomy tube placement by another physician for presumed recurrent otitis media. She had daily otorrhea despite topical and oral antibiotics. She had no history of trauma or ear surgery. Temporal bone CT and MRI imaging demonstrated fluid filled mastoid and middle ear spaces with multiple large tegmen defects and temporal lobe encephaloceles bilaterally, consistent with bilateral spontaneous CSF (sCSF) leaks. She underwent sequential middle fossa craniotomies to repair the encephaloceles and skull base defects without complications. At last follow up, she was 9 months and 3 months out from right and left sided repairs respectively, with resolution of her otorrhea and improvement in her conductive hearing.
Conclusions: sCSF leaks can mimic common otologic conditions such as otitis media. When symptoms fail to resolve with conservative treatment, skull base imaging is instrumental in diagnosis. High-risk patients include obese, middle age females with obstructive sleep apnea. Failure to repair sCSF leaks is associated with risks of intracranial infection and meningitis. Surgical repair of sCSF leaks with middle fossa craniotomy allows for repair of multiple skull base defects, is highly effective with a long-term leak rate of <1% and has a low complication profile.
Clinical Significance: sCSF leak is a pathology that presents with conductive hearing loss and otorrhea most commonly in obese, middle aged women. The incidence of sCSF leaks has more than doubled in the past decade corresponding with a rise in obesity. Accurate recognition and repair is important for symptom relief as well as preventing meningitis complications. Currently, middle cranial fossa craniotomy is the main method for surgical repair of sCSF leaks and is linked with favorable outcomes, including low morbidity and fewer complications.

Dynamic Three-Dimensional Mapping of Anterior Cruciate Ligament Attachment Sites on the Tibia and Femur

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Purpose: The purpose of this study was to 1) map the length changes of the MWLFC with respect to various points about the tibial ACL footprint to determine the area that demonstrates the least amount of length change through full range of motion and 2) to identify a range of flexion that would be favorable for graft tensioning.
Methods: Six fresh-frozen cadaveric knees were obtained from screened individuals with no prior history of arthritis, cancer, surgery, or any ligamentous knee injury. For each knee, 3D CT point-cloud models were obtained in succession from 0-135 degrees of flexion. A point-grid was placed on the medial wall of the lateral femoral condyle (MWLFC) and the tibia. Intra-articular length was calculated for each point on the femur to the tibia at all flexion angles and grouped to represent areas for bone tunnels. Normalized length changes were compared.
Results: Areas anterior/distal on the MWLFC increased with increasing flexion, and areas proximal/posterior decreased with increasing flexion. The area about the intersection of the lateral intercondylar ridge and the bifurcate ridge was most isometric throughout flexion as no significant change in ligament length was found throughout flexion. The normalized length changes from the central position of the tibia showed no significant difference compared to the anterior or posterior tibial position.
Conclusions: No area of the LWMFC is truly isometric through flexion. Femoral tunnel placement slightly anterior to the center of the anteromedial and posterolateral bundles was most isometric. Minimal length change occurs between 10-40 degrees, which reflects the range where graft tensioning most often performed. The results of this study provide further support for an anatomic ACL reconstruction.
Clinical relevance: The femoral tunnel location for ACL reconstruction with the least amount of length change through range of motion should encompass the direct fibers of the ACL.

Interferon Stimulated Gene 20 Knock-Down and Differential Transcriptome Profiling

◆ **AZAD NEUPANE**
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Purpose: Interferon stimulated gene 20 (ISG20) is a ribonuclease that can degrade Hepatitis B viral RNA with basal expression and when upregulated by interferon-α (IFN-α). It achieves this by binding to a secondary epsilon stem-loop structure and promoting degradation. Besides the antiviral function of ISG20, it is imperative to discover its cellular functions in uninfected cells, which are currently unknown.
Methods: To accomplish this, two HepG2-NTCP12 (sodium taurocholate cotransporting polypeptide) cell lines were created. A cell line with the ISG20 gene knocked down via lentiviral transduction and a short hairpin RNA (shRNA) control cell line were made first. These two untreated cell lines were then treated with IFN-α for 36 hours to create four distinct cell conditions for the experiment. RT-qPCR and Western Immunoblotting were performed to gauge success of the lentiviral knockdown procedure. RNA was then isolated for high-throughput next generation total RNA sequencing.
Results: We reported that in the untreated condition, 868 genes were upregulated and 1012 genes were downregulated, while in the treated condition 2332 genes were upregulated and 2205 genes were downregulated.
Conclusions: Next steps include performing validation experiments and gene ontology analysis and examining genes of interest one by one to generate novel hypotheses about the mechanism of ISG20 in healthy cells. Learning how ISG20 alters the RNA profile of healthy cells can inform us about whether ISG20's antiviral mechanism of action in other pathogens is via direct action such as binding viral RNA already shown in human Hepatitis B virus or indirect action such as changing host cellular gene expression.

Circulating Unmethylated CHTOP DNA as a Potential Biomarker of β Cell Death in Type 1 Diabetes

◆ **KYLE O'MALLEY**
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Background: Type 1 diabetes (T1D) is characterized by autoimmune-mediated destruction of pancreatic β cells. Identification of biomarkers of β cell death would allow for the early detection of β cell destruction and the possible institution of therapeutic interventions to prevent hyperglycemia. Expanding upon previous studies conducted by members of our group, we hypothesized that CpG sites throughout the human genome may contain differential methylation that are unique to β cells and may enable detection of β cell death.
Methods: We utilized whole-genome DNA methylation arrays to compare the methylation of CpGs in human islets compared to non-islet human tissue, and verified prospective β-cell-specific CpG sites using DNA deep sequencing. We used droplet digital PCR to measure differentially methylated CpG sites in serum samples collected from 43 youth with new onset T1D, 23 first-degree relatives (FDR) of T1D subjects who were autoantibody (AAb) negative, and 8 healthy control youth without AAb positivity as part of a comprehensive discovery approach to validate potential biomarker genes.
Results and Conclusions: Droplet digital PCR analysis demonstrated that circulating levels of unmethylated CHTOP DNA were found to be significantly higher in subjects with new onset T1D. We also observed an elevation of unmethylated CHTOP DNA from serum samples of individuals who are first-degree relatives of T1D subjects, but were AAb negative. In conclusion, our data suggests that circulating unmethylated CHTOP DNA may be a useful biomarker in early detection of β-cell death in individuals with T1D and those with high risk for development of T1D.

Dermatofibrosarcoma Protuberans Imitating Pilonidal Cyst

◆ **SAVANNAH PAFFEN**
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Case: A 68 year-old African American female presented with a 3-year history of an enlarging intergluteal soft tissue mass. Given findings not consistent with pilonidal cyst, an MRI was ordered. The MRI demonstrated a large, heterogeneously enhancing subcutaneous gluteal cleft mass with a smaller lobulated extension, consistent with pilonidal cyst. The mass was then resected in the operating room. Final pathologic evaluation indicated dermatofibrosarcoma protuberans with focal fibrosarcomatous transformation involving peripheral and deep margins. The patient was referred to surgical oncology and underwent wide excision with loop colostomy given positive margins and close proximity to the anus.
Conclusions: Dermatofibrosarcoma protuberans (DFSP) is a rare tumor with an incidence of 4.2 per million in the United States. It is found on the trunk and proximal extremities and is most common in African Americans and people aged 20-59. The tumor has traditionally been more common in men; but, in recent years, incidence in women has increased by 3.2% annually while incidence in men has decreased. In contrast, pilonidal cysts are found on the sacrococcygeal region in young adult men. Risk factors include hirsute nature, obesity, sedentary occupation, and local irritation. DFSP tumors range in appearance from flush to protuberant, solitary to multiple, and flesh colored to violaceous. This variability extends the differential diagnosis. Rarely, DFSP may mimic a skin tag or cyst. However, there is no literature documenting DFSP imitating a pilonidal cyst.
Clinical Significance: DFSP is a rare but important tumor with increasing incidence in women. The tumor tends to locally recur, and fibrosarcomatous transformation, though rare, drastically increases metastatic potential. Providers must keep a high index of suspicion for DFSP in patients with a subcutaneous mass. Biopsy should be used to confirm diagnosis and adequate treatment requires excision with 2-3 centimeter margins.

Atypical Progression of Enteroviral Meningoencephalitis

◆ **PRIYA PARIKH**
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Purpose: To investigate an atypical progression of enteroviral meningoencephalitis.
Background: Enterovirus is a common cause of meningoencephalitis in children. Most children recover without long-term sequelae, but there are predictors of poor outcomes, such as MRI findings as seen in this case.
Case Presentation: A 6-year-old previously healthy female presented with altered mental status after a prolonged seizure and fever. Initial infectious work up was negative, including cerebrospinal viral studies and bacterial culture. After the seizure she experienced residual right-sided hemiparesis and aphasia. Initial MRI showed subtle T2 and FLAIR signal hyperintensity in the left hippocampal tail but was otherwise normal. On day three of admission, repeat infectious work-up along with autoimmune studies revealed positive enterovirus PCR from cerebrospinal fluid. Repeat MRI revealed left cerebral subcortical white matter restricted diffusion and cortical T2 prolongation consistent with her clinical symptoms. Her hospital course was complicated by continued seizures, right-sided weakness, aphasia, and incontinence. She was eventually discharged to the inpatient rehabilitation unit with remarkable recovery, including the abilities to walk and speak. Six months after the initial presentation, MRI findings included significant left cortical volume loss.
Conclusions: This case illustrates at least two important points. First, when clinical suspicion is high, it is crucial to repeat testing for infectious meningoencephalitis as initial tests can be negative early in the disease process. Second, while MRI findings due to enterovirus in brainstem encephalitis are well established, this case illustrates rare neuroradiographic sequela of enteroviral meningoencephalitis.

The Role of Post-synaptic Cell-adhesion Molecules in the Trafficking of AMPA-type Glutamate Receptors

◆ **ASHLEY RILEY**
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Purpose: To investigate the role of neurologin 1 (NL1), a post-synaptic cell adhesion protein that binds to pre-synaptic neurexin, in long-term potentiation (LTP), a form of synaptic plasticity implicated in learning and memory that has been implicated in multiple neuropsychiatric disorders. LTP is dependent on trafficking of AMPA receptors (AMPARs) at the post-synaptic membrane.
Methods: We first generated various neuroligin constructs in which different functional domains of NL1 are mutated. We then prepared primary dissociated mouse hippocampal cell cultures from NL cKO mice and infected the cultures with lentiviruses containing Cre recombinase with either WT NL1 or mutant NL1 constructs. We induced chemical LTP using glycine and measured the resultant increases in surface expression of endogenous AMPARs using immunocytochemistry.
Results: Stabilization of AMPARs during chemical LTP is impaired upon deletion of neuroligin 1, can be rescued solely by the extracellular domain of neuroligin 1, does not require neuroligin dimerization, and is impaired when NL1 binding to neurexin is inhibited.
Conclusions: The trans-synaptic interaction between NL1 and presynaptic neurexins appears to be necessary for the increase in surface expression of endogenous AMPARs following the induction of chemical LTP in dissociated cultures prepared from NL cKO mice.

Use of 3D Printing for Complex Vascular Anatomy in Interventional Radiologic Education and Medical Student Engagement

◆ **JOSHUA SCANTLAND**
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Purpose: To address demand for Interventional Radiologic and procedural exposure prior to residency while enhancing medical student engagement and education.
Methods: Used DICOM CT angiogram files and converted them to stl files and printed them as 3D models with help of staff at Ruth Lilly Medical Library in Indianapolis, Indiana. The 3D models were used for simulation for inferior vena cava (IVC) filter deployment and education on vascular anatomy. A model of an abdominal aortic aneurysm (AAA) was used to discuss methods of repair for such vascular diseases.
Results: Significant increase in medical student engagement and drastic increase in IR student interest group (IRSIG) membership. IRSIG now has 86 members with 63 pre-clinical students. Over 20 of pre-clinical students expressed a "new strong interest" in IR specialty. Many expressed that the simulation and models contributed to their education outside of the classroom.
Conclusions: Use of 3D printed models and simulations is useful in engaging pre-clinical students with limited understanding of IR to a procedurally complex field while providing additional educational value. Trainees of all levels, including residents and fellows, could derive benefit-especially those at institutions without access to live animal labs. Future considerations include increasing simulations for medical students as taught by residents and faculty in IR or other procedurally complex fields. Our team is currently coordinating with School of Informatics and Computing at Indiana University-Purdue University Indianapolis (IUPUI) to produce different materials better suited for simulation and procedural education. Anticipating further investigation on if use of 3D models with simulation helps trainees to gain greater appreciation of angles, visuospatial associations, and changes in physiology of surgically altered anatomy superior to conventional illustrations and didactic lessons.

Fall Prevention: A Multicomponent Analysis of Fall Risk Factors

◆ **NATHAN SCHLEINKOFER**
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Purpose: To determine and evaluate possible fall risk factors and assess current approaches to fall prevention, specifically at the Center for Aging and Health (CAH) located in the Parkview: Randallia campus in Fort Wayne, Indiana.
Methods: Initially 490 patients of the Center on Aging and Health were assessed for this study. Upon applying exclusion criteria, 205 were included in this study. Variables analyzed include: age, sex, diagnosis of neuropathy, parkinsonism, stroke, syncope, depression, compliance with exercise, medication usage, vision impairment, leg weakness, deconditioning, physical wellness and orthostatic hypotension.
Results: Factors observed to increase numbers of falls in patients included: female gender ($p<0.05$), depression ($p<0.05$), poor physical wellness ($p<0.05$), and orthostatic hypotension ($p<0.05$). Other factors individually did not significantly affect number of falls experienced ($p>0.05$).
Conclusions: The Fall Prevention Clinic of CAH was successful in reducing the number of falls for those patients who underwent fall risk assessment and received fall prevention recommendations. It was reaffirmed that for successful prevention of falls, an individualized strategy must be adopted for each patient as only rarely two patients experienced the same combination of risk factors.

Barriers to Hepatitis B Vaccination in Rural Indiana

◆ **ARA SCOTT**

Purpose: Despite free childhood vaccination services for underserved populations, Vigo County completion rates are among the lowest in Indiana. This study examined barriers to Hepatitis B vaccination of infants in Vigo County, and assessed parents' opinions regarding vaccinations and sources of information on the subject.
Methods: The questionnaire targeted parents aged 18 years and older who had children seen at the Midwest Child and Adolescent Specialty Group. Only parents bringing in their children for well child checks were asked to participate, to avoid confounders from other health conditions.
Results: Twenty-three surveys were collected, with demographics closely matching those of Vigo County. Only one participant had not had her child vaccinated against Hepatitis B in the first 48 hours of life, explaining that she did not "sleep around" or "share needles". She planned to vaccinate future children but was unsure whether Hepatitis B was a serious condition. She also felt that too many vaccines could weaken a child's immune system, that children are given more vaccines than are good for them, and that childhood vaccines should be limited to diseases that are very disabling or lethal. All participants agreed that their healthcare provider was a trustworthy source of information about vaccines, but the non-vaccinating parent found the media trustworthy as well.
Conclusions: Based on the only participant not to vaccinate her child at birth, possible barriers to vaccination include lack of education about disease transmission and conflicting sources of information. As the sample size was small, further study is needed to explore these possibilities. A future study might benefit from implementation in a maternity ward to reach parents at the time they are making the decision. A follow-up longitudinal study could determine how many of their children completed the standard vaccination schedule.

Aicardi Syndrome: A Timely Diagnosis

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Aicardi syndrome is an x-linked disorder characterized by agenesis of the corpus callosum, infantile seizures and chorioretinal lacunae. This rare condition which affects 4,000 individuals worldwide may go undiagnosed due to infrequent occurrence. It occurs in about 1 in 105,000 to 167,000 newborns in the US. Nearly all known cases are sporadic. The genetic mutation has not been identified, however it is believed to be located on the X chromosome. Nearly all individuals with Aicardi syndrome are female, therefore the condition is suspected to be neonatal lethal for males.

A 28-year-old G3P2 gave birth to a term female infant at 39+4 weeks. Prenatal ultrasound and fetal MRI showed progressive worsening of interhemispheric cysts and partial agenesis of the corpus callosum. Birth weight and head circumference were above the 90th percentile with APGARs 8 and 9. Postnatal head ultrasound showed cystic parenchymal abnormality of the brain. MRI at 2 weeks showed callosal dysgenesis, interhemispheric cysts, right frontal lobe pericystic interstitial edema, and right frontal polymicrogyria. Aicardi syndrome was suspected after a neurology evaluation at 1 month. A pediatric ophthalmology exam revealed chorioretinal lacunae. At 2 months the patient had episodes of infantile spasms. Video EEG was performed 2 weeks later showing frequent epileptiform discharges arising from the right greater than left temporal regions. Focal tonic seizures episodes were identified. A 5 months physical exam showed delayed development and decreased tone. Radiography showed T10-T11 hypoplasia.

This case demonstrates early recognition features of the rare Aicardi syndrome. Aicardi syndrome has characteristic MRI findings of corpus callosum agenesis and interhemispheric cysts that may be identified in-utero. Infantile spasms begin to occur in the first few months. Chorioretinal lacunae evident on ophthalmology exam is a pathognomonic finding. Early diagnosis is important to prevent the progression of seizures and commencement of appropriate developmental and physical therapy.

Drug-Loaded Mesoscale Nanoparticle Therapy for Cisplatin Induced AKI

◆ **ELIZABETH MERCER**
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Purpose: Cisplatin is a chemotherapy treatment with a dose limiting side effect of nephrotoxicity. It presents as acute kidney injury (AKI) in 20-30% of patients and causes proximal tubular necrosis. Mesoscale nanoparticles, approximately 400nm in diameter, have been found to target the proximal tubular epithelium of the kidneys in vivo. A free radical scavenger drug has been shown to have a protective effect against the development of AKI by reducing oxidative damage in the renal cells. Our hypothesis was that drug-loaded mesoscale nanoparticles would prevent cisplatin-induced renal cell death in vitro. This targeted therapy allows for increased local drug concentration while decreasing systemic side effects.
Methods: Drug-loaded mesoscale nanoparticles were synthesized with a polymer and characterized based on size, zeta potential, and percent drug loading. AKI was induced in normal adult proximal tubule epithelial cells in vitro with cisplatin. The AKI induced cells were initially plated with free drug to assess the effect of the drug. Subsequently, AKI induced cells were plated with the drug-loaded mesoscale nanoparticles. Cell viability was assessed after two days. Delivery time course of the nanoparticle treatment was also investigated.
Results: The results of the study showed that the drug was successfully loaded into 376nm nanoparticles. Free drug was shown to significantly reduce renal cell death due to cisplatin therapy. Both 1.9mM and 3.5mM drug-loaded nanoparticles were found to significantly reduce renal cell death in vitro. Administering 3.5mM drug-loaded nanoparticles two hours before cisplatin or 24 hours after cisplatin significantly decreased renal cell death.
Conclusions: There is a clinical need for a therapy that prevents cisplatin-induced kidney cell injury. A free radical scavenger drug can be loaded into mesoscale nanoparticles and can reduce cisplatin-induced renal cell death in vitro. Future studies will investigate this drug delivery system as a viable solution to treat various renal diseases.

Reviewing Current Ocular Imaging Trends in Traumatic Brain Injury

◆ **OSAMA MUFTI**
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Purpose: To conduct a literature review of published individual and population-based studies to explore current imaging techniques in ocular physiology following Traumatic Brain Injury (TBI).
Methods: Electronic databases utilized in the search strategy for journal articles included Pubmed, Google Scholar and Web of Science. Journal article inclusion criteria were based on diagnostic approaches, and ocular disturbances in TBI. The exclusionary criteria implemented included congenital brain injuries and assessments solely focusing on vestibular aspects of TBI. Key words used in search strategy consisted of TBI, ocular factors, vasculature, diagnostic modalities, OCT, and retina.
Results: Mean global cerebral blood flow was significantly lower in veterans with TBI compared with non-TBI veterans. Several studies on rodents have shown a decrease in the optic nerve diameter and a thinning of the retinal nerve fiber layer following TBI. Direct macular Retinal ganglion cells (RGCs) thinning have also been demonstrated in patients with optic tract lesions and in cases of chiasm compression. Atrophy of the RGC layer is a good predictor for poor visual function, and correlates at the topographic level with the visual field deficits.
Conclusions: No studies have been previously conducted measuring the retinal thickness and blood flow in patients with TBI. Several studies have demonstrated changes in cerebral blood flow following TBI. but its effect on retinal blood flow has never been studied. Similarly, there have been no studies on humans measuring the changes in the oxygen saturation in the retinal vessels following TBI. In theory, using SD-OCT, SD-OCTA, retinal flowmeter and retinal oximetry, one can offer a novel, safe, noninvasive, and comprehensive approach to quantify changes in retinal thickness, retinal blood flow and oxygen saturation after TBI.

Omental Infarction in a Pediatric Patient

◆ **MOHSIN MUKHTAR**
Contributing authors: Riley K

Purpose: Omental infarction is an uncommon cause of acute abdominal pain in pediatric patients, who account for less than 15% of all reported cases. This case report examines the clinical course of a child who was diagnosed with omental infarction and discusses the differential diagnosis in pediatric patients.
Methods: We reviewed the clinical presentation, diagnostic imaging results and clinical course of a child with a probable diagnosis of omental infarction at our institution. We also reviewed all relevant literature pertaining to the differential diagnosis.
Results: A six-year-old girl presented with three days of worsening right lower quadrant abdominal pain. A CT scan was performed and the diagnosis of omental infarction was favored. The patient was managed conservatively and then discharged.
Conclusions: Omental infarction is a rare cause of right lower quadrant abdominal pain in children. Because the clinical history is nonspecific, patients are often misdiagnosed with appendicitis. Since omental infarctions can be managed conservatively, accurate diagnosis is critical and can dramatically change patient management.

Breaking the Cycle of Painful Love

◆ **KRISTEN SWANSON**
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Case: A 16 year old female presented to Methodist ER with severe bruising to the face and neck after being physically and sexually assaulted by her 17 year old boyfriend. The patient had attended two counseling sessions, but admitted that it "wasn't helping." Three months after the assault, the patient came in for a well-adolescent visit and shared her thoughts about the situation. Her boyfriend had been subjected to two months of jail time for domestic battery and had recently been let out of jail. The patient had been contacting the boyfriend via text message and was planning to meet with him. She shared that he had told her that his time in jail had changed him and that he has learned from his mistakes. He wanted to get back with her since he was still in love with her. During the visit, a discussion of the cycle of violence was relayed to the patient as "anticipatory guidance."
Conclusions: A lack of knowledge and supportive measures regarding intimate partner violence perpetuates a cycle of violence and victimization. Changes in behavior at the individual level won't occur without a supportive social environment. Advocacy needs to be continued to persuade policymakers of the importance of primary preventative measures. More programs need to be implemented during adolescence, a period of significant impact and vulnerability. These programs should be provided for not only women, but also men, who can serve as empowered individuals capable of making a positive change. If gender equality can be improved along with better access to programs focused on education at the individual level, then primary prevention has the power to change social norms regarding violence, masculinity, and gender roles.
Clinical Significance: Programs geared toward prevention and awareness of intimate partner violence are key when dealing with adolescent patients.

Anterolateral Ligament Incidence in the Knee of Sus Scrofa Domestica

◆ **GARY ULRICH**
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Background: Sus scrofa domestica – more commonly known as the domestic pig – has served as a respected model for human knees, especially regarding the anterior cruciate ligament (ACL), over time. In 2013, researchers rediscovered the anterolateral ligament (ALL) in humans, originating from the lateral epicondyle of the femur and inserting midway between the fibular head and Gerdy's Tubercle (GT) on the proximal tibia. Due to its anatomical placement, the anterolateral ligament restrains internal tibial rotation. While the anterolateral ligament has been identified in human knees, the question still remains as to whether the domestic pig possesses an anterolateral ligament. Many terrestrial vertebrates across the animal kingdom, including species such as dogs, bonobos, gorillas, rhesus monkeys, tigers, lions, deer, and tortoises, do not possess an anterolateral ligament.
Methods: After dissection, Sus scrofa domestica was found not to possess any indication of an anterolateral ligament in any of the specimens examined. The other structures that were present on the anterolateral aspect of the knee, including the lateral collateral ligament (LCL), tibialis anterior tendon (TAT), and lateral retinaculum (LR), were harvested and tested to determine their biomechanical properties.
Results and Conclusions: The tibialis anterior tendon was found to have the largest average tangent modulus, followed by the lateral collateral ligament, and then the lateral reticulum. The lateral reticulum was found to have the largest average toe region, followed by the tibialis anterior tendon, and then the lateral collateral ligament. The properties of these anterolateral structures, the lifestyle, and the evolutionary path of Sus scrofa domestica likely offer insight into why this species might lack an anterolateral ligament.

Orthopaedic Outpatient Procedures in the Morbidly and Super Obese

◆ **SHREYA VEERA**
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Purpose: Recent studies have explored the relationship between BMI and skeletal injuries indicating that obesity is related to an increased risk of fracture at different skeletal sites regardless of BMD. While it is accepted that a BMI over 35 is indicative of a greater incidence of spine and lower extremity joint injury, the impact of the severity of obesity is unclear. The purpose of this study was to describe differences in injury types in orthopaedic outpatient surgeries based upon BMI classifications.
Methods: Patients with a BMI greater than 30 who underwent an outpatient surgical procedure between 2014 and 2017 were identified from the surgical database at a single institution. The electronic medical records were retrospectively chart reviewed to determine demographic information, reoperation rates, comorbidities, history of bariatric surgery, and Patients were divided into subgroups for analysis based on "super" obesity (BMI >50), "morbid" obesity (BMI 40-40.9), and obesity (BMI 30-30.9).
Results: A total of 6546 procedures (2859 males, 3687 females) with a mean age of 60 and a mean BMI of 37.8 were identified. The most common comorbidities were found to be hypertension (36.4%), arthritis (25.4%), depression (21.8%), and sleep apnea (21.5%). Spine procedures were found to be the most prevalent (56.5%) while shoulder and hand procedures were the least prevalent (18%). Of those who self-reported tobacco use, 48.7% denied any tobacco use, 18.5% were former smokers, and 32.8% currently smoke.
Conclusions: This supports previous findings that obesity frequently contributes to soft tissue damage and osteoarthritis. It is important to note the increased prevalence of spinal, hip, and knee injuries. Future analysis could help identify predictors of injury to aid in development of strategies for bone loss and fracture prevention. These data could contribute to mitigating the substantial health risk and financial costs associated with orthopaedic injuries in the morbidly and severely obese.

Healing of critical-sized bone defects using genetically modified human bone marrow mesenchymal stem cells overexpressing BMP-2

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Purpose: The purpose of this study is to evaluate the osteoinductive potential of human bone marrow mesenchymal stem cells (BMSCs) transduced to express BMP-2 via a two-step transcriptional amplification (TSTA) lentiviral vector in a rat femoral defect model.
Methods: Human bone marrow was harvested from 10 healthy patients (3 female, 7 male), 57.9±11.5 years of age, undergoing elective primary total hip arthroplasty. BMSCs were isolated and expanded in culture and then transduced overnight with a TSTA lentiviral vector overexpressing BMP-2 or green fluorescent protein (GFP). BMP-2 production over a 24-hour period was quantified by ELISA. An established critical-sized femoral defect (6 mm) model was used to evaluate the in vivo osteogenic potential of human BMSCs. The BMSCs were delivered to the femoral defect on a compression resistant matrix. Eighteen athymic nude rats were randomly assigned to one of the following groups: LV-TSTA-BMP-2 transduced BMSCs (Group I; n=10), LV-TSTA-GFP transduced BMSCs (Group II; n=4), and non-transduced BMSC (Group III; n=4). Groups II and III served as controls. The animals were euthanized 12-weeks post-operatively and bone formation was evaluated via plain radiographs, micro-CT, histologic, histomorphometric and biomechanical analyses.
Results: Mean BMP-2 production following transduction was 89.6±10.7ng/24h/million cells. In group I (BMSCs/LV-TSTA-BMP) 9/10 femora demonstrated complete radiological healing at 12 weeks. In contrast, the control groups (GFP and non-transduced BMSCs) demonstrated minimal bone formation at all time points. Volumetric assessment of total new bone formation via micro-CT revealed significantly higher bone volume fractions ($p<0.001$) in group I (26±3.6%) compared to group II (4.7±1.7%) and group III (5.4±2.2%).
Conclusions: To our knowledge, this is the first study to evaluate the use of lentiviral-mediated BMP delivery via human BMSCs to induce bone regeneration. Our results indicate that human BMSCs transduced to express BMP-2 via a TSTA lentiviral vector can induce bone formation in vivo.

Baseline Capillary Blood Flow Correlates with Changes in Visual Function in Open Angle Glaucoma Patients of African Descent

◆ **AADITYA SHAH**
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Purpose: To examine the relationship between baseline visual function and changes in capillary blood flow in open angle glaucoma (OAG) patients of African (AD) and European descent (ED) after 4 years.
Methods: 83 patients with OAG (18 AD, 65 ED) were assessed for capillary blood flow by Heidelberg retinal flowmetry (HRF) and for visual function by 24-2 Swedish interactive threshold algorithm visual field exam using the Humphrey visual field machine every 6 months for a 4-year period. Pearson correlations were used to test for associations between measurements, with $p<0.05$ considered statistically significant.
Results: Baseline superior 10th% was 85.77 (95% CI: 76.73, 95.86) and 78.74 (72.27, 85.78), 25th% was 199.94 (179.39, 222.85) and 177.97 (163.67, 193.51), 50th% was 378.25 (339.37, 421.59) and 341.25 (313.90, 370.99), 75th% was 606.25 (543.31, 676.48) and 551.81 (507.25, 600.29), 90th% was 874.97 (779.41, 982.24) and 807.32 (739.21, 881.71) in patients of AD and ED, respectively. In OAG patients of AD, changes in mean defect were positively correlated with baseline superior 10th% ($r= 0.52$, $p= 0.0259$), 25th% ($r= 0.52$, $p= 0.0239$), 50th% ($r= 0.49$, $p= 0.0374$), 75th% ($r= 0.51$, $p= 0.0275$), 90th% ($r= 0.49$, $p= 0.0387$), leading to a significant difference between race groups (superior 10th%: $p= 0.0254$; 25th%: $p= 0.0240$; 50th%: $p= 0.0353$; 75th%: $p= 0.0271$; 90th%: $p= 0.0467$).
Conclusions: In OAG patients of AD, baseline capillary blood flow are positively correlated with changes in visual function after 4 years.

Striking Enhancement at the Site of Radiation for Nivolumab-induced Stevens-Johnson Syndrome

◆ **KISHAN SHAH**
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Stevens-Johnson Syndrome (SJS) is a rare adverse cutaneous drug reaction characterized by epidermal detachment of <10% body surface area (BSA) with an average mortality rate of 1-5%. The mechanism of SJS is not fully understood. Nivolumab is a monoclonal antibody directed against programmed cell death-1 (PD-1), with immune checkpoint inhibitory and antineoplastic activities.
We present a case of SJS in a patient being treated with anti-PD-1 therapy nivolumab for metastatic squamous cell carcinoma of the oropharynx. This case is unusual because of the severe accentuation with striking enhancement at his prior radiation site and in the cutaneous region with heavier tumor burden from his metastatic disease. This reaction may give insight to the underlying pathophysiology of SJS, suggesting that immune checkpoint inhibitors can activate T-cells to target keratinocytes and that external factors may be involved in creating distinct epitopes for T-cell recognition. We hope this case adds to the body of knowledge in the pathogenesis of Stevens-Johnson syndrome and cutaneous adverse events seen with checkpoint inhibitors.

Artifical Intelligence in Healthcare: Coding an Intelligent Webapp for Pre-visit Patient Interview

◆ **PAUL SHEN**

Purpose: To improve efficiency, cut costs, and increase quality in outpatient visits by autonomously gathering information via a custom designed webapp before the visit.
Methods: We engineered a webapp that intelligently interviews the patient for symptoms, gathers visit specific details, generates a differential diagnosis, and summarizes the information in charting format. The patient would use the webapp before the visit or in the waiting room. The information is then sent electronically to the physician can then more succinctly conduct the in-person interview, better address remaining concerns, and save time charting.

We used the python programming language alongside with the Django web framework. The backend database comprises of relationships between diseases, symptoms, symptom qualities, epidemiology and risk factors. Some of it is compiled from publicly available data from the Mayo Clinic Symptom Checker.
Conclusions: Our webapp holds promise for streamlining outpatient and telemedicine care by augmenting symptom checking capabilities with intelligent information gathering and automatic note generation.

FANCC Prevents Aneuploidy Through its Regulation by CDK1 During Mitosis

◆ **ADAM STEPANOVIC**
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The Fanconi anemia signaling network, which consists of 19 different genes/proteins, operates during interphase and mitosis as a guardian of genome integrity. Inherited germline mutations in these genes can cause a pediatric syndrome known as Fanconi anemia, which is characterized by congenital malformations and predisposition to cancer. Fanconi anemia genes can also be sporadically mutated in certain tumors. Our lab has shown that many Fanconi proteins (including FANCC) localize to the centrosome and spindle apparatus during mitosis and are essential for regulating the spindle assembly checkpoint (SAC). This checkpoint ensures that all of the chromosomes are attached to the mitotic spindle before anaphase begins. Loss or mutation of Fanconi genes results in chromosome mis-segregation, aneuploidy, and multi-nucleation. Our study sought to explore how the interaction between the Fanconi protein FANCC and the master mitotic kinase CDK1 is implicated in regulating the SAC. Using co-immunoprecipitation studies and immunofluorescence microscopy, we confirmed that CDK1 and FANCC interact during mitosis and localize to the mitotic spindle. Using an in vitro kinase assay, we verified that CDK1 does phosphorylate FANCC in vitro. FANCC localization is impaired in cells treated with a CDK1 inhibitor and in cells transfected with a phospho-dead version of FANCC. When FANCC-deficient patient cells are treated with the anti-mitotic drug taxol to challenge the SAC, these cells show a higher degree of multi-nucleation. The SAC impairment of FANCC-deficient cells can be partially rescued by transfection of a plasmid with wild-type FANCC, while transfection of phospho-dead FANCC fails to rescue the cells. These results help us to better understand the signaling mechanisms involved in the regulation of the SAC and could potentially have therapeutic implications by allowing physicians to tailor treatment to the FANCC status of each patient's tumor.

A Multifactorial Severity Score for Congenital Diaphragmatic Hernia (CDH) using Fetal MRI

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Background: The prognostic value of multiple prenatal imaging biomarkers in diagnosis and treatment of CDH is well-established. Our purpose was to combine qualitative and volumetric analysis of various fetal MR biomarkers within a single population and use weighted indices from these biomarkers to calculate a severity score in patients with CDH. This score might then be used to estimate risk of mortality in high-risk CDH patients and to assist in family counseling.
Methods: We retrospectively identified all cases of prenatally-diagnosed CDH at a single institution during 2004-2016. Factors identified on MRI included observed-to-expected total fetal lung volume (O/E TFLV), percent predicted lung volume (PPLV), and spleen, liver, and stomach position. Prenatal factors were compared with mortality. The ROC was optimized for O/E TFLV of 24% for mortality (sensitivity 64%, specificity 82%, AUC 0.72). Analysis was performed using bivariate and multivariate regression methods. Using weighted and normalized coefficients from the logistic regression of mortality, severity scores were calculated. The probability of mortality used to determine relative risk within this population was estimated using the resulting algorithm.
Results: Within our cohort of 41 CDH patients, Mean (±SD) O/E TFLV was 32% ±22%, and survival was 41% (n=17). 48% had major comorbidities. Bivariate analysis identified O/E TFLV (p=0.007) and stomach position (p=0.049) as significantly associated with mortality. Multivariate regression revealed a relative weighting of prognostic factors as follows: O/E TFLV, stomach position, liver position, PPLV, and spleen position. These factors contributed to the probability of mortality results.
Conclusions: Using qualitative and volumetric assessment of various MRI biomarkers in patients with CDH, these biomarkers are valuable collectively when assigned relative weighting, and multivariate analysis appears to stratify mortality. When combined into an algorithm after weighting, they can be used to estimate the probability of neonatal mortality and guide prenatal family counseling.

Factors Contributing to Quadriceps Muscle Weakness after Adductor Canal Blocks: A Multivariate Analysis of 1,085 Primary Total Knee Arthroplasties

◆ **ELLIOTT YEE**
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Background: Adductor canal blocks (ACB) have emerged as the preferred regional blockade for pain control after total knee arthroplasty (TKA) due to quadriceps preservation. The study purpose was to identify (1) the prevalence and (2) factors associated with quadriceps weakness (QW) with ACB use in TKA.
Methods: 1,085 consecutive primary TKAs performed by four fellowship-trained arthroplasty surgeons using identical perioperative protocols were reviewed. Patient demographics; ACB anesthetic type, volume, and concentration; steroid and epinephrine use; and postoperative quadriceps weakness were recorded. QW was documented if the physical therapist indicated quadriceps strength less than or equal to 3/5 (can lift leg/no resistance/no muscle contraction); if the patient demonstrated QW attempting to bear weight, perform short/long arc quads or straight leg raises; or if knee immobilizer was required.
Results: After exclusions for confounds, the analysis sample comprised 1,038 patients. The prevalence of QW was 8.9% (92/1,038). Gender, height, epinephrine use, and dose (mL/kg) were related to QW in univariate analysis ($p \leq 0.061$). In binary logistic regression, independent predictors of QW were dose (mL/kg) and epinephrine use. For every 0.1 mL/kg increase in ACB dose, patients were 1.5 [95% CI: 1.2, 1.9] times more likely to develop QW ($p = 0.003$). Patients who received epinephrine were 1.8 [95% CI: 1.0; 3.3] times more likely to develop QW ($p = 0.032$).
Conclusions: To our knowledge this is the first report of clinically significant QW prevalence with ACBs in TKA. The observed rate of 9% was dependent on anesthetic dose and associated with epinephrine. At lower dosages of ACB per body weight, patients were significantly less likely to suffer QW and gait disturbance. This suggests that dosage should be optimized for each patient to maximize safety, prevent falls and facilitate early discharge in the outpatient setting.

Testing MTM Analogs for Novel Drug Therapeutics in Alzheimer's Disease

◆ **RYAN XU**
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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder, characterized by amyloid-beta (Aβ) plaques and neurofibrillary tangles, without any effective medication. Aβ is generated by secretases, such as β-secretase or BACE1, and β-secretase from Aβ precursor protein (APP). We hypothesize that APP regulation is central to Aβ generation. The transcription factor specificity protein 1 (SP1) plays a significant role in APP and BACE1 regulation. Our rationale is to block SP1 binding by specific drugs: Mithramycin A (MTM) and its analogs. We propose testing MTM and its analogs such as MTM-SDK and MTM-SK in mammalian cell cultures, expecting a non-toxic MTM analog to be a novel therapeutic for AD.
Methods: Different doses of MTM and analogs were tested in two neuronal cultures. Differentiated rat neuronal PC12 and human neuroblastoma SK-N-SH cells were separately treated with differing doses of i) MTM, ii) MTM-SDK, iii) MTM-SK, iv) combination and vehicle control. Further, we tested two additional drugs: Acamprosate and Lithium in neuronal cultures. Endpoints included assaying morphology, cell viability and neuronal proteins. Live cell imaging Incucyte®ZOOM was performed to monitor neuronal changes of treated cells over time. Lysates were collected, cell viability measured, and specific proteins (APP, BACE1 and β-actin) analyzed by Western blots.
Results: Cell viability assay provided a non-toxic dose-range of each drug. IncuCyte® Neurite Analysis revealed significant increases in neurite length and neurite outgrowth with MTM analogs in differentiated neuronal PC12 and SK-N-SH cells. Western blotting showed that expression levels of APP and BACE1 are decreased by MTM and/or its analogs. In this poster, we are not showing the WB data, which we will present in another future meeting.
Conclusions: These results suggest that MTM and analogs are able to maintain/promote neurite length and neurite outgrowth in neuronal cultures. Further research in human iPSCs and in AD relevant animal models is warranted to optimize these drugs for AD.

Screening Mammography Guidelines for Transgender Patients

◆ **DANIELLE YIN**
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Background: Mammography guidelines differ between many leading national organizations and are even more poorly defined for transgender patients, especially those at an increased risk of breast cancer due to hormone replacement therapy. There is limited research and evidence to guide decisions on the best practices for this vulnerable population that faces many barriers, which can lead to missed diagnoses.
Case: In this case, a 61-year-old male-to-female transgender patient presents with no significant past medical history. She has a family history of breast cancer in three of her paternal aunts as well as a sister who was diagnosed with breast cancer in her early 60s. The patient presents for screening mammograms after being over the age of 50 and having been on hormone replacement therapy for at least five years. Her screening mammograms demonstrate the typical progression of breast changes in a male-to-female transgender patient including an increase in breast tissue developed over time. This particular patient falls into the "heterogeneously dense" breast tissue category, which decreases the sensitivity of mammography by obscuring small masses. However, this patient's screening mammograms have been negative to date.
Discussion: Driven by limited data, screening guidelines recommend that transgender women begin annual mammography after the age of 50 if they have any of the following risk factors: estrogen hormone therapy for at least 5 years, BMI > 35, or a family history of breast cancer. In this case, the patient qualifies for annual screening mammograms. Unlike many patients who undergo male-to-female transition, her records provide comprehensive imaging of progressive breast changes during hormone therapy. Understanding the normal progression of breast development in male-to-female transgender patients is an important first step in establishing standard of care in transgender medicine.

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