Insight

INDIANA UNIVERSITY MEDICAL STUDENT RESEARCH JOURNAL

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From the Editor's Desk

To our readers:

August 2020

First, we wish to thank all the authors, IUSM faculty and support staff, our financial sponsors, and the students who make Insight possible. When we started this journal as first year medical students, we did not know, nor did we anticipate, the demands of running and publishing an annual journal while studying and working as medical students ourselves. With your support, we were able to:

- Start and manage an online version of our journal;
- Publish annual print versions of this journal with original IUSM student pieces as well as faculty interviews;
- Obtain recurring financial support from the School of Medicine, program subdivisions, as well as from the Clinical and Translational Science Institute;
- And inspire incoming first year medical students to pursue research endeavors while offering words of encouragement as they start medical school.

This journal was intended to reach all those of the IUSM community, to help students develop a better understanding of not only the scientific process and their future career paths, but also of themselves and the society in which we participate in.

That society now is at a critical juncture in history. We have learned of the widespread effects of the COVID pandemic and the impact it has on minority communities. We have learned of the deep roots of individual and systemic racism that still plagues us and our institutions. However, we have also learned of the impact a few dedicated individuals can have on effecting change. We saw this with our school's White Coat for Black Lives event, where numerous students, residents, and faculty staff marched in solidarity for all those who have suffered from racism. We are experiencing this on a national level as well where countless protests are becoming catalysts for long-lasting systemic change.

For this reason, as we step down as Editors-in-Chief and move on to the next chapter of our lives, we have hope that our collective futures will be all the better.

"*Never doubt that a small group of thoughtful, committed, organized citizens can change the world. Indeed, it's the only thing that ever has.*" - Margaret Mead

Sincerely,

Honglin Xiao
Editor in chief
Class of 2021

Monica Cheng
Editor in chief
Class of 2021

We extend our deepest gratitude to Anne Nguyen, Dr. Brittney-Shea Herbert, and the Indiana Medical Student Program for Research and Scholarship (IMPRS) for their support and guidance since the founding of this journal.

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

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insight

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In This Issue

From the Advisor >>

RICHARD GUNDERMAN

Richard Gunderman, MD, Ph.D. is the Chancellor's Professor and John A. Campbell Professor of Radiology, and the faculty advisor of Insight Medical Student Research Journal.

The Woman Who Opened America's Eyes to Dehumanization

She came from a family of 13 that included two of the most famous men in America, one of whom lived and worked for a decade in Indiana. The mother of seven children herself, she also managed to write 30 books. One became the best-selling American novel of the 19th century and did more than any other to open the eyes of Americans to the blight of slavery's dehumanization. President Lincoln is said to have greeted her by saying, "So you are the little women who wrote the book that started this great war." Her name, of course, is Harriet Beecher Stowe, and her book is "Uncle Tom's Cabin."

Physicians in training need to know Stowe and her book. At a time when options for public service for women were highly limited, she rose to become one of the most influential voices in American history. She did it not through wealth, fame, or political office, but simply through the power of words. And she told that story not for her own benefit but in service to oppressed peoples and an entire nation sickened by a corrupt and corrupting institution. Her story offers inspiration to young physicians who seek not only to care for sick patients but also to help heal our society.

Stowe

Stowe was born in Connecticut in 1811, the sixth of her parents' 11 children. Her father was the great preacher Lyman Beecher, who served as president of Lane Seminary in Cincinnati. Her brothers included Henry Ward Beecher, at one point perhaps the most famous person in the United States, whose services in rousing support for the Union causes in the Civil War Lincoln regarded as essential. Henry Beecher was also the first pastor of Second Presbyterian Church in Indianapolis. Several other siblings also rose to prominence, including her sister Catherine, who ran a female seminary that Harriet attended.

At 21, she moved to Cincinnati to join her father. Her 18 years there profoundly shaped her life. She met her husband, seminary professor Calvin Stowe, and they were married in 1836. Just across the river from slaveholding Kentucky, Cincinnati was a boom town teeming with escaped slaves and bounty hunters. Her father's seminary hosted debates on slavery, which prompted such ferocious attacks by those fighting the abolition of slavery that he prohibited further discussion of the topic, sparking an exodus of students to the newly founded Oberlin College.

Calvin and Harriet Stowe were staunch opponents of slavery and even hosted multiple escaped slaves in their home, as part of the Underground Railroad. In 1850 they moved to Maine, where Calvin had accepted a faculty position at Bowdoin College, and during that same year Congress pass the 1850 Fugitive Slave Act. The law required that even slaves in free states be returned to their owners and made the federal government responsible for doing so. In effect, the law seemed to abolitionists to transform the United States into a slave nation, and the Stowes were horrified.

While the Fugitive Slave Act was an important factor in Stowe's decision to write her most famous book, another was the death of her son, Samuel Charles Stowe, the year before. Known to the family as "Little Charley," the boy died during a cholera epidemic. Writing to her husband within just two days the event, Stowe described the scene of the boy's death:

> *My Charley, my beautiful, loving, gladsome baby, so loving, so sweet, so full of life and hope and strength, now lies shrouded, pale and cold, in the room below. Never was he anything to me but a comfort. He has been my pride and joy. Many a heartache has he cured for me. Many an anxious night have I held him to my bosom and felt the sorrow and loneliness pass out of me with the touch of his little warm hands. Yet I have just seen him in his death agony, looked on his imploring face when I could not help nor soothe nor do one thing, not one, to mitigate his cruel suffering, do nothing but pray in my anguish that he might die soon.*

"Uncle Tom's Cabin"

Instead of giving in to despair, Stowe vowed to draw on her suffering for the benefit of her country. She wrote, "Having experienced losing someone so close to me, I can sympathize with all the poor, powerless slaves at the unjust auctions." She wrote to the editor of an anti-slavery journal, indicating

that she planned to compose a story that would evoke the sympathies of readers for the plight of the enslaved: "I feel now that the time is come when even a woman or a child who can speak a word for freedom and humanity is bound to speak."

She published the first installment of what later became the book, "Uncle Tom's Cabin," in 1851, and further installments appeared on a weekly basis for nearly a year. When published as a book, it immediately established itself as a runaway bestseller, with purchasers snapping up tens of thousands of copies per week. The book sold even more briskly abroad, where in Britain alone more than a million copies were purchased. Translated into many languages, "Uncle Tom's Cabin" is often said to be the second-bestselling book of the 19th century, after the Bible.

Subtitled "Life among the Lowly," the book profoundly shaped attitudes toward slavery and, as Lincoln's remark suggests, set the stage for the Civil War that would end it permanently. In it, a Kentucky farmer facing mounting debt feels compelled to sell two of his slaves, one of whom is the married father Uncle Tom. While onboard a riverboat to the slave market, Tom befriend a little girl, Eva. When she falls into the river, Tom saves her, and he is purchased by her grateful father. After two years with the family, Eva dies, but not before she shares a vision of heaven and universal brotherhood.

Before Eva's father can free Tom, he is killed, and his wife sells Tom at auction to a cruel plantation owner named Simon Legree. When Tom refuses to whip another slave, Legree tries to break his deep religious faith, almost succeeding. But Tom has two visions that renew his belief. Ordered to disclose the whereabouts of two escaped slaves, Tom refuses, and Legree orders his death. As Tom is dying, he forgives the two men who have killed him. Awed by what they have experienced, the men convert to Tom's faith. Just then, the Kentucky farmer's son arrives to buy Tom's freedom, but he is too late.

Although there is nothing Tom's former owner's son can do for him, he resolves to have no further truck with slavery. As he sets his slaves free, he vows:

> *It was on his grave, my friends, that I resolved, before God, that I would never own another slave, while it is possible to free him; that nobody, through me, should ever run the risk of being parted from home and friends, and dying on a lonely plantation, as he died. So, when you rejoice in your freedom, think that you owe it to that good old soul, and pay it back in kindness to his wife and children. Think of your freedom, every time you see Uncle Tom's cabin; and let it be a memorial to put you all in mind to follow in his steps, and be as honest and faithful and Christian as he was.*

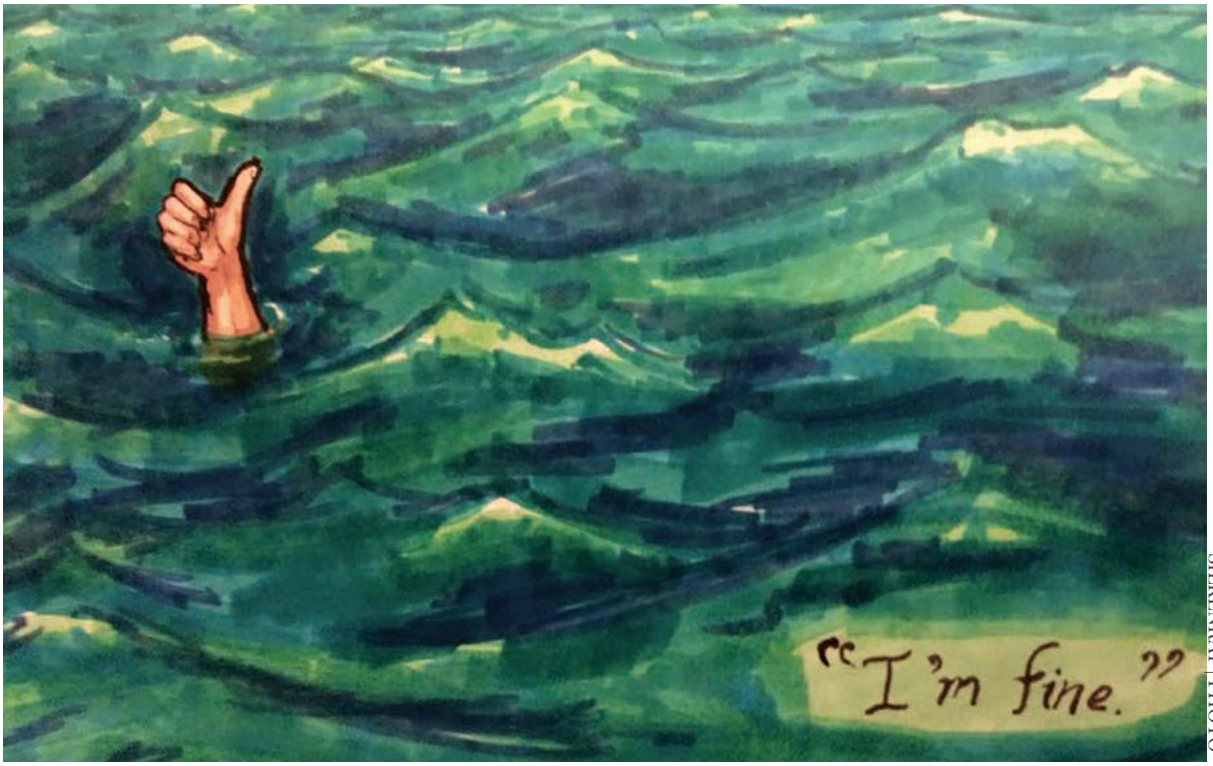
Stowe's Lessons

Stowe managed to exert more influence over American public opinion than any previous woman in American history. And she did it with words – words shaped and energized by her own experience. She drew on her sense of moral outrage over the treatment of slaves she had witnessed, as well as her heartbreak over the loss of her beloved Charley, resolving that he should not die in vain and that some good should come of her grief. Physician-advocates, too, need to look deep within themselves and their life experiences for wellsprings of inspiration and sustenance.

Stowe dramatizes the evils of slavery in a way that tugs at the heartstrings of readers, an approach that physicians seeking to build better communities neglect at their peril. Physicians sometimes suppose that only scientific principles and empirical data can be trusted, but when it comes to the art of persuasion, appeals to emotion are equally important. Reams of tables, charts, graphs, and diagrams may change a person's understanding, but it is often a well-told story that proves most memorable and most likely to summon others to act.

Stowe, deeply moved by Charley's death and horrified by the Fugitive Slave Act, decried the evils of slavery by cultivating her readers' sympathies for the plight of the enslaved. Regardless the color of his skin, Uncle Tom is a transparently noble human being, a person of deep faith and principle who is prepared to sacrifice himself for the sake of others. Stowe invites readers to see themselves in the stories of separated families, to imagine how they would feel in such circumstances. In seeking to build better communities, physicians too need to draw on wellsprings of indignation and sympathy.

While the rights of women in Stowe's day were highly constrained, she believed that if slavery were to be banished from the land, it would require their concerted efforts. Men owned the property, held public office, and fought the battles, but perhaps the most important victory to be won was in the hearts of wives and mothers everywhere. Once they felt for themselves what it meant for a family to be torn apart, no woman could fail to recognize the inherent evil of slavery. Likewise, for medical advocacy to thrive, physicians must see beyond formal power to the real sources of moral authority.



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The Emotional Plight of the Medical Student

An introduction to mental health struggles and to the necessity of system-wide changes.

BY LUCAS MORGAN AND NICHOLAS HEITKAMP

Studies reveal a high prevalence of mental health struggles amongst medical students; levels of anxiety, depression, and general distress are significantly greater in U.S. and Canadian medical students compared to those of the general population and age-matched peers by the later years of training.[1] In a larger context, the global pooled prevalence of clinically-significant anxiety for medical students is 33.8%.[2] Global depression and/or depressive symptom prevalence is at 27.2%, with suicidal ideation present in 11.1% of all med students.[3] While our conversation will revolve around U.S. students, it is important to realize that the issue is universal.

A question comes to mind: are the students entering medical school already suffering in their mental health? Brazeau and her colleagues would suggest not – that compared to matched college graduates, matriculating medical students in the U.S. have higher scores on quality of life measures, as well as fewer symptoms of depression.[4] Thus it would appear that there is a correlation between medical school and distress, with few solutions to confront the issue.

Many medical schools have fantastic advertisement for mental health services; they are encouraged to "(i) provide better links between the university and external mental health providers" and to "(ii) increase students' awareness of existing support services within and external to the university".[5] While such encouragement is incredibly valuable, as is supportive resource availability, why do we seek to mitigate the result rather than neutralize the problem? It's like treating headaches – if they are consistent and distressing, we focus on prophylaxis, not just abortive therapy. So, let's focus on the sources of anxiety, depression, and distress in order to provide prophylaxis. There are many things within the medical education program which are integral and may be less conducive to alterations, but we should seek both acknowledgment of the flaws and efforts of change.

A Source of Stress

Yerkes and Dodson, as early as 1908, realized the limiting nature of stress on performance (**Figure 1**).[6,7] There is an obvious decline in productivity at a certain level of anxiety, demonstrated in both mice and the slightly more sophisticated species, humans. Medical schools promote the mental health of students, yet continue to perpetuate the culture of competition and perfection. The high rates of anxiety demonstrate that students are being shoved to the right side of the Yerkes-Dodson bell curve for unnecessary reasons, which are discussed in the following section. It seems that many students are stressed beyond the optimal performance peak, and carry-over effects may influence the efficacy of practice as a resident and physician.

In response to grievances with the system, students hear counters of "I know it's tough - we all have to go through it." The intensity of med school is treated as a rite of passage. But why should emotional lability be a required part of the curriculum? Medicine comes with its own humanitarian emotions, such as dealing with loss and with responsibility, but there are avoidable stressors in the medical school curriculum, including 1) excessively challenging academic measures, 2) subjective evaluations from preceptors, and 3) minimal control over schedules.

Curricular Issues

On Evaluations

Would you rather your doctor have spent time learning how to please their preceptor in the 3rd year of medical school, or have spent time learning the material and interacting with patients to better their future practice? Med students resort to chasing an evaluation and are distracted from key material and clinical skills. Yet it is for good reason – up to 50% of their final grades are dependent on these evaluations, and grades play a role in competitiveness for residency placement.

Furthermore, what merit the evaluations hold is dissolved if some evaluators are tougher than others. They become an arbitrary assessment, based on where the medical school places the student for a rotation and what physician is on duty that month. In addition, not all preceptors are the ideal model whom medical students should be looking to for emulation and guidance, thus what is their authority in evaluating students? There is much left wanting in the evaluation system.

On Academic Measures

Med students tend to have type A personalities, or are at least high achievers. The standards of medical school exams/assignments often curve toward the student with exceptional performance - not simply the well-prepared, hardworking student who has all the qualifications of a future physician. Therefore, averages are often low on assessments. While this may be intended to motivate the student and to encourage improvement, for most students, it has the opposite effect. There is either emotional distress or annoyance at the seemingly impossible standards. Feelings of inadequacy and/or shock yield an immediate mental barrier, which is not conducive to student learning.

Some grading systems use a scale that includes the gambit of 1st-4th year expectations, with the assumption that students will improve steadily over the course of their schooling and that they will be satisfied to see a score in the range of their year's expectations. However, as high achieving individuals, medical students push themselves to get top scores. While this may not be the intention of the grading system, the conclusion is the same: students are anxious that they are not obtaining the best results.

On a more specific note, one grading issue involves the history and physical documentation. There is such a range in severity of grading, and again, as with evaluations, a student's final grade is dependent on who they happen to have marking their documentation. The scores become arbitrary, especially when there is such grand variation in the characteristics and quality of practicing physicians' notes.

On Autonomous Control

A simple conundrum, though tough to fix, is the lack of control that some schools allow students in deciding their schedules. The first two years are fairly regimented, with little choice for the types of classes and minimal exposure to clinics/hospitals. Students must then zoom through 3rd year rotations (many of which are core/required) and are expected to find a career path, with little time for autonomous exploration. Yes, shadowing is a possibility, but the amount of time for that amidst studying and clinical duties is minimal.

A New Model

A state-wide study in Florida looking at the stressors of medical students found that, in addition to concerns over time management, finances, and health, students were also concerned about medical school administrative failures, lack of assistance with career planning, and assessment-related performance pressure.8 As Hill and her colleagues expressed so well, "though individually focused interventions have demonstrated some success, medical students self-report stressors that may be better addressed through system-level changes".[8]

St Louis University School of Medicine, in an effort to institute such system-level changes, created a model that included a pass/fail system for pre-clinical courses, reduction of contact hours and unnecessary detail, and longitudinal electives for first and second year students which allowed them to explore their interests in addition to completing required coursework.[9] The school also established learning communities (service and advocacy, research, global health, wellness, and medical education) with a combination of passionate faculty and students that investigated opportunities for education and outreach, allowing for more autonomous expedition of the medical world.[9]

In further rounds of change, the school 1) implemented a resilience and mindfulness program (just 6 hours over the semester) to address cognitive distortions, cultivate mindfulness, and diminish stress, and 2) reduced the amount of performance information given to students, by only showing the median score and 75th percentile of each exam. Lastly, the med school dean instructed anatomy professors to create a test with a higher mean score so that students would

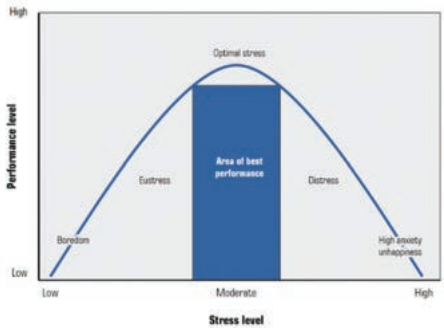

Figure 1. Depiction of Yerkes-Dodson law.

feel less at risk of failing.[9]

Data analysis revealed improvement in depression and anxiety levels of medical students with the new curriculum compared to the old, but was limited in its applicability due to a lack of comparison groups and longitudinal measures.[9] That being said, these alterations appear to be the promising start to a new and improved medical education system.

Discussion

There are many issues with current medical education; evaluations, grades, and lack of schedule control are amongst the most prevalent. In observing the alterations made by St Louis SoM, we see improvements to the system that may benefit the mental health of medical students. With this in mind, we have considered potential implementations based on the most pressing issues, some of which mimic the St Louis model.

On Evaluations

Preceptor evaluations are necessary to assure that a student is well-rounded and is able to interact empathically with patients - to build rapport and trust. However, the worth of the evaluations makes their quality and honesty all the more important. We suggest a scaled score based on the trends of each preceptor's evaluations; some tend to score students high and some low, so a balance is required. In addition, a more rigorous screening of preceptor caliber must be implemented, based on teaching skills, quality of patient interactions, and willingness to participate in student learning. Schools should not enroll someone as a preceptor simply to have enough preceptors - this is unjust for students' education and their futures.

On Academic Measures

As mentioned, there is often a scale to assess performance which includes a range of expectations for all 4 years of medical school. The simple question is, why do we need a scale such as this? Why not create a separate scale for each year? In other words, assess 3rd years with a scale for 3rd years. We assess whether students are where they need to be for that year, in the grand scheme of progress.

As for tests and quizzes, a simple and effective way to combat mental health challenges for students is to write slightly more straightforward assessments with intention to raise averages. The effect is the same - students are stratified based on knowledge and preparation. Yet the numbers are less powerful in yielding distress. This is not a way to "coddle" students; these are intelligent women and men, and mental health is a pressing issue in their world. If there is resistance to altering assessments, professors should, at the least, consistently reinforce that students are not always expected to be in the 80s, 90s, or 100s - that the tests are intentionally created to push students' learning strategies.

The issue of variability in note assessment is more difficult to solve. Each physician was trained differently and has their own interpretation of what notes should look like. One solution is to have more standardized grading, with fewer physicians assessing the notes and each one given the agreed-upon expectations of what a note should look like. Another solution is to create an elaborate, standardized rubric that mentions all key components. This may involve specifics, such as "includes comment on rhythm and rate of heart in cardiovascular physical exam." With a laid-out rubric, there is less room for preceptor interpretation.

On Autonomous Control

Lack of control yields anxiety. More control over schedules allows time for students to find what they enjoy; there is less rush to "figure everything out." Our suggestion is to offer more clinical time, in areas of the students' choice, during the first 2 years of school. This could be something as simple as reserving 2 hours each week for "career exploration," with administration helping to find community physicians for exposure to specialties. Our second suggestion is to allow more free time for 3rd year electives. For example, instead of having just one month (which may also be available as a vacation), protect 2 months during the year for electives amongst the required clerkships.

We have a few suggestions for the redistribution of time during medical school's first two years to allow more clinical exploration. Firstly, for schools that do not already, the anatomy course material should be integrated into systems-based courses (i.e. cardiology, neurology, etc.); the information will be more applicable and memorable in the setting of clinical problem-solving. This alone will free up time for more electives, and will minimize anatomical detail that students will likely not use in their careers. Secondly, much of the time in clinical foundation courses can be streamlined. The curriculum of such courses can allow autonomous exploration and focus on identifying interests in addition to mastering clinical skills.

Conclusion

The journey to become a physician is a difficult one, with long hours of studying, minimal autonomy, and numerous assessments. The end goal is to be a compassionate, well-informed, and hard-working provider; the medical school environment often impedes students from doing so, by chipping away at mental health. Administrations and the education system as a whole must be aware of student struggles and work to implement curricular changes that will shape a more empathetic, healthy, and content student.

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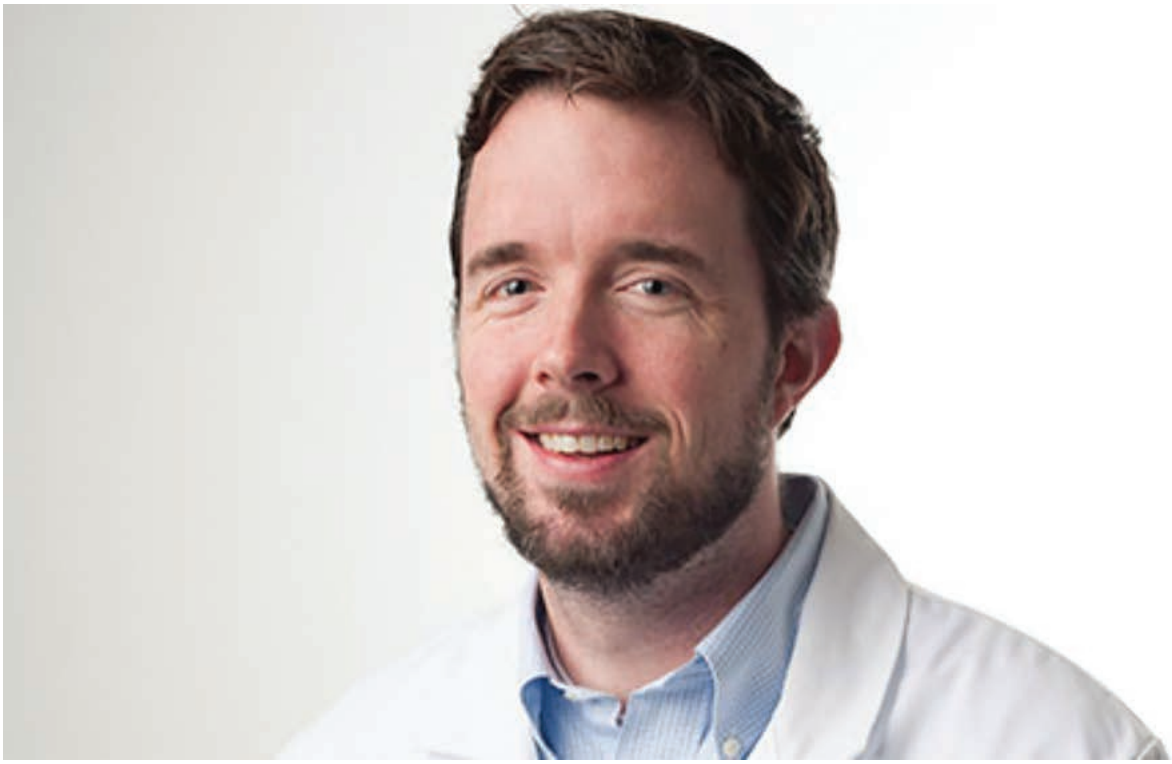
Lucas Morgan and Nicholas Heitkamp are fourth year medical students. Morgan is an aspiring child neurologist, and Heitkamp is interested in pursuing pediatrics. All opinions are their own.

Creating the Class He Would Hav



WILLIAM G. CARLOS | PHOTO

BY NEETA PATWARI

It's rare for medical students to agree much on anything, much learning. One exception seems to be Pulmonary Grand Rounds. In 2019, 89.5 percent of students across the state found that pulmonary ground rounds (PGR) either highly or very highly required higher order thinking skills. Almost 79 percent believed that PGR hit the perfect note between board preparation and clinical experience. That begs the question, what is the respiratory course at IU doing in order to catch such praise and what can other courses do to continue this trend.

In order to answer this question, Neeta Patwari sat down with Dr. William Graham Carlos III, Chief of Internal Medicine at Eskenazi Health and the creator behind the pulmonary ground rounds on his inspiration behind the course, changes in medical education, and his opinion on technology's role in future medical education.

Neeta Patwari: What inspired the idea of teaching respiratory in a grand rounds style?
William Graham Carlos: So I was asked to take over the respiratory teaching initially for just the Indianapolis campus and I was honored and thrilled to do that because I love to teach. So as I sat down at my desk, I really truly thought about if I were a student right now in the second year class, how would I want it to be when I was a student here. And I remembered how hard it was to try to memorize all the information and then I always struggled both in seeing some of the clinical application for some of the stuff I was being asked to learn but I also struggled with putting it all together because there would be a lecture on pharmacology and a lecture on physiology and then there be clinical lectures.

And I just wish they could all be together. And so this dream was that I could learn respiratory, pharmacology and physiology in the context of a clinical case with everything together at the same time so I could see the relevance of why this drug matters for this disease because of this bit of pathology and this physiology. So that was the original inspiration bring everything together at once for learning.

NP: How have you seen a change in medical education from when you were a student to now?
WGC: I have seen some shifts. For example, I've seen more of an emphasis on small group non-didactic style teaching. I have seen students go from studying off of transcribed notes, which

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is the way I studied as a student because we didn't have lecture recordings. There weren't very many board review books back then too. Now, students are embracing online learning and watching videos at two and three times speed and rushing the content. I know that students are adapting to the challenges of being a student and I feel like we need to adapt with our students by leveraging video technology and being really good about engaging students with technology and with board relevance and keeping an emphasis on how this [material] is clinically relevant as well.

NP: Did your education involve a lot of physical textbooks and transcribing from that or transcribing from lecture?
WGC: Yes, we had both. And we also had Harrison's textbook of Internal Medicine. I remember trying to study and read about adrenal insufficiency and just being overwhelmed flipping through the pages. Now, I have a smartphone and I can look up adrenal insufficiency and have my answer in seconds. I find that in our day and age of medicine, I think the equality of accessing quality information and identifying what is reliable to use and take care of patients is equally or maybe more important than memorizing the key components of a particular disease. I don't memorize doses of medications anymore because the EMR helps me through it. If I've forgotten something I now can look it up instantly. We used to actually go to the library and look stuff up like literally. We didn't have up-to-date. We didn't have the electronic resources that we have now. That's definitely changed as well.

The amount of information that you guys have to learn has also grown and I worry about the amount of stuff that we now have to teach you about. A great example in my field of pulmonary medicine is all these tumor markers. We didn't have and thus, didn't need to know about them way back when. Now, you have to remember ALK mutations and EFGR mutations in lung cancers and why they're important. I don't know that we have subtracted the stuff that's no longer relevant as much as we should have in order to make the amount of information coming at you appropriate. I need to do a better job with that too.

NP: Different professors have different ideas on outside resources and board material for studying. Do you have an opinion?
WGC: Yeah, so I buy them all and I make sure that I'm covering what's in them. I've written letters to some of the officers when I found some errors in those books actually, but I embrace it. I think that they present the information succinctly and in ways that help you remember them like in a mnemonic or a picture in a sketchy. It just helps you remember things deep in your hippocampus. So whatever students are doing to learn the information, I am all for. I embrace it and welcome it.

NP: Do you have any concerns about some of the ways the material is presented?
WGC: My overarching concern is that it seems a tremendous focus of the first couple years of medical school leading up to step 1 is just memorization, and I wish it was more application. When I work with third and fourth year students, I'll ask them questions that were objectives from class in second year that I knew were clearly presented and clearly stated, and they'll have forgotten the information. And that's just the way the brain works. There has to be a relevance for it to stick. So I believe learning should be in the context of deliberate practice where you're taking and applying the information. That's why there seems to be more of a push towards small groups style learning.

In pulmonary grand rounds, what I've tried to do through using engagement questions and Top Hat questions is to achieve the same goal of practice and relevance by having students ask questions and answer questions in class.

NP: If you could change anything about IUSM curriculum what would you change?
WGC: I'm biased in my answer but I feel like after three years of multi-campus live stream pulmonary grand rounds, we have

WILLIAM G. CARLOS | PHOTO

accumulated enough feedback from students and have made enough changes that I recognized the students really like this style of learning that they're not afraid to participate online as long as they have the ability to ask and get their questions answered. The style that we use enables me to hand pick the panelists in the discussion, so I know that the content delivery is strong at each campus. And so I like this format of engaging online learning coupled with small group application exercises. So I think it's a both and situation.

I know from statistics that didactic PowerPoint lectures are often not well attended for various reasons. But after pulmonary grand rounds through what we saw on top hat and our engagement data, we had over two-thirds of the class of 2022 this past fall zoom in for a non-mandatory session live. So I feel like we figured out it out. It's hard to really figure out what are the hooks to get students to engage in class. Make it high-quality make it relevant make it efficient. Make it fun. Make it must-see TV if you're zooming in.

NP: I know in terms of students that students at other campuses sometimes feel the material is presented between the different campuses in a disjointed manner and I'm sure it was a similar situation when you were a student. Is there anyway, you can think of that allows us to bridge the gap between the nine campuses?
WGC: Yeah, so that was one of the great things about the way we did the pulmonary grand rounds is that it was the same professor for all 9 campuses. Everybody was running the same stuff the same way at the same time and I know the students highly value that. I asked a question at the end of Indianapolis Grand rounds and there were about 200 students who responded. The question was "was it worth it to only have one live session at your campus and have the other eight live stream in order to have a an equivalent experience across all 9 campuses in this course?" And we got I believe it was 190 responses and 189 were yes, and one was no. So 99.9% of the class says yes, there is value in having us all learn the same material from the same doc in the same time. So to get to there we need to identify professors who are at each site who are great at whatever topic it is that needs to be learned by the whole school and get them in front of the live stream so that the students from all over the state can benefit from their teaching methods and style and what they have to share. It's also nice to have as we did one professor who has a top of the mountain view and is able to see what is repetitive information and what's new information so that you're not teaching in silos. And then you have that big view.

Finally, it's great to feel as a student, that you're not missing anything. Medical students are all very driven and worried that something is given a different emphasis in one campus because it might be on the exam or something is explained more clearly and another campus that would enable the students to understand it better and memorize it better. And that creates anxiety, and anxiety increases cortisol levels and cortisol stresses people out and we want it to be stress-free. So having one talk across all 9 campuses or one discussion is great. Then when it comes to the smaller groups, I don't think students freak out as much because that's just application and there is usually an answer sheet and the experience can be more organic in that regard. So yeah, I think you're onto something with the different campuses and the worried students have about disparity between them.

WILLIAM G. CARLOS | PHOTO

NP: Compared to the way you and your colleagues have learned medicine, do you think there has been a shift in how the material is presented? What are some aspects from your education and what would you have wished you would have had when you were studying?
WGC: Well, I studied off of transcribed lecture notes and we paid a fee to one of the classmates to type up their tape from a cassette tape player recording of the lecture. So, the student would sit in the front row, type whatever the professor said and then sometimes he would couple that with like a printout of the slides. Sometimes you didn't have that. For example, gross anatomy was taught with an overhead projector and colored markers drawing on plastic overhead projected images without a recording.

So imagine what that would be like to try to learn Anatomy with no visual.

You had Netter and you had a transcript and you had the anatomy lab. So it forced me to spend a lot more time in the anatomy lab with the cadaver.

The library and having to look stuff up on clinical rotations brought us together as a team when we were all trying to figure out the answer to a question. I miss some of that.

I've noticed that the amount of resources, podcasts, things online is so huge that it is hard for student to figure out what resource they should be using for each course and each question. Back in the day, you didn't have all of these different resources. It was this or nothing. So that maybe is a new challenge for students that didn't exist when I went through.

Lastly, I'll say that just using electronic medical record has been a huge game changer. We used to have to write out our notes and order on paper and it would take much longer. So nowadays, we should be able to leverage technology to use more time for teaching moments. At the bedside with an ultrasound, looking at the heart, learning aspects of the clinical exam. But what I've seen instead is that the EMR has caused more students, residents and faculty to spend more time in front of a computer, typing notes, looking stuff up, answering questions, and doing transfers and discharge summaries. So that's a challenge both ways. They didn't exist when I was a medical student.

The last thing I'll say is that Step One has changed. Because the applications for residencies have gone sky high, residency program directors need metrics to screen students. And they cannot look at 10,000 applications. So, they set a Step One cut-off line. Which is unfortunate because I believe it causes a lot of medical students a lot of anxiety and grief. And it causes residency programs to miss fantastic applicants.

I would, if I were in charge, give students a cap on the number of programs that they can apply to. With the idea being that number one, you would be more likely to go to the programs you apply to. Then I would do a secondary match or a modified version of the way they do scrambling now to fill the remaining spots. I hope that cutting down the number of applications that residency programs get each year will afford them more time to be intentional with their screening and avoid setting this hard cut line that creates so much of this anxiety over Step One and casts a shadow over the first two years of medical school. I have had countless students complain about hearing stories about patient care during first and second year and professors talking too long about clinical things that may not appear on step one but are immensely clinically relevant.

While these students embrace hearing more about what's its like being a doctor, they are worried that the amount of information that is coming at them is so huge, that if it not relevant to step one, they don't have space for it in their brain. And they don't want to spend time on it. I think that's a travesty because you really do need to know more than what is just one step one. But unfortunately, that other stuff you need to know doesn't count in the same way that step one does. It will pay off when you are on your clinical rotation third and fourth year when you've learned and heard more clinically relevant things. So, that the other big change since I was a medical student: this huge emphasis on step one.

NP: Other doctors have mentioned buzzword culture for medical students where they remember four key words. Was that also a thing when you were a medical student?
WGC: I don't remember it a lot like that. We had a small book at the time called Surgical Recall, it may still be published. Surgical Recall would have things on it like Beck's Triad, and Light's criteria and memorizing things in three words. Or common associations like parakeet and lung problem equals psittacosis and making those connections. I think I use a little bit of that style in my teaching. In pulmonary grand rounds in South Bend, we did a lot of buzzwords. Legionnaires, you think hyponatremia, diarrhea, and pneumonia, and you put it together. I find that this way helps remember things through association.

The problem with buzzwords is that it doesn't help you apply things. So, I think you need both. Both strategies and tools in order to memorize such as mnemonics but you also need to try and apply those things to a case in order to achieve a diagnosis or start the right treatment.

NP: For future medical student classes, you and other course directors have talked about implementing changes from student feedback, class feedback, LCME recommendations. What do you think the future of technology in medical education will look like in five to ten years?
WGC: I believe artificial intelligence is coming with the ability of computers and systems to make diagnoses and put things together. But I think that the future of medicine will always have to have great emphasis on humanism, because a computer cannot replace a touch or an encouraging word. It might be able to help a surgeon to remove part of a prostate but it cannot talk the patient into having part of their prostate removed.

So, I'm hopeful that as AI helps the information overload that we have right now in medicine, that doctors will be able to have more time with patients and with the actual caring of medicine, with counseling, with teaching and with enjoying what it's like to be a part of somebody's recovery.

I think the future of medicine; we need to embrace systems and strategies to help with the amount of information that needs to be retained. That might be through artificial intelligence because it just keeps getting bigger and bigger and bigger.

Finally, I'll say that medical students nowadays are on Reddit and on Snapchat and getting information so quickly through their phones. I also think there may become a space to use those types of things to teach medicine. So, in pulmonary grand rounds this year, we created a twitter hash tag. I have slowly been growing my Twitter presence. So, what I've noticed is that rather than having intentional study time, just flipping through Reddit and finding a healthcare topic of interest you learn an incredible amount of information. Based on who you follow on twitter, if you want to become an orthopedic surgeon and you're on Reddit or twitter and are following people who are educators and respected in their field, you're going to learn things. So I think that's another thing we could look to embrace in medical education.

Follow Dr. Carlos on Twitter for updates on his work.
Twitter: @GrahamCarlos

IMPRS

INDIANA MEDICAL STUDENT PROGRAM FOR RESEARCH AND SCHOLARSHIP

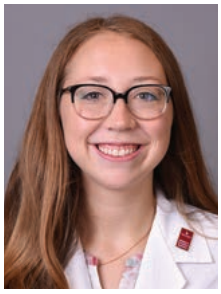
The following works represent a selection of the student research that took place at the 2019 IMPRS summer internship program—a collaboration of Indiana University School of Medicine and Indiana CTSI—including finalists who were selected to give oral presentations to a panel of judges.

Oral Presentation Finalist

SHROOM3 is a Novel Component of the Planar Cell Polarity Pathway Whose Disruption Causes Congenital Heart Disease

◆ **Alison Schmidt**, Matthew Durbin, James O'Kane, Stephanie M. Ware, Nina Jain

Background: Congenital heart disease (CHD) is a significant contributor to neonatal mortality, yet the molecular mechanisms underlying most disease remain unknown. In a patient with CHD we previously utilized whole exome sequencing to identify a novel CHD candidate gene, SHROOM3. SHROOM3 is implicated in human neural tube and kidney defects but mostly unexplored in CHD. SHROOM3 encodes a protein which localizes to the apical portion of cells and induces cytoskeletal changes, including ACTOMYOSIN constriction. In addition, SHROOM3 binds DISHEVELED2 and ROCK1, both key components of the noncanonical Wnt/planar cell polarity signaling pathway (PCP). PCP signaling influences numerous developmental processes, in part through regulating ACTOMYOSIN constriction. In previous studies, the Ware Lab identified that Shroom3gt/gt mice have incompletely penetrant heart defects, including ventricular septal defects (VSD), double outlet right ventricle (DORV) and left ventricular noncompaction, and Shroom3gt/gt mice have diminished cardiac neural crest cell staining in the outflow tract; this CHD spectrum phenocopies PCP disruption. We hypothesize that SHROOM3 is a novel component of the PCP pathway and disruption of this gene results in CHD.
Methods: Heterozygous SHROOM3gt/+ and DVL2-/+ mice are phenotypically normal and fertile. To demonstrate that SHROOM3 interacts with DVL2 and the PCP pathway during cardiac development, we analyzed compound SHROOM3gt/+;DVL2-/+ embryos for CHD phenotypes. We also employed immunohistochemistry (IHC) to assess for evidence of PCP disruption in homozygous SHROOM3gt/gt embryos.
Results: There is a decreased frequency of compound SHROOM3gt/+;DVL2-/+ embryos as compared to anticipated Mendelian ratios (observed: 18.4%; expected: 25%; n=76), suggesting potential embryonic lethality. One compound SHROOM3gt/+;DVL2-/+ embryo has DORV and VSD, characteristic of PCP disruption. IHC also demonstrates disrupted actomyosin in the SHROOM3gt/gt mice, characteristic of PCP disruption.
Conclusion: These data help strengthen SHROOM3 as a novel CHD candidate gene and a component of the PCP Signaling pathway. Further characterization of this gene is important for CHD diagnosis and therapeutic development.



Alison Schmidt is a third year medical student currently undecided on a specialty; however, she's especially enjoyed her experiences with neonatology and maternal fetal medicine. For Schmidt, "it is evident that genetics will play a major role in shaping the way we care for patients in the future." She explains that her research experience "illustrated the complexity behind translating a piece of genetic information into an understanding of the molecular implications on embryogenesis and ultimately hopefully into improved diagnosis and therapies."

Oral Presentation Finalist

Inhibition of Type 2 Sodium-Glucose Transporters and Na+/H+ Exchanger-1 Produces Similar Cardioprotective Effects in Response to Ischemia-Reperfusion Injury

◆ **Bianca S Blaettner**, Hana E Baker, Adam G Goodwill, Hannah E Clark, Michael C Kozlowski, Johnathan D Tune

Background: Recent studies indicate that inhibition of Type 2 Sodium-Glucose Transporters (SGLT2i) augments diastolic filling volume and mitigates myocardial ischemic injury. During the course of a summer research experience, our group initiated a study testing the hypothesis that inhibition of the Na+/H+ Exchanger-1 (NHE-1) mimics the cardioprotective effects of SGLT2i in response to ischemia-reperfusion injury.
Methods: Lean swine (~50 kg) were anesthetized, a thoracotomy performed, and perivascular flow transducers placed around the left anterior descending (LAD) and circumflex coronary (LCX) arteries. A pressure-volume (PV) catheter was then inserted into the left ventricle. Swine received a 15 min infusion of vehicle (DMSO; n = 3), the SGLT2i Canagliflozin (30 μM; n = 3), or the NHE-1 inhibitor Cariporide (1μM; n = 3) prior to a 60 min total occlusion of the LCX and 2-hour reperfusion period. Following reperfusion, the LCX was re-occluded and a 2.5% Patent Blue 5 solution was administered to identify area at risk. The heart was excised, sectioned, and incubated in a 2,3,5-triphenyltetrazolium chloride (TTC) solution. Images were collected and analyzed for area at risk and infarct size.
Results: In the vehicle treated group, 2 of the 3 swine studied died prematurely before the completion of the protocol; one at baseline and one during ischemia. Our preliminary findings showed that left ventricular end diastolic volume increases in response to regional myocardial ischemia in the swine that received either Canagliflozin or Cariporide. This increase in diastolic volume was associated with an increase in stroke volume (i.e. Frank-Starling effect) and a reduction in myocardial infarct size in both treatment groups. Blood pressure tended to decrease to a similar extent in all groups.
Conclusion: These preliminary studies demonstrated that inhibition of SGLT2 and NHE-1 produce similar functional and protective effects in response to regional ischemia-reperfusion injury. Further experiments are necessary to verify these findings and examine the extent, if any, to which SGLT2i directly modulates NHE-1 activity.

Bianca Blaettner is a third year medical student who is currently interested in general surgery. "I love being in the operating room and hope to work with Doctor's Without Borders to provide medical care to developing countries." While she entered the summer without any expectations of pursuing research after medical school, Blaettner said, "I had such a great time with the Tune lab doing pig surgeries, learning how to suture, and how to analyze data. The summer I spent with them opened my eyes to the different aspects of research and I hope to continue doing research for my last years of medical school and into my professional career." She also adds a shout out to the Tune Lab for a great summer (even with the 6 AM start time). If you don't like research, a great lab will change your mind!

Oral Presentation Finalist

Asthma in Indiana – Using a Community Health Matrix to Determine Asthma Health Factors for Indiana Counties

◆ **Mikayla Burrell**, Rachael Casey, Dennis Savaiano

Background: Asthma and its appropriate treatment are public health issues in Indiana that Indiana Joint Asthma Coalition (InJAC), a partnership within CTSI, is attempting to address. This is done through state-wide coalition building, which unifies efforts regarding asthma health and education and promotes interprofessional collaboration. Because time and resources are limited, InJAC must choose the areas that would benefit most from their focused work. A matrix was developed to establish the 10 counties with poorest asthma health and highest vulnerability to social determinants to aid in this choice. We hypothesize that the 10 counties with the highest vulnerability to social determinants of health will have the worst asthma health.
Methods: Asthma health outcomes, contributing asthma-related variables, and social determinants of health were identified in all 92 counties in Indiana. Counties were compared by composite z scores to determine the top 10 counties with the poorest health statistics for asthma and social determinants. In addition, qualitative data will be used to identify local health coalitions that have the capacity and desire to work with InJAC to improve asthma treatment. InJAC will begin sessions with these counties to determine if long-term, sustainable, health promotions are feasible.
Results: The top 10 counties that were identified as having the poorest asthma health and factors were Lake, Grant, Madison, Marion, Huntington, Vanderburgh, Howard, La Porte, Blackford, and Noble. These are represented as the blue counties in **Figure 1**. The top 10 counties with highest vulnerability to social determinants were Owen, Ripley, Daviess, La Grange, Fayette, Wayne, Elkhart, Newton, Switzerland, and Marion. These counties are represented as the orange counties in Figure 1. The majority of current asthma-related resource clusters for the state of Indiana are represented as white circles in **Figure 1**.
Potential Impact: The data from this matrix will help direct InJAC to the areas of Indiana with the most need for asthma coalition efforts. This will be done through improvement on education, awareness, and quality of care based on the Indiana State Asthma Plan.

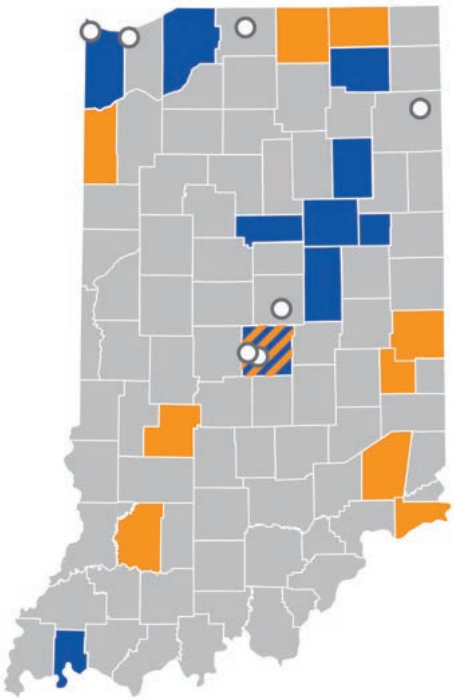


Figure 1.

Mikayla Burrell is a third year medical student who is currently interested in pediatrics. She believes that "motivating children will help the next generations to make the world a better place."

What is your most important takeaway from your research?

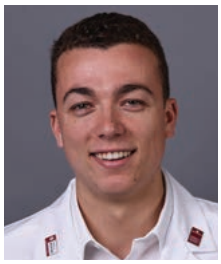
There are great disparities in health care and health outcomes throughout our own communities. I learned that the best way to address this is through involving our own communities and community leaders and through policy change. While these new, innovative ways of treating or addressing health issues are vital, they serve no purpose if this research cannot be disseminated or integrated into the communities which need it most.

Oral Presentation Finalist

Perception and Performance of PEM Fellows Following POCUS Curriculum Implementation

◆ **Steven Dawson**, Benjamin Nti

Introduction: Point-of-care ultrasonography (POCUS) in the emergency department provides the clinician with a real-time, non-invasive and rapid assessment of their patients. Currently, there is a lack of published POCUS curriculum guidelines for pediatric emergency medicine (PEM) trainees. In this regard, we developed a POCUS curriculum for fellows at a newly established PEM fellowship at our institution to understand their perception and its effectiveness.
Methods: We enrolled all current PEM fellows (n = 4) who had limited to no prior experience with POCUS to participate in program implementation in January 2018. Their progress was followed over time until graduation. The curriculum included didactics hands-on training in the presence (supervised) and absence (solo) of an expert instructor. In addition to the curriculum, the fellows were also required to complete a pre- and post-survey assessment.
Results: Before curriculum implementation, barriers of POCUS common to all fellows (100%) included image interpretation and comfort level. Conversely, this improved with only 1 fellow (25%) suggesting these barriers. Interestingly, nearly all fellows (75%) found POCUS to be time-consuming following the curriculum implementation. Knowledge-base assessment showed improvement from an average score of 50% pre-test versus 79% post-test. The number of scans increased with time, but qualitative measures of image acquisition had a minimal improvement on a self-assessment quality assurance (QA) Likert scale. Average solo QA rating by an expert was slightly higher (Mean 3.22 + SEM 0.06) but comparable to the average by the fellows' self-assessment QA (3.11 + 0.15). Overall sensitivity of POCUS examinations were 90.32% (80.12%-96.37%) and specificity was 99.11% (97.44%-99.82%).
Conclusion: POCUS curriculum implementation can improve the PEM fellow's skills while enhancing their experience. While there are challenges for the utilization of POCUS, this study shows that the implementation of such a curriculum may have a positive effect on skill, knowledge development as well as perception.



Steven Dawson is a third-year medical student currently undecided in his specialty of interest.

What is your most important takeaway from your research experience?
While POCUS may seem tedious and difficult to learn, I think it has the potential to become integrated into everyday medical practice. Learning how to use POCUS can expedite a physical exam, providing real time imaging at the patient's bedside. This form of expedited imaging is especially useful in emergent situations, in which wasted time can be the difference between good and bad patient outcomes. Going forward, I think that all physicians can benefit from proficiency in POCUS, and I only expect its usage to continue to increase in the coming years.

Oral Presentation Finalist

Intraperitoneal Mesalamine Does Not Restores Mesenteric Perfusion or Prevent Mucosal Injury Following Intestinal Ischemia and Reperfusion

◆ **Thomas Knowles**; Brian Hosfield; Chris Shelley; Troy Markel

Background: Acute Mesenteric Ischemia (AMI) is characterized by a sudden decrease in blood flow to varying segments of the small intestine. It can lead to cellular damage, life-threatening intestinal necrosis and, if corrected, subsequent reperfusion injury. Reducing inflammation is key to preventing further cell damage. We therefore hypothesized that administration of mesalamine prior to intestinal ischemia would reduce epithelial cell damage by I/R and restore mesenteric perfusion.
Methods: C57Bl6J wild type (WT) mice were assigned to mesalamine or vehicle treatment groups (N=8/group). Prior to surgery, mice underwent intraperitoneal injection of treatment. Midline laparotomy was performed. Intestines were eviscerated, superior mesenteric artery (SMA) located, and baseline intestinal perfusion determined using Laser Doppler. SMA was then occluded to induce intestinal ischemia for sixty minutes, thereafter the occlusion was removed. Mesenteric reperfusion was then determined by Laser Doppler. Midline incisions were reapproximated with suture and animals were allowed to recover. After twenty-four hours, animals were re-anesthetized and underwent final assessment of mesenteric perfusion by Laser-Doppler. Animals were then euthanized, and intestines explanted. A portion of tissue was snap frozen for assessment for proinflammatory cytokines by ELISA. Another portion of tissue was stained with H&E and scored for intestinal mucosal injury. Data were assessed for normalcy and compared by Mann-Whitney-U test. P<.05 was significant.
Results: Preliminary data suggests mesalamine treated mice show no significant change in mortality compared to vehicle. Mesalamine treated mice also show an insignificant increase in histological damage score. Despite this, they show an insignificant improvement in oxygen perfusion.
Conclusion: Intraperitoneal mesalamine administration does not appear to be a useful method for limiting cell damage in GI diseases associated with AMI such as necrotizing enterocolitis. A larger sample size is needed to further elucidate treatment effects.

Thomas Knowles is a third year medical student who is currently undecided on his specialty choice but considering internal medicine, radiology, anesthesia, and emergency medicine. "The most important takeaway from my IMPRS experience is the value of the team. While following proper scientific methods and forming evidence-driven hypotheses are vital, the ability to surrounding yourself with a team of positive and supportive people proves invaluable to achieving large goals and having a healthy mindset throughout. Science doesn't solve anything without quality people behind it."

Oral Presentation Finalist

Identification of Microbes Associated with the Urethra During Health and Inflammation

◆ **Jonathan Alessi**, Rowan Farrell, Evelyn Toh, Xiaoli Zhang, David E. Nelson, Stephen J Jordan

The number of cases of urethritis, or inflammation of the male urethra, in the US has been estimated to be 2.8 million each year in the United States.1 It is the most common reason young men seek primary care and this syndrome is associated with acute proctitis, epididymitis, and orchitis.2 Approximately half of the cases are idiopathic, meaning that a causative agent cannot be identified. The goal of my project is to identify and characterize novel microorganisms that may be associated with male idiopathic urethritis. We used a variety of approaches to cultivate microorganisms from archived urethral swabs collected from men with idiopathic urethritis and healthy controls. We defined the phylogeny of the isolates using 16S rRNA sequencing to identify organisms that are not presently represented in microbial databases. Currently, we are scaling up a number of novel taxa we identified for genome sequencing. By adding these new genome sequencing to the existing databases we will be able to assign a higher proportion of reads from corresponding metagenomic sequence data and achieve a more complete survey of the male urethral microbiota in health and urethritis. This will provide crucial information which may permit us to identify urethritis associated organisms, develop new molecular diagnostics for these organisms, and discern if how these organisms are sexually transmitted.

Jonathan Alessi is an MD/PhD student currently interested in Med/Peds for its broad range of training and problem solving involved in approaching novel scenarios. "After studying the microbiome for just a few weeks, it becomes highly apparent that even the most complete medical text cannot encapsulate all the complexity of Medicine." His new research interests include the science of human behavior change and learning to leverage human psychology to aid people in extinguishing their self-determined "vices."

Oral Presentation Finalist

Risk Factors for Unplanned Admission to the Pediatric Intensive Care Unit in Pediatric Trauma Patients

◆ **William Schrock**, Jodi Raymond, Matthew Landman

Background: A number of risk factors for unplanned pediatric intensive care unit (PICU) admission and readmission have been identified. However, little is known of the risk factors associated with unplanned admission to the PICU in pediatric trauma populations. We hypothesize specific risk factors can be identified which may be associated with unplanned admission to the PICU following traumatic injury.
Methods: For this national retrospective study, we queried the 2016 National Trauma Data Bank for patients younger than 18 years experiencing a traumatic injury requiring hospital ad-mission from the Emergency Department (ED). We excluded patients who had experienced burn injuries. Statistically significant ($p<.05$) risk factors for unplanned PICU admission were identified in bivariate analysis and used to build a multiple logistic regression model.
Results: Patients experiencing unplanned admission to the PICU had lower ED Glasgow Coma Scale (11.83 vs. 14.31; $p<0.001$), higher Injury Severity Scores (ISS) (17.96 vs. 7.32; $p<0.001$), and were older (age 11.35 vs. 9.60; $p<0.001$). Initial ED disposition to the PICU was significant-ly associated with unplanned admission to the PICU ($p<0.001$). Initial ED disposition to the OR was significantly associated with unplanned admission to the PICU ($p=.018$). After multiple lo-gistic regression, ISS ($p<0.001$), initial ED disposition to the PICU ($p=0.002$), initial ED disposi-tion to the OR ($p=0.005$), and older age ($p=0.005$) remained statistically significant risk factors for unplanned admission to the PICU.
Conclusion: ISS and ED disposition to the PICU, OR disposition to the PICU and age are sig-nificant risk factors for unplanned admission to the PICU in pediatric trauma. These findings will assist in identifying patients at risk for unplanned admission to the PICU, thereby reducing the adverse effects of unplanned PICU admission and ultimately improving the quality of care for pediatric trauma populations.

William Schrock is a third year medical student who's currently interested in surgery and radiology due to their proximity to a number of exciting and innovative medical technologies. For Schrock, one of his most important takeaways from the IMPRS program was his deepened appreciation for "the vital role patient data plays in healthcare's ability to efficiently study, identify, and prevent various medical risk factors and adverse health outcomes."

Oral Presentation Finalist

Telepresence and Provider Communication Predict Veteran Satisfaction with Telestroke

◆ **Griffin Selch**, Holly Martin, Teresa Damush, Michelle LaPradd, Susan Ofner, Linda Williams, Michael Lyerly

Background: Telestroke has been demonstrated to be a cost-effective means to expand access to care and improve outcomes in stroke; however, information on patient perceptions of this system of care delivery are limited. This study seeks to examine patient feedback of a national telestroke system within the Veterans Health Administration.
Methods: Patients who received a telestroke consultation were eligible for a phone interview two weeks later, including questions about technology quality, telepresence, and telestroke provider communication. Satisfaction scores ranged from 1-7, (higher = more satisfied), and for analyses were dichotomized as 6-7 indicating high satisfaction vs. < 6. Patient variables including stroke severity (measured by the NIH Stroke Scale) were obtained from study records. Bivariate logistic regression models were used to determine what factors were associated with patient satisfaction.
Results: Over 18 months, 186 interviews were completed and 142 (76%) reported high satisfaction with telestroke. Patients with more severe stroke were less likely to recall the consultation. Factors significantly associated with patient satisfaction were higher ratings of the technology ($p < 0.0001$), telepresence ($p < 0.0001$), provider communication ratings ($p < 0.0001$), and overall VA satisfaction ($p = 0.02$). In the multivariate model, telepresence (OR 3.10, 95% CI 1.81-5.31) and provider ratings (OR 2.37, 95% CI 1.20-4.68) were independently associated with satisfaction. Veterans that were satisfied were more likely to recommend the technology ($p < 0.0001$).
Conclusion: Provider qualities, including telepresence and provider ratings, were associated with overall Veteran satisfaction with the telestroke consultation. Technology quality may be necessary but not sufficient to impact patient experience. Training providers to improve telepresence could improve patient experience with telestroke consultation.

Griffin Selch is a third year medical student currently undecided on specialty choice and keeping an open mind going into clinical rotations. "My research taught me that telemedicine (which is quickly becoming an essential component of healthcare as a whole) can be very satisfying for patients, and that physicians can enhance that satisfaction by how they communicate using this platform. This is important to keep in mind as more doctors interact with their patients virtually."

Neurology

"Since both research and the practice of medicine are constantly changing, it's important to identify what is constant. Know yourself, both your strengths and your weaknesses. Be confident but always eager to learn from others. Bring your passion to bear in a place of need and you will be content in your life and your work."

Linda S. Williams, MD
Director, Roudebush VAMC JC Primary Stroke Center
Professor of Neurology, IU School of Medicine

Oral Presentation Finalist

It's Complex: Predicting Gastroschisis Outcomes Using Prenatal Imaging

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Abstract

Introduction: Gastroschisis occurs in 1 out of 2,000 births with survival rates partially contingent on intestinal complications and time to establishing feeding. Enhancements in prenatal imaging have given better insight into postnatal outcomes. The goal of this study was to examine the gastroschisis patient population at a single children's hospital in the modern era and to utilize prenatal ultrasound to develop new prenatal prognostic indicators.
Methods: We performed a retrospective review of gastroschisis patients at a quaternary care referral children's hospital from 2010 through 2018. We recorded demographics, prenatal data and imaging, early postnatal data, operative data, and patient outcomes. We compared patients within our cohort born with complex gastroschisis (bowel atresia/ perforation) to uncomplicated gastroschisis patients. Second trimester and third trimester prenatal ultrasounds (US) were evaluated for changes in amount of external bowel, bowel dilatation, and bowel wall edema to identify prognostic indicators of the status of the bowel at birth. For categorical variables, Chi-square tests were used to assess for significance. Univariate and multivariable analyses were used to asses significance between categorical and continuous variables using medians and interquartile ranges or means.
Results: 134 patients were included in the study: complex (24), uncomplicated (110). Compared to uncomplicated gastroschisis, complex patients required longer median days to feeding initiation (44 vs 10, $p<0.001$), full feeding (80 vs 23, $p<0.001$), length of stay (LOS) (83 vs 33, $p<0.001$), and TPN at discharge ($p=0.004$). Full US data was available on 81% of patients, and partial data was identified on 19%. Prenatal US analysis showed significantly more complex patients had polyhydramnios amniotic fluid on third trimester US (4.3% to 23.5%, $p=0.018$). US analysis between complex and uncomplicated patients showed large amount of external bowel (41.2% vs 22.3%, $p=0.129$) and prevalence of internal bowel dilation (29.4% vs 10.6%, $p=0.053$) on third trimester US and increase in bowel edema (29.4% vs 13.8%, $p=0.148$) and external bowel dilation (64.7% vs 51.1%, $p=0.429$) from second to third trimester US. Multiple multivariable logistic regression analyses revealed amniotic fluid on third trimester US to be the most significant predictor of complex gastroschisis. However, there were no differences in perioperative or long-term complications in the complex group when compared to the group with uncomplicated gastroschisis.
Conclusions: Markers on prenatal ultrasound can predict intestinal complications at birth. Complex gastroschisis is associated with increased time to feeds and LOS.

Sarah Fisher is a third year medical student currently interested in general surgery. "Spending time in the pediatric surgery department at Riley not only displayed the variety of surgeries performed, but also the ever-changing day to day tasks other than surgery, such as time in clinic, multidisciplinary care conferences, and research." Her most significant takeaway from this research experience was "being able to see the research through from an idea, to developing and then completing the project. Working at Riley researching gastroschisis and concurrently observing surgeries on gastroschisis babies was an incredible learning experience."

Introduction

Gastroschisis is an anterior abdominal wall defect that occurs in 1 out of every 2000 births with varying outcomes based on intestinal complications [1]. Two of the most important variables in the care of gastroschisis patients include timing of reduction of the bowel back into the abdominal cavity and establishment of full enteral feeding. A patient with complex gastroschisis is diagnosed based on bowel complications present at birth, including intestinal atresia, perforation, or both [Figure 1]. Complex gastroschisis patients experience higher mortality and morbidities, including increased infections and functional bowel deficits, such as short bowel syndrome [2]. Complex and uncomplicated gastroschisis patients experience a significant difference in outcomes, making prenatal identification of complex gastroschisis imperative for parental counseling and perinatal management.

Gastroschisis is often diagnosed on prenatal ultrasound (US) in the second trimester [3]. However, complex gastroschisis is only definitively diagnosed postnatally. Enhanced prenatal imaging has driven studies to identify prognostic factors for complex gastroschisis. Three-dimensional ultrasound has been used to evaluate fetal stomach volume and stomach-bladder distance as prognostic indicators. However, no significant difference was found in these variables between complex and uncomplicated patients [4]. A meta-analysis showed intra-abdominal bowel dilation, polyhydramnios, and gastric dilation could be used to identify a high-risk group more likely to experience post-natal complications [5]. More recently, Dewberry and colleagues identified internal bowel dilation on prenatal ultrasound as a significant predictor of complex gastroschisis and increased time to full enteral feeding [6]. Despite these findings, the prenatal indices identified to date have been mostly subjective and difficult to translate between institutions. The goals of this study were to identify novel indices on serial prenatal ultrasound that can help prognosticate complex gastroschisis and adverse outcomes, and to characterize complex and uncomplicated gastroschisis within our patient population. Our hypothesis was that there are identifiable objective differences between these two groups that can be delineated on prenatal US.

Method

This study retrospectively evaluated 134 patients with surgically-repaired gastroschisis at a quaternary-care referral children's hospital from 2010 to 2018. Following consent-exempt approval by the Indiana University Institutional Review Board, records of patients admitted with gastroschisis were queried using hospital and surgical billing records. Newborns with gastroschisis and other major comorbidities, such as complex congenital heart disease, lethal genetic conditions (trisomy 9, 13, 18), major central nervous system abnormalities, and infants who died on transport prior to arrival at the Riley Hospital NICU were excluded. All data was collected and stored in a secure online REDCap database. Birth weight, presence of complex gastroschisis (atresia, perforation), day of life (DOL) of abdominal closure, type of closure (primary closure or use of a silo), presence of infection or sepsis, days until feeding initiation, days until full feeding, requirement for total parenteral nutrition (TPN) at discharge, length of hospital stay, and long-term intestinal complications (dysmotility, volvulus, NEC, adhesive bowel obstruction) were collected for each patient to identify complex patients and evaluate outcomes between complex and uncomplicated patients. Complex gastroschisis was diagnosed based on clinical determination of an atresia, perforation, or both present in the bowel at birth. In patients with matted bowel, the determination was made at a later time. Sepsis was defined as documented or suspected sepsis from any source.

119 patients had either complete or partial prenatal data. 15 patients had no available prenatal medical record. US images were evaluated for bowel wall dilation (internal and external), bowel wall edema, and amount of external bowel (small(<40mm2), moderate(40-70mm2), or large(>70mm2)). The first prenatal US was generally in the second trimester (median EGA 20 weeks [IQR 17.5-22.5 weeks]), and we defined this study as "second trimester" for the remainder fo the manuscript. Similarly, the final prenatal US was generally in the third trimester (35 weeks [IQR 33.5-36.5 weeks]) and was defined as such for consistency in the manuscript. Measurements of bowel wall thickness [Figure 2] and total area of herniated abdominal contents were obtained using sonographic PACS software measuring tools (GE Viewpoint). The "area of external defect" was defined as the point of ventral wall defect to the farthest extending loop of bowel in the horizontal plane, and from cranial to caudal extension in the vertical plane [Figure 3]. Additional prenatal information included quantity of amniotic fluid (normal, polyhydramnios or oligohydramnios), as well as estimated fetal weight (EFW) determined from abdominal circumference (AC) for gestational age at time of scan. Any genetic anomalies or major comorbidities seen on US were noted. Finally, second and third trimester US measurements of bowel wall thickness, area of external defect, and wall edema were compared, and any progression or reduction of disease was correlated with outcomes to identify prenatal US prognosticators.

Data from the REDCap database was exported to IBM SPSS Statistics 24 software, which was used to complete Chi-square tests (Fisher's exact or Pearson chi-square) for categorical variables and univariate analyses of continuous variables. Univariate and multivariable analyses were used to asses significance between categorical and continuous variables using medians or means. Univariate analyses were completed for several grouped cohorts using the nonparametric independent-samples median test. Multivariate logistic regression analyses were used to assess the significance of prenatal US factors as predictors of complex gastroschisis. A reduced model

Figure 1. Patient with complex gastroschisis, including small bowel necrosis, small bowel atresia, and colonic atresia.

multivariate logistic regression analysis was performed on significant prenatal US factors. Sensitivity and specificity analyses were completed on these significant prenatal US factors and positive and negative predictive values were evaluated.

Results

Complex vs Uncomplicated Gastroschisis Outcomes

Of the 134 patients included in this study, 24 (17.9%) had a complex gastroschisis, and 110 (82.0%) were uncomplicated. There was 100% survival in the complex group and a 99.1% survival in the uncomplicated group. The sole mortality in the uncomplicated group was a result of acute NEC totalis that proceeded to septic shock. The patient was progressing well on full feeds before abruptly becoming ill. This patient was born prematurely at 33 weeks EGA, which could have contributed to the development of NEC Of the complex patients, 3 presented with both atresia and perforation, 16 presented with atresia only, 3 presented with perforation only, and 2 presented with other indications of complex gastroschisis (matted bowel, primary bowel dysfunction). Table 1a shows a comparison of patient characteristics and Tables 1b-1c show a comparison of outcomes for complex vs uncomplicated patients.

There were no significant differences in rates of adhesive bowel obstruction, dysmotility, postoperative infection, and ventral hernia between complex and uncomplicated patients. 16.7% (p=0.02) of complex patients had a central line infection and 20.8% (p=0.02) suffered documented or suspected sepsis in the first 30 days postop, compared to 2.7% and 4.8%, respectively, of uncomplicated patients. [Table 1c]

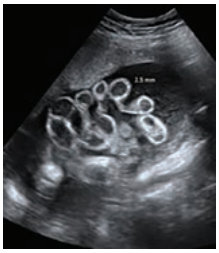
Prenatal Ultrasound Indices

Median EGA for second trimester US was 20 weeks (IQR 17.5-22.5 weeks) and 35 weeks (IQR 33.5-36.5 weeks) for third trimester US. Median EGA for second trimester US was 20 and 21 weeks for uncomplicated and complex patients respectively and 35 and 34.5 weeks respectively on third trimester US. Complex patients had a mean defect area of 932.25 mm2 on second trimester US and 4918.88 mm2 on third trimester US. In contrast, uncomplicated patients had a mean defect area of 996.62 mm2 on second trimester US and 3920.62 mm2 on third trimester US. Pearson chi-square and Fishers Exact tests revealed polyhydramnios was significantly increased in complex patients from second to third trimester US (4.3% to 23.5%). Though not statistically significant, other differences in groups were noted, including increased amount of external bowel (p=0.129) and increased internal bowel dilation (0.053) among complex patients on third trimester US. From second to third trimester US, complex patients had an increase in external bowel dilation (51.1% to 64.7%, p=0.429) and an increase in bowel edema (13.8% to 29.4%, p=0.148). Mean defect area, bowel thickness, and abdominal circumference were evaluated between complex and uncomplicated patients on second and third trimester US without a significant difference between groups. [Tables 2-3]

All factors on third trimester US and change in external bowel, bowel edema, and bowel dilation from second to third trimester US were assessed as predictors for complex gastroschisis using multivariate logistic regression models. In a multivariable regression model including all US factors, amount of external bowel (p=0.031), amniotic fluid (p=0.011), change in external bowel (p=0.044), and change in bowel edema (p=0.032) were found to be significant both alone and in the full model. In a multivariable regression model including only these four factors, polyhydramnios amniotic fluid was found to be the only factor significantly associated with complex gastroschisis at birth (p=0.011) [Table 4]. Sensitivity and specificity analyses were completed for these four factors, where an increased amount of external bowel on third trimester US compared to second trimester US showed the highest sensitivity (58.8%) and polyhydramnios amniotic fluid on third trimester US showed the highest specificity (95.7%) [Table 5].

Discussion

The goal of this study was to compare complex and uncomplicated gastroschisis patients in a large single institution cohort and use serial prenatal US to identify new prenatal markers to predict complex disease. Since this study was done at a single institution, characterization of the patient



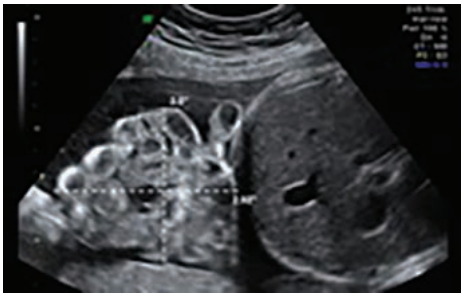


Figure 2 (left). Measurement of bowel wall thickness
Figure 3 (right). Measurement of area of external defect

Table 1a Patient characteristics for complex vs uncomplicated

	Complex (n=24)	Uncomplicated (n=110)	P
Sex	13 (54.2%) male 11 (45.8%) female	49 (44.5%) male 61 (55.5%) female	0.499
C-section	5 (20.8%)	39 (35.5%)	0.231
Silo placement	18 (75%)	97 (88.2%)	0.110
*EGA at birth	35.4±2.9	36.5±1.5	0.087
*Birth weight (grams)	2369.1±685.2	2496.7±517.9	0.397
*APGAR 1 minute	6.5±2.6	6.4±2.5	0.936
*APGAR 5 minutes	7.8±1.5	7.8±1.7	0.890

*Values represent means +/- standard deviation.

Table 1b Comparison of outcome data for complex vs uncomplicated

	Complex (n=24)	Uncomplicated (n=110)	P
Days intubated in first 30 days of life (DOL)	9 (3-30)	5 (0-18)	0.074
DOL abdominal closure	7 (1-20)	5 (1-20)	0.054
Days to feeding initiation	**44 (5-92)**	**10 (3-71)**	**0.001**
Days to full feeding	**80 (17-356, n=23)**	**23 (10-179, n=109)**	**< 0.001**
Length of stay	**83 (28-263)**	**33 (16-113, n=109)**	**< 0.001**

Values represent medians and range.

Table 1c Postnatal complications for complex vs uncomplicated

	Complex (n=24)	Uncomplicated (n=110)	P
TPN required at discharge	**7 (29.2%)**	**7 (6.4%, (n=109))**	**0.004**
NEC	1 (4.2%)	2 (1.8%)	0.450
Adhesive bowel obstruction	3 (12.5%)	5 (4.5%)	0.153
Dysmotility	7 (29.2%)	23 (20.9%)	0.420
Central line infection	**4 (16.7%)**	**3 (2.7%)**	**0.020**
Postoperative infection	7 (29.2%)	18 (17.1% (n=105))	0.250
Sepsis in first 30 days post-op	**5 (20.8%)**	**5 (4.8% (n=105))**	**0.020**
Ventral hernia	3 (12.5%)	21 (19.1%)	0.566

		Complex (n=24)	Uncomplicated (n=110)	p
Amount of external bowel (2nd tri US)				
	Small/moderate	22 (100%, n=22)	96 (98%, n=98)	1.000
	Large	0 (0%)	2 (2%, n=98)	
Amount of external bowel (3rd tri US)				
	Small/ moderate	10 (58.8%, n=17)	73 (77.7%, n=94)	0.129
	Large	7 (41.2%)	21 (22.3%)	
Amniotic fluid (2nd tri US)				
	Normal/ oligohydramnios	22 (100%, n=22)	96 (98%, n=98)	1.000
	Polyhydramnios	0 (0%)	2 (2%)	
Amniotic fluid (3rd tri US)				
	Normal/ oligohydramnios	**13 (76.5%, n=17)**	**90 (95.7%, n=94)**	**0.018**
	Polyhydramnios	**4 (23.5%)**	**4 (4.3%)**	
Internal bowel dilation (2nd tri US)				
		2 (9%, n=22)	2 (2%, n=97)	0.155
Internal bowel dilation (3rd tri US)				
		5 (29.4%, n=17)	10 (10.6%, n=94)	0.053
External bowel dilation (2nd tri US)				
		2 (9%, n=22)	2 (2%, n=98)	0.153
External bowel dilation (3rd tri US)				
		10 (58.8%, n=17)	47 (50%, n=94)	0.602
Bowel edema (2nd tri US)				
		0 (0%, n=22)	1 (1%, n=98)	1.000
Bowel edema (3rd tri US)				
		4 (23.5%, n=17)	17 (18.1%, n=94)	0.736
Change in bowel edema (2nd tri to 3rd tri US)				
	Same	12 (70.6%, n=17)	81 (86.2%, n=94)	0.148
	More	5 (29.4%)	13 (13.8%)	
Change in amount of external bowel (2nd tri to 3rd tri US)				
	Same	7 (41.2%, n=17)	32 (34%, n=94)	0.590
	More	10 (58.8%)	62 (66%)	
Change in bowel dilation (2nd tri to 3rd tri US)				
	Less/ same	6 (35.3%, n=17)	46 (48.9%, n=94)	0.429
	More	11 (64.7%)	48 (51.1%)	

Table 2. Comparison of US factors from second trimester (2nd tri) US and third trimester (3rd tri) US for complex and uncomplicated patients

Ultrasound Factor		Complex	Uncomplicated	P
Defect area (mm^2)				
	2nd Trimester US	1003.8±787.3 (n=12)	1094.4±891.5 (n=60)	0.214
	3rd Trimester US	3937.9±2377.6 (n=15)	3584.9±1712.2 (n=81)	0.792
Bowel Thickness (mm)				
	2nd Trimester US	2.3±0.4 (n=12)	2.1±0.6 (n=62)	0.726
	3rd Trimester US	3.3±1.5 (n=15)	3.4±1.3 (n=82)	0.590
Abdominal Circumference (cm)				
	2nd Trimester US	16.4±4.4 (n=22)	15.1±3.5 (n=96)	0.210
	3rd Trimester US	26.3±3.3 (n=14)	27.0±3.0 (n=86)	0.473
Values represent means +/- standard deviation.				

Table 3. Comparison of prenatal US measurments for complex and uncomplicated gastroschisis patients

Ultrasound Factor	Reduced model (p-value)	Full model Odds ratio [CI] (p-value)	
Amount of external bowel on 3rd tri US	0.054	Large	3.586 [0.980-13.123] (0.054)
		Small or moderate	Reference
Amniotic fluid on 3rd tri US	**0.013**	**Polyhydramnios**	8.754 [1.646-46.548] **(0.011)**
		Normal or oligohydramnios	Reference
Change in external bowl	0.092	Large	0.291 [0.077-1.102] (0.069)
		Small or moderate	Reference
Change in bowel edema	0.064	More	3.320 [0.857-12.858] (0.082)
		Same	Reference

Table 4. Multivariate logistic regression analysis of predictors of complex gastroschisis on third trimester (3rd tri) US

Predictor of complex gastroschisis on 3rd trimester (tri) prenatal US	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Large amount of external bowel	41.2%	77.7%	25%	88%
Polyhydramnios amniotic fluid	23.5%	95.7%	50%	87.4%
More external bowel compared to 2nd tri US	58.8%	34%	13.8%	82%
More bowel edema compared to 2nd tri US	29.4%	86.2%	27.8%	87.1%

Table 5. Sensitivity and specificity for significant US predictors of complex gastroschsis

population was important. Our comparison of uncomplicated and complex gastroschisis patients showed increased morbidities in complex patients including more post-operative days to initiate enteral nutrition, wean TPN, and achieve full enteral nutrition. Complex patients had a significantly higher rate of central line infections and documented or suspected sepsis, including line, intra-abdominal, urologic, and unknown source, in the first 30 days post-operation, anticipated by increased days with a central or PICC in place for parenteral nutrition. Similarly, a previous study comparing outcomes for complex and uncomplicated patients showed complex patients also had more days to enteral feeding initiation and full enteral feeds, a longer LOS, prolonged parenteral nutrition, and increased rates of sepsis [2]. Previous studies, one of which was conducted at the same institution as this study, also showed an increase in mortality for complex patients, which differed from our study, in which the mortality in the complex group was zero [2,7]. A more recent study from the Children's Hospital of Pennsylvania showed no increase in mortality for complex gastroschisis, similar to the results of this study [8]. Interestingly, there were no significant differences in many long-term complications between complex and uncomplicated patients. Trends showed an increased percentage of complex patients had an adhesive bowel obstruction, dysmotility, and post-operative infections. However, these differences were not significant. A previous study showed a significant increase in NEC in complex patients, which was predictive of poor outcomes, however, we did not see NEC complications among complex patients in this study [8]. Similar data for increased rates of surgical re-intervention for adhesive bowel obstruction in complex patients was demonstrated in another previous study [9]. Overall, however, other studies confirmed our data that high rates of dysmotility and hernia repair occur in both complex and uncomplicated patients [9]. These findings could indicate complex patients experience more short-term complications after birth and during their significantly increased hospital stay. However, having complex gastroschisis did not appear to influence long-term outcomes and intestinal function.

On prenatal US, patients with complex gastroschisis were more likely to have polyhydramnios on third trimester US. Interestingly, there were no significant differences between patients who eventually had complex vs uncomplicated gastroschisis on second trimester US. Polyhydramnios amniotic fluid on third trimester US was the most predictive factor for complex gastroschisis. Trends showed more complex patients had an increase in both external bowel and bowel edema

from second to third trimester US and an increased amount of external bowel on third trimester US, but these values were not statistically significant. These findings make physiologic sense, as threatened bowel can be expected to become more edematous over time, even in relation to the amount of bowel injury normally expected with the exposure to amniotic fluid in gastroschisis. While the initial second trimester US itself may not be helpful to predict complex gastroschisis, third trimester US and change over time may be more useful in prenatal counseling, thus serial US into the third trimester is valuable. This data validates previous studies showing polyhydramnios [5] on prenatal US is predictive of complex gastroschisis and adds additional factors predictive of complex gastroschisis.

Large amount of external bowel on third trimester US, polyhydramnios on third trimester US, and an increase in bowel edema from second to third trimester US all had a high specificity, which makes identification of these factors on prenatal US useful in identification of patients that may be more likely to be born with a complex gastroschisis. All three of these factors also had a high negative predictive value making patients without these factors on prenatal US less likely to be born with a complex gastroschisis. These results indicate evaluation of third trimester US and trends from second to third trimester US are valuable in identification of factors related to complex gastroschisis at birth. These factors can be used to plan for delivery, help with team readiness for what to expect at birth, and to inform family of LOS and complications they can expect for their baby.

Limitations of this study include a small sample size, specifically of complex patients, due to the rare nature of these intestinal complications. The single institution nature of this study also introduced institutional bias of particular methods to treat gastroschisis patients, whereas patients with the same presentation may be treated differently at other institutions. The solution to both of these challenges would be to expand this study to a multi-institutional cohort to increase the patient number and level out treatment biases of a particular institution. Other limitations in evaluation of prenatal data include missing prenatal US data for 15 patients in the study. The sample size of 119 patients, however, showed significant predictive value of complex gastroschisis from US factors.

Conclusion

Not surprisingly, complex gastroschisis patients had a significantly longer LOS, time to initiation of enteral nutrition, and time to full enteral nutrition postnatally. We were able to identify polyhydramnios in third trimester US as a strong predictor of complex gastroschisis at birth, and several other ultrasound factors, including a large amount of external bowel on third trimester US, and an increase in bowel edema from second to third trimester US, with a high specificity and negative predictive value. Using these prenatal markers to prognosticate which patients will fall into the complex gastroschisis category can inform prenatal family counseling and immediate postnatal care. Future studies will work to validate these prenatal markers in a larger multi-institutional cohort.

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Oral Presentation Finalist

Classification of Cell types in the Human Kidney Using 3D Nuclear Morphology

◆ **Andre Woloshuk**, Seth Winfree, Tarek M. El-Achkar

Background: The evaluation of human kidney biopsies, a cornerstone for diagnosing renal disease, relies on subjective interpretation and semi-quantitative analysis of 2D images from thin-sections of tissue. Advances in 3D confocal fluorescence imaging and machine learning approaches such as neural networks provide the opportunity for an automated and quantitative approach, and the potential for extracting new data from 3D space. In this project, a convolutional neural network (CNN) was designed to automatically identify cell types in the kidney cortex based upon nuclear morphology.
Methods: Individual cells in human kidney tissue were isolated and assigned a ground truth classification based on validated cell markers. Images of the nuclei as 2D projections and 3D volumes were extracted and classified based on these markers using 3D tissue cytometry analysis. Two CNN architectures were trained using the image dataset. The accuracy of each network was assessed by its ability to classify specific cell types within the biopsy.
Results: A database of 1946 images of fluorescently stained nuclei collected from human renal tissue was created to train, validate and test the CNNs. Classification of different cell types was based solely on their nuclear features. With minimal training, the best performing CNN was able to classify a volume of all nuclear staining with an accuracy of 88.7%. This is likely to improve with additional training time. The network was also robust to changes in signal to noise ratio and image resolution.
Conclusion: A CNN was designed to classify cells in the human kidney cortex using only the nuclear staining in 3D fluorescence images. When implemented in an imaging workflow, this network could improve the efficiency of exploration and interpretation of the data, while sparing the need to incorporate specific cell markers in a multiplex design. Such approach can be leveraged to link imaging data at the single cell level from biopsy specimens to various clinical outcomes, thereby providing the prospects of precision medicine in kidney disease.

Andre Woloshuk is a third year medical student currently undecided in specialty choice, but interested in practicing in an academic setting with an emphasis on both teaching and clinical research. "Regardless of my specialty, I hope to translate scientific advancements into meaningful improvements in my patients' care." For Woloshuck, the most important part of his research project was working with excellent clinicians, mentors, and researchers. He said, "These individuals allowed me to ask important questions and gave me the tools to answer those questions."

ANTWIONE HAYWOOD | PHOTO

Shifts in Medical Education

__Antwione Haywood__, Ph.D. is the Assistant Dean of Student Affairs and an Assistant Professor of Clinical Radiation Oncology. He oversees various aspects of the student experience including wellness, diversity programming, and student success initiatives.

BY SEUNGYUP SUN

Seungyup Sun: Thank you for sitting down with me today. Could we start with your educational background and your path to medical student education?
Antwione Haywood: What's most interesting is starting even before myself. I have four siblings and most of us have terminal degrees. But my mom has a 6th grade education and immigrated here. I think people who search for the American dream often want life to be so much better for their kids. And when you're in a space where everyone is talented, it's hard to step back and reflect back on your accomplishments or have some sense of gratitude to the possibilities that have played out.

I grew up in LA and went to college in Virginia at Old Dominion University. I had these great experiences with student government and as a resident assistant. At some point, an advisor told me that I could work with college students in a similar capacity and get paid to do it. So, for the past 15 years or so, I've been studying and practicing the art of working with college-level students. My background and training are in college-age student development and the development of human potential.

I received a masters from the University of Kansas and then a doctorate from IU Bloomington. In between all that, I've also worked for Drexel University in Philadelphia, the higher learning commission in Chicago, and Purdue before being recruited for this position. In many ways, it's my job to fill in the gaps by providing subject matter expertise in student affairs.

SS: In what ways do you find that you're helping to fill in those gaps?

AH: There are several things that our students today take for granted that were nonexistent when I first arrived. For one, students weren't assigned advisors until the end of 3rd year. And that was the model. When you're in the thick of medical training, you don't realize how that sounds. So, my role is to share what the current practices are in higher education and what students are expecting.

And there are little things here and there that I've helped develop. For example, the connection days. We used to have mega-blocks, which were blocks consisting of three clerkships and no days off in between. The only clerkships that had what were called "changeover days" were those with inpatient services, where you may go from four weeks of inpatient to four weeks of outpatient rotation. Outside of that, it was very possible you could end a rotation on Thursday in Evansville and start the next rotation on Friday in South Bend.

SS: During your six years at IUSM, what are some of the biggest shifts you've seen in medical education?

AH: One of the things I'm particularly proud of is orientation. Last year, in the class of 2023, they had less than three hours of didactic time at orientation. Previous students spent a lot of time in a lecture hall with a lot of people talking at them. There's this idea in many organizations: when you have leaders reflect back, there's no great rationale for why we do things the way we do. So, what is the rationale for talking to people for two days straight? Instead, we spent a lot of time developing a thrive mentality and trying to do a better job of creating pride, community, and a sense of belonging. We went from the service project being optional to it being the first experience for all students. It's amazing to have 370 students participate in service across the area. We also did all kinds of small group activities around wellness, community building, and dealing with conflict.

With regards to the curriculum, I was on a committee responsible for making the argument for why we should go to pass-fail. I was also a representative on the curriculum counsel steering committee where I, along with others, brought up questions around curricular inequities. Before your time, every campus delivered a Phase 1 experience differently. Different classes, different credit hours, different grading schema… it felt like nine different medical schools. And we had grades and rankings. To me, a logical question was how can you have a ranking system that's not based on equitable evaluation of students? The Phase 1 curriculum has come a long way. Curricular experiences in the clinical years are continuing to become better too.

Outside of the curriculum, I've been happy and pleased with the efforts of medical student council. It used to be, in my opinion, a campus activities programming board. They've really shifted to representing the student voice in a governance capacity and expanding its reach by making sure relevant leaders and issues are brought to the forefront of the student body.

My baby project that has taken off has been around wellness. My personal interests and passions are around lifestyles and prevention medicine. I'm a certified life coach, I'm a trainer for Mind, Body, and Medicine, and I teach physical fitness classes. I work behind the scenes to develop relevant evidence-based medicine to support why we should be teaching more lifestyle and preventative approaches in our curriculum.

SS: Why do you think we should be incorporating those approaches in our curriculum?

AH: Lots of people ask, "How do we deal with burnout?" I think the issue is that we think about burnout as an acute disease. Burnout didn't just happen yesterday. It's really the collection of symptoms that have built up over time that have led to your anxiety or depression. And what we can do in the front end is to educate about pitfalls and preventative practices from the start.

For example, it's hard to feel the effects that lack of sleep have on patient care when you're involved. Maybe there's usefulness in studies showing that residents or physicians who lack sleep have safety issues. Or maybe it's useful to just show what happens in your brain when you don't sleep. We could be teaching that. Information is power. And then people could develop in a prescriptive way preventative tools to support them. So, on exam week or a busy rotation, when you know you're going to be working late at night, you can prepare for that. What ends up happening currently is that you're already deep in it and you don't have the knowledge and tools to be well.

There's something called the G.I. Joe fallacy. Back in the 80s, there was this cartoon called G.I. Joe and they always ended it by saying, "Now you know. And knowing is half the battle." They call it a fallacy because reality is not like that. Again, as an example, medical students are very smart people; I don't have to break down to you that you should be sleeping eight hours a day. You've likely seen some data that sleep is important. Yet, I feel like if I spoke to every medical student about how much they slept, most of them would say they sleep less than 7 hours knowing that it's

"The reality is that we don't connect the science and knowledge to ourselves. We never look at medicine with the lens that we benefit the most from knowing that information…Self-care is important and I think what happens to many students is that they dismiss a practice before even trying it, looking at the evidence, and considering how knowing that information might help someone else."

probably bad for them.

The reality is that we don't connect the science and knowledge to ourselves. We never look at medicine with the lens that we benefit the most from knowing that information. It's the same analogy of being in an airplane where they tell you to put on your oxygen mask and life vest first before worrying about the person next to you. Self-care is important and I think what happens to many students is that they dismiss a practice before even trying it, looking at the evidence, and considering how knowing that information might help someone else.

SS: What are your thoughts on cultural aspects of medical training that impact wellness?
AH: There's this concept called Maslow's hierarchy of needs. At a fundamental level, people don't make rational decisions if their basic needs aren't met, such as food, sleep, shelter, etc.

At a basic level, there are things that we don't address that are real problems. Debt load is a major concern for students and as a result, they make poor decisions when it comes to food choices. As much as everyone loves free Yats or pizza, you know processed foods are not the best for your body. But it's hard to pass up on because it's free, you're broke graduate students, and it saves you time from cooking. Then does this kind of food become your habit or a thing you do occasionally?

The second layer of that is around safety. It's hard to feel psychologically safe in medicine because you're always being evaluated. In Phase 1, you're being compared based on your score. In Phases 2 and 3, you're essentially focused on impression management with faculty who don't know you but need to make an assessment of how well you're doing based on limited interactions. It's such a simple concept but it really plays out in how people operate behaviorally. There are other models of graduate school; for example, there are systems where everyone is considered a junior colleague, much like PhD students are considered in their labs. There are systems with no grades that are instead criterion based; you either know the content or are working towards learning it. In the clinical environment, there are models such as having a coach or seeing yourself as an apprentice. I imagine implementing those models would have a profound impact on the psychological safety of students, and thus their decision-making and wellness.

SS: How do you personally find a work-life balance and what are your keys to happiness?
AH: My routine: I go to bed early. When I was a student, I used to go to bed around midnight. Now I go to bed around 9 or 9:30 PM. I wake up around 5 AM and I have some time to myself. I go to the gym every morning and do a fasted workout. Your body releases cortisol and insulin in the morning and that's part of what wakes you up, so I go through that practice. And I take pride in taking my son to school every day.

When I park in Lockfield, I do a 10-minutes or less meditation and reflect on three things I'm grateful for. I also do a little bit of free writing. I've found the only way I do it is by making it a part of something that's right in my face and I can't avoid. I sit, I meditate, and I reflect on what I'm thankful for.

And I'm pretty good at checking out once I leave work. I'll look at my email to see if there are any emergencies or if there's a message from a student. If it's an emergency, I'll respond. If it's a student that's across the state that doesn't know me well, I'll respond and let them know that I've seen their email but that I'll respond in a business day or so. I think people deserve that courtesy to know that you're listening to them. I want to acknowledge their interest but let them know that I have some boundaries.

The final piece is that through a lot of the practices that I've been exposed to, including spirituality, I've realized the only thing I can control are my own emotions. I've evolved around not idolizing other people, whether it's my spouse or my son, because I can't control their actions. I can only display the love and kindness that I want to. When you put all of your purpose into something that you can't control, like how do you compare to someone else or whether your kid is an exact mini-me of you, those things are going to lead to disappointment because rarely do things work out 100% how you want them to. It's been important to my mindful practices to be more forgiving of others and more reliant on controlling my own behaviors, anger, and frustration. And when you do that, it gives you power. Once I started getting into this stuff, it's become a gateway into other dimensions of wellness and support. I try to experience as much as I can and practice what I preach.

SS: For medical students interested in education, do you have any advice on how they can get involved?
AH: There's a lot of potential in our scholarly concentrations. A lot of disciplines say that they want people who have depth in a field of study and a range of skills. You want T-shaped individuals: people with broad aspects of knowledge outside of their depth of knowledge so that they can connect with people and be a better person.

Post-graduate, there are lots of deans and leaders I've seen who went back and got a masters in higher education, curriculum and instruction, educational psychology, or a related field. There's an entire profession out there with various pathways that can support an interest in education. Certainly, some students have pursued degrees in anatomy education.

One of the first things students can do is to get involved in committees, learn about the curriculum, learn about student affairs, learn about course design, and then share their voice. The second big step is getting involved in a scholarly concentration that supports medical education, and then ultimately pursuing post-graduate education.

Dean Haywood can be contacted at haywooda@iu.edu

Oral Presentation Finalist

Association Between IL6R Polymorphisms and Cachexia Phenotype in Patients with Pancreatic Ductal Adenocarcinoma

◆ **Nicholas J. Polster**, Joseph E. Rupert, Andrew R. Young, Teresa A. Zimmers

Background: Cachexia, manifested as progressive adipose and muscle wasting, affects up to 80% of patients with pancreatic ductal adenocarcinoma (PDAC) and significantly increases morbidity and mortality. Increased inflammation is an underlying mechanism in almost all cases of cachexia. Trans-signaling of Interleukin-6 (IL-6) via the soluble form of its receptor (sIL6R) has been shown to promote inflammation. Certain polymorphisms of the IL6R gene such as rs2228145 (Asp358Ala substitution) are associated with increased levels of sIL6R. We hypothesize that patients with PDAC possessing IL6R alleles correlated with higher levels of circulating sIL6R will have increased systematic inflammation manifested as increased cachexia prevalence or severity.
Methods: DNA was extracted from prospectively collected blood samples acquired from patients with PDAC and from non-cancer controls. Genotype at the rs2228145 polymorphism was determined by TaqMan qPCR genotyping. The resulting genotypes (A/A, A/C, C/C) were compared against cachexia-related metrics, including presence of cachexia (>5% body weight loss in the prior 6-months), body mass index (BMI), BMI-adjusted weight loss grade (BMI-WLG), and muscle and adipose volumes calculated from height-adjusted surface areas obtained from CT scans at the level of the third lumbar vertebra.
Results: 83.3% of patients with PDAC heterozygous (A/C) and 84.6% of the patients homozygous for the rs2228145 polymorphism (C/C) exhibited cachexia, versus 57.9% of patients homozygous for the reference allele (A/A), (P = 0.0364, Chi-square test). No significant difference was found among genotypes for BMI, 6-month weight loss, BMI-WL grade, or muscle and adipose tissue indices.
Conclusion: Patients with PDAC who are possess at least one copy of the rs2228145 polymorphism have a higher incidence of cachexia than those who are homozygous for the reference allele. This association suggests a causal role for sIL6R in cancer cachexia.

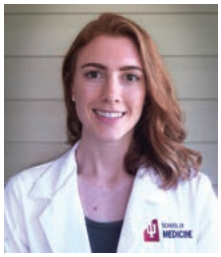
Nicholas J. Polster is a third year medical student interested in pathology and anesthesiology. "I'm fascinated by the science heavy natures of the fields," he said, "as well as how I can make an immediate difference for my patients." Polster's most important takeaway from his research experience: "It can be easy to dissociate the horrible diseases we read about in the first two years of medical school from actual patients, but working with real data from dozens of critically ill patients with cancer put it into perspective for me how important it is to master the art of medicine so that we can help these people to the best of our abilities."

Oral Presentation Finalist

"Women Never Use Drugs Alone": Assessing Stigma & Access to Care among Women who Use Drugs

◆ **Amanda Essex**, Carrie Lawrence, Brooklyn Sean Turner

Background: Substance misuse remains a significant health threat in communities across Indiana. Despite the 2015 HIV outbreak in Scott County, Indiana's health systems continue to lack the capacity to reduce health harms associated with substance misuse. Unlike general patient populations, people who use drugs (PWUD) face various social and structural barriers that impede access to health care and result in poorer health outcomes. Such impediments are of more significant concern for pregnant women who use drugs (PWWUD) who experience greater stigma, complex health needs, and require more specialized care. The purpose of this study was to assess access to healthcare and related services among women of childbearing age with a history of substance misuse.
Methods: For this qualitative study, participants (n=20) completed a sociodemographic questionnaire and semi-structured interview. Interview questions included perceptions of their overall health, healthcare experiences, and how to improve access to and retention in these services.
Results: The results reported reflect a thematic analysis of the interview transcripts. Two key care barriers identified were: (1) experiences of stigma related to professionals' attitudes towards PWWUD and (2) fear of losing custody of their child as a result of physician mandated reporting to child welfare.
Conclusions: Addressing social and stigma related barriers experienced by PWWUD are key to increased linkage to and retention in care as well as improved health outcomes. Additionally, our findings call for mandated student and physician education on patients who use drugs as well as reform of mandated reporting laws to reduce barriers and increase care access among PWWUD.

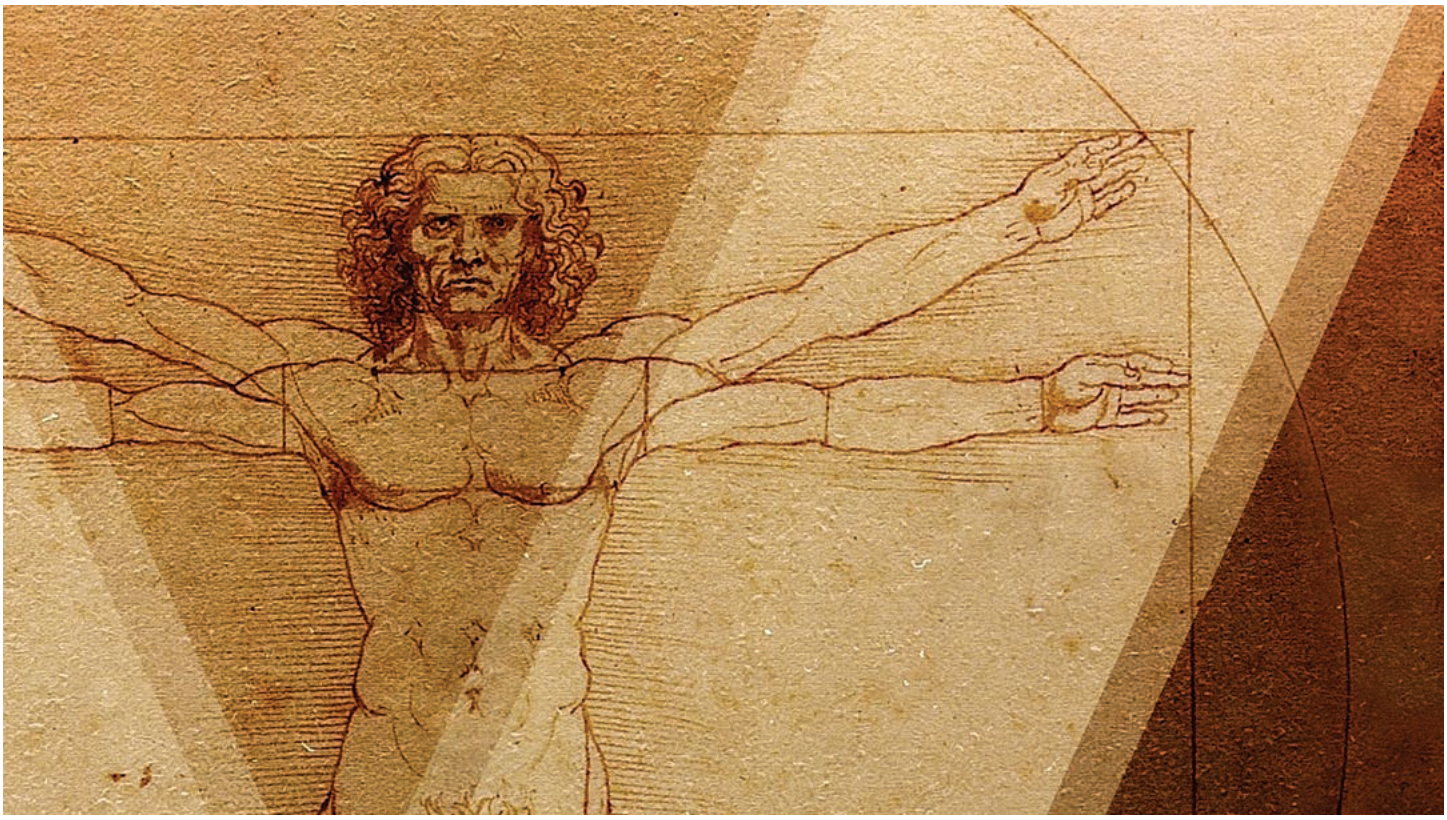


Amanda Essex is a third year medical student who is currently undecided on her specialty of interest, but considering OBGYN.

What is your most important takeaway from your research experience?
The interviews I conducted throughout the summer were emotionally taxing but also one of the most valuable experiences I've had throughout medical school. Collecting the stories of stigma and barriers that so many of these women faced when trying to get medical care was disheartening, but it also inspired me to continue working to improve care for these patients so future women don't have to experience the same hardships.

The Institutional Accomplice

How Medical Schools Have Quietly Contributed to a Step 1 Culture That Hurts Students and the Profession



HORRORGAMES | PHOTO

BY NICHOLAS HEITKAMP

Medical trainees today take a three-part licensing examination consisting of multiple choice questions created by the National Board of Medical Examiners (NBME). The first part of this series, the United States Medical Licensing Examination (USMLE) Step 1 exam, is the most important of the series, not only because it serves as a prerequisite for later examinations, but because scores are frequently used by residency programs to screen applicants for postgraduate medical training.

Usually taken after the first two years of medical school, students' scores on this exam largely determine the medical specialties to which they can match, with the most competitive specialties requiring the highest percentile Step 1 scores. Students with low Step 1 scores are generally limited, regardless of their career ambitions, to lesser competitive specialties. Although the USMLE Step 1 exam has recently been changed to pass-fail, the prevailing Step 1 culture that had existed leading up to this change still merits important discussion.

History of the NBME Exam

How did the career choices of medical students become dependent on the result of a single-day multiple-choice assessment of basic science knowledge in the first place? The original intent of this exam was to provide a comprehensive assessment of physician knowledge and skill that would be recognized by all states, obviating the need for physicians to take individual licensing exams to practice in each state. The original NBME examinations themselves were grueling, multi-day affairs that utilized hospitalized patients and oral presentations.1 Scores were reported in a binary fashion—students either passed or they did not. The exam has evolved over the years, with scores provided initially due to the belief that doing so benefitted examinees.[1] As scores began to be used for other purposes, the NBME began to include a disclaimer on using scores in residency selection: "It is important to understand, however, that the examinations have not been developed for the purpose of assessing preparation for postgraduate education."[2]

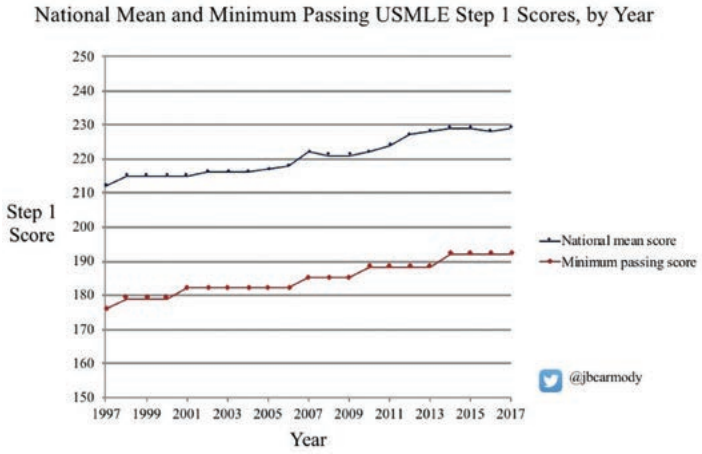
The exam has evolved over the past 100 years to its current-day form. Historically, physicians had several options for licensure testing. Until the 1960s, many states offered their own licensure examinations. Until 1992, there was also another licensing examination provided by the Federation of State Medical Boards (FSMB) known as the Federation Licensing Exam (FLEX). However, in 1992 the NBME gained total market control when the Federation of State Medical Boards agreed to merge the FLEX and NBME exams, giving rise to the USMLE series.[3] Students are now required to purchase and take the USMLE licensing examination, without any alternative options, from a private 501(c)(3) nonprofit company whose decisions come from its own board of directors. As recently reported by Stanford Dean of Medical Education, Dr. Neil Gesundheit, "the NBME has a deep and inescapable financial conflict of interest."[3]

We find ourselves in the midst of a current crisis in medical education, aptly described as "Step 1 mania."1 A national conversation has emerged analyzing the risks and benefits that the USMLE exam offers. Many discussions have been raised in the literature and via social media outlets which outline the effects that the USMLE has on students, several of which are mentioned below. The NBME not only has a monopoly on the administration of the exam, they have a financial conflict of interest in leveraging their ownership of the exam with profit they earn from study aids. Some residency program directors have also been implicated in the testing crisis as they contribute to perpetuating the behavior.[6] Yet what hasn't been discussed thus far is the role that medical schools play in Step 1 mania. Their lack of advocacy on behalf of students and their widespread use of NBME exams in the medical school curriculum make schools complicit in the high costs medical students pay for NBME profit.

The Financial Burden of Success

The USMLE exams are a financial burden for medical students. Prices for USMLE Step 1 have increased briskly over the past fifteen years, to a degree that outpaces inflation, despite the fact that the number of students taking the exam has remained stable.[4] This non-profit organization in fact makes a handsome annual profit. While the company makes some money from the sale of the Step exams themselves, their largest margins come from practice and shelf exams. Medical schools purchase the rights to practice exams and subject exams from the NBME at very high costs which are then transferred to students in forms of increasing tuition. In fact, many schools now require that their students then take these practice exams as a way of gauging their 'progress' prior to taking Step 1. In essence, indebted medical students are required by their school to take exams purchased from the very company that will license them to be a physician. It has been estimated that the cost that students incur from USMLE services, not including use of the Customized Assessment Services (CAS) by schools, is an average of $4,000 per student.[3]

Although the cost of exams and services most directly contributes to the substantial financial burden that students bear, there is another issue that deserves discussion. The minimum passing score and the average score of the Step 1 exam have increased at similar rates over the past twenty years,[1] as seen in this graph from JB Carmody:



Each year, the NBME itself sets the minimum passing score for the Step 1 exam rather than outsourcing this important task to an independent organization free of bias and financial conflict. Thus, the NBME embraces a policy that continuously increases the pressure on our country's medical students to improve exam performance. Many would argue that the intellectual capacity of students has not increased beyond the margin of new discovery but rather they have been forced to utilize smarter and more efficient resources to stay competitive with the rising exam averages. As minimum passing and average scores

go up, students feel they must remain competitive by re-prioritizing their time and resources. Dozens of expensive proprietary resources have now become the new normal for students studying for Step 1. In fact, they are so widely used that schools unofficially recommend the usage of these resources as a means to stay "minimally competitive". Sadly, these resources are usually financed at prevailing rates for medical school loans. Included in this lucrative market for Step 1 resources is, of course, the NBME itself, which sells practice tests directly to students.

The Medical School Shadow Curriculum

A majority of lectures in the first half of medical school now have an optional attendance policy. That is to say, students can choose to come to a traditional in-person lecture or skip the lecture and study the material on their own. Yet some tenured professors disagree with this new policy and feel that it is in the students' best interest to be present in class. So why the disconnect? There are likely two parts to this answer. First, medical schools today make student feedback a very high priority, as data from student surveys play a central role in LCME accreditation.[7] Second, schools now recognize the pinch that students are in during their preclinical years. They know how important Step 1 is to students—that residency program directors use the scores to stratify applicants for interviews. Schools want to advertise a high match rate for their students and realize that good Step 1 scores are an integral part of achieving this goal. In the same way that schools advocate for the use of efficient third-party review material, they are contributing to the Step 1 culture by carving out study time from the official medical school curriculum. Indeed, schools have enabled a new shadow curriculum to thrive.

Medical Schools Are Hurting Student Wellbeing

Perhaps the most worrisome aspect of the Step 1 culture is how it impacts student wellbeing. A 2014 study by Dyrbye and colleagues showed that compared to aged-matched college graduates, medical students demonstrated significantly higher rates of burnout and depression.[5] Step 1 is certainly a major source of stress for students in the preclinical years, with so much riding on the outcome of the exam.

To the extent that medical schools have enabled Step 1 preparation to become the de facto curriculum in preclinical medical education, they are complicit in the deleterious effects it has had on student wellbeing. In this population already known to be at higher risk for burnout and depression, schools must recognize the undue mental health burden that the NBME places on students.

Next Steps Forward

It is time for medical schools to publicly recognize the problem they've helped to perpetuate and vow to purposefully advocate on behalf of students in the future. While it can be argued that carving out room for Step 1 preparation within the preclinical curriculum and requiring students to utilize NBME preparatory materials helps students prepare for these important exams, such actions also implicate medical schools as accomplices to the adverse effects that standardized exams like Step 1 have on students' financial and mental wellbeing. While access to reliable institutional mental health services has improved for most medical students over the past ten years, more needs done to prevent the root causes of student stress and burnout, rather than relying on mental health resources as a safety net. It is time that medical schools make the difficult decision to prioritize student well-being over a Step 1-influenced curriculum that delivers positive feedback on student surveys.

There are a number of ways schools can demonstrate leadership and improvements. First, schools can utilize the change to the pass/fail system of Step 1 as an opportunity to reflect on how far the NBME enterprise has disadvantaged their own students. This is the right time to reflect on the past and implement change moving forward. Second, schools can demand more transparency from the NBME itself as terms for its usage. With detailed financial reports, stakeholders will see the actual cost of products and where the margins are allocated. Third, in addition to financial transparency, schools need to demand the use of independent review boards for determining the minimum passing scores. The NBME's current practice of choosing their own standards is a direct financial conflict of interest that potentially affects both their profits and students' mental health. An independent board created by nationally recognized physician-leaders without ties to the NBME would create a fair system. Fourth, encouraging and recognizing a second licensing organization would end the current monopoly enjoyed by the NBME, allow for diversity of licensure exam products, end of the financial monopoly, and likely drive improved quality and innovation.[8] Lastly, schools have the opportunity to redeem their past oversights by intentionally advocating on the side of their students during the impending Step 2 frenzy.

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Nicholas Heitkamp is fourth year medical student interested in pursuing pediatrics. All opinions are his own.

From Mentee to Mentor

Dr. Emily Walvoord's Path to Medical Student Education

BY ALLISON YOUNG AND ERIC CHEN

Dr. Emily Walvoord is a Pediatric Endocrinologist, Professor of Clinical Pediatrics and the Associate Dean of Student Affairs. In addition to overseeing medical student education at all nine campuses, she serves an advocate and mentor for students across IUSM.

First off, thank you for joining us today and we really appreciate it! Can you start us off by telling us a little bit about your background and how you got into your field of pediatric endocrinology?
EW: I actually went to college thinking that I would be a veterinarian. I worked for a vet between the summer of my junior and senior year of college and I absolutely loved it. But the vets actually talked me out of it and into human medicine. I changed my mind and took a gap year, which at that time people didn't do. In my year off, I did a lot of volunteer work for the St. Jude's Midwest Affiliate in Peoria, Illinois and I loved it. This is when I first thought that maybe I would want to work in pediatrics.

I ended up going to Northwestern for medical school, and as a 4th year medical student I still wanted to do pediatrics. I decided to do a rotation in Peoria so I could also be home with my parents for a month and I just picked something random, pediatric endocrinology, and it turned out that I absolutely loved it. The people that I worked with were two women, and they were super inspiring and great role models for me. When I went to medical school about ~30% of the students were women and there also weren't a lot of female role models either, so this was a big deal. As I went into residency, I loved being in the hospital, taking care of complicated cases, teaching, and being in an academic environment. By the end of my chief resident year I had decided to do peds endocrinology.

One of the aspects of pediatric endocrinology that I enjoy most are the connections that I have with my patients and their families. I get a lot more time with my them than some other specialties and I see them at the minimum once per year and some patients I see every 3-4 months, so I get to know them really well. I also love teaching the medical aspects of endocrinology, and how most things in endocrinology are thankfully quite treatable. But what I love most are the patients, watching kids grow up, knowing their family, and the relationships you build. I've been very lucky and have been invited to people's weddings, graduation parties, and get sent baby pictures; it's just wonderful and the best part of my job.

What motivated you to get involved with medical school education?
EW: For sure it started when I was a chief resident. I was always interested in clinical education and teaching, and during that time, Chief Residents were in charge of an inpatient teaching service, so I worked closely with the residents and students. I actually liked the administrative aspects too; I liked thinking about how to change the systems to make things better for people.

It was during my time as the assistant dean in faculty affairs at IU when the school started the process of curriculum reform. I joined one of the curriculum reform teams, then I led a curriculum reform team for the next step in the process, and eventually I was lucky enough to be included in a very small group of faculty and two students who put together the entire curriculum. That was how I met Dr. Allen and in 2017 Dr. Allen approached me for this job, which had been vacant for a few years. I initially said no since I loved my job in faculty affairs and professional development because the people I worked with in that office were amazing, I learned a ton, and was super fun. But he kept at it. I knew that in truth I loved working with students the most, and I was getting ready for a new challenge. I had been in that role for 7 years and I was ready to take on a different challenge to continue to grow and that's what led me to where I am now.

Do you have a feeling or know when it's time for something different?
EW: It's interesting, I think that you just have to listen to your inner voices. It's good to listen and to keep pushing yourself to take on new challenges and not get bored. When you're pushing yourself for something new, you've really got to give your best effort all the time and that's something I really enjoy.

It sounds like mentors have played a significant role in how you got here, could you tell us more about that? And now that you are in this new role, what excites you about mentorship?
EW: I've had so many wonderful people that have invested in me as a person, encouraged me, given me opportunities and wanted to see me continue to grow. And there are a lot of different kinds of mentors. There are people who help you with projects, and others who encourage you, introduce you to the right people, sponsor you, and share opportunities with you. And there are peer mentors, people who I call friends that are peers, and we share back and forth and encourage each other, and they have helped me to grow.

My biggest mentor when I was starting out was Dr. Ora Pescovitz, who was the head of pediatric endocrinology at the time. She was the reason I came to IU so that I could work with her. When I met her at the interview for Fellowship, I drove back to Chicago and told my husband about the interview; I was going on and on about her and he said, "so it looks like we're moving to Indiana". She was amazing, so encouraging, so brilliant, so warm, and she believes in you and pushes you to be your best. She's role modeled for me how to be a mentor and how to care for people- how to help and encourage them.

My other important mentors have been Steve Bogdewic, the inaugural EAD of FAPDD who gave me my first assistant dean job, Mary Dankoski the current EAD of FAPPD and Megan Palmer who is also dear friend. She is a great example of a peer mentor but I have learned so much from her since she has a different perspective as a PhD in Higher Education and has taught me so much about faculty affairs and student affairs. I'm always nervous that I'll leave someone out, but there are so many more individuals who have been a mentor along the way. So many people who I've worked with in Peds endo, when I was a resident, when I was doing research as a fellow, from faculty affairs, my peer mentors, Dr. Allen, and many, many others.

"To be a good mentor, you have to put your own interests aside and think of that person and what's right for them; it might even be something that's totally different from something that you would personally do."

What excites you most about working with students and being a mentor?
EW: YES! The other side, I love that. I can never say no when students want to meet with me. It's super fun just to be encouraging and to help people. One of the things that I enjoy most is helping people make connections with someone that they want to do research with, for a shadowing experience, or just to talk to. I also see being a mentor as part of my role as a woman in medicine. Now that half the class are women in medicine, it maybe doesn't seem that big of a deal, but there still is a huge dearth of women in leadership positions in medicine. To be a good mentor, you have to put your own interests aside and think of that person and what's right for them; it might even be something that's totally different from something that you would personally do. Lastly, you all are highly intelligent, highly capable, motivated young adults, and I try to role model that everyone needs to treat you as such.

Besides all the work roles that you do, is there anything that you do to promote your own wellness or hobbies that you have?
EW: I like to exercise, I run, and I go to the gym sometimes (pre Covid-19!). I actually run with my best friend in the early mornings and it's like double-dipping, I get exercise and we get to chat. I also have two children that I adore, one's in college and one is a senior in high school and they're always a big focus for me. And I love to read - that's why I have a little free lending library outside my office. I love being social and going out with my husband and friends or with my girlfriends. It's important to keep those connections and friendships; they are a part of who I am. I love my friends, and we're always there for each other when we need it. I promised myself early on in my medical journey that I never wanted to be so absorbed in my career that I don't have time for my family or friends or don't know what's really going on with my family.

If there's one piece of advice that you could leave with your medical school self, what would that be?
EW: Don't underestimate yourself! I was waitlisted to Northwestern and I had this feeling that I wasn't as smart as everyone else. My two best friends in medical school went to Ivy Leagues and my classmates were from all these high-powered undergrads. I knew I was smart and I knew I would work hard and become a doctor, but I had decided up front I wasn't going to be top of the class or even had it in my

sights. And that was stupid; not that it would have made a difference but why didn't I try for it? I should have pushed myself a little more, had a little more confidence and told myself that I could accomplish that. Don't sell yourself short, you never know what you can accomplish.

Is there one thing you wanted to leave us with?
EW: There's so many people that are here to help you. Don't ever feel like you can't reach out. If you reach out and if it isn't what you expected, reach out to someone else - there's plenty of people to click with. Don't think your problem is too small or that you don't matter. People care; we are all here, and we want to help you.

This year has been difficult for many students for a multitude of reasons. Are there any words of encouragement that you would like to give?
EW: These are incredibly challenging times. COVID-19 has taken a huge toll on the lives of people across the globe, including family and friends. I feel quite down myself intermittently and super frustrated with what I consider to be a travesty in the national response to this crisis. At the same time, I am also sad about personal "losses" - not being able to have a live IUSM match day or graduation, my daughter's high school graduation, etc. but then think that I am being small and ridiculous when people are losing their lives. But, I have realized that it is OK to grieve lost plans and things that I have looked forward to, even if it feels small within all that is going on, as long as you keep the big picture in mind. I am also incredibly sad and mad about what has been going on in the US for years in terms of systemic racism. At the same time, I am mad and upset with myself for not seeing this more clearly and doing more. I am truly hopeful that this unrest and current spotlight on these issues will result in real change. I am recommitting myself to exploring my own white fragility so that I can contribute positively to making our school a more safe and equitable place for everyone.

So—I guess my words of encouragement are that turbulent times can bring out the best in us. Give yourself some grace, but at the same time, commit to being part of solutions. We can get through this. "Great things are done by a series of small things brought together." – Vincent Van Gogh

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NEUROLOGY

Novel Large Vessel Occlusion Stroke Identification Scale in the Pre-hospital Setting

◆ **Daniel Torolira**; Sara Brown; Fen-Lei Chang

Objective: To develop a scale used by EMS in the pre-hospital setting to better identify large vessel occlusion (LVO) stroke patients.
Background: With the proven effectiveness of thrombectomy within 24 hours of stroke onset, a short scale composed of clinical presentations used by EMS to identify potential LVO stroke patients who are prime candidates for thrombectomy is urgently needed. So far there are several scales being used but none of them have shown consistently high sensitivity and specificity. A possible contributing factor is that all available stroke scales incorporate only positive scale values in identifying LVO based on clinical presentation consistent with LVO such as cortical signs. No scale has incorporated negative scale values for common presentations of non-LVO stroke subtypes such as embolic strokes and small vessel strokes or mimics. We hypothesize that a scale using differentially weighted positive and negative scale values may help to better identify LVO stroke from other stroke subtypes.
Methods: This is a retrospective chart review analysis of 148 patients evaluated for stroke between January 2017-May 2018 at a regional medical center with imaging confirmed stroke. Stroke scale scores were calculated from patients' initial NIHSS and presentation upon ER arrival, using the C-STAT stroke scale findings for comparison.
Results: C-STAT stroke scale had a sensitivity of 66.7% and a specificity of 73.0% in differentiating LVO from other stroke subtypes. Compared to C-STAT, our scale showed a significantly higher sensitivity of 93.8% ($p < 0.001$) and a non-significantly increased specificity of 81.0% ($p = 0.084$).
Conclusion: Findings suggest that our new scale may allow for a more accurate determination of LVO stroke in the pre-hospital setting without significant delay. A prospective, larger patient cohort in a pre-hospital setting is needed to validate these findings.

Evaluating the Effect of Acarbose Treatment on Insulin Secretion and Sensitivity in Early Diabetes Using a Novel Interpretation of the Disposition Index Equation

◆ **Clarissa Hanna**, Tamara Hannon, Robert V. Considine, Kieren J. Mather

Background: In pathologic states such as obesity and insulin resistance, there is a progressive decline in insulin sensitivity requiring greater insulin secretion to maintain normoglycemia. The inverse relationship between insulin sensitivity and secretion is mathematically defined by the Disposition Index (DI), a measure of beta-cell function adjusted for insulin sensitivity. We are working to generalize the DI equation to allow direct physiologic interpretation of the DI term, and of the slope relating insulin secretion with insulin sensitivity. We tested study treatment effects hypotheses using these new analytic methods.
Method: We used data from hyperglycemic clamp procedures and from standardized oral glucose tolerance testing performed in the Early Diabetes Intervention Program, a randomized controlled study evaluating the effects of acarbose, an alpha-glucosidase inhibitor, on beta-cell function. We applied our novel analytic method to 1-year treatment data comparing acarbose versus placebo effects on DI, secretion-sensitivity coupling slopes, and the joint change in secretion and sensitivity with intervention. Multiviarate analysis of variation was the primary statistical approach to evaluate joint changes in secretion and sensitivity; ANOVA was used to compare DI terms.
Results: These analyses revealed statistically significant 1-year changes in DI, in secretion-sensitivity coupling slopes, and in the joint changes in secretion and sensitivity. However, these treatment effects did not differ by randomized treatment group, suggesting an on-study effect beyond the randomized treatments.
Conclusion: We have applied a novel analytic approach to evaluate the secretion-sensitivity relationship modeled by the disposition index equation to investigate the effect of randomized therapy on beta-cell function in a placebo-controlled randomized clinical trial. These analyses revealed study effects on the secretion-sensitivity relationship that have not been previously described, suggesting that this novel approach will have value in clinical studies of beta-cell dysfunction and treatment effects.

Targeting the Warburg Effect to Overcome Lapatinib Resistance in Esophageal Adenocarcinoma

◆ **Samantha Holmes**, Sazzad Hassan, Victoria Makuru, Urs von Holzen

Background: Esophageal adenocarcinoma (EAC) is known to overexpress HER2. Lapatinib, a dual tyrosine kinase inhibitor blocking HER1 and HER2 pathways fails to improve patient survival. The molecular mechanisms of this lapatinib resistance remain largely unclear. Therefore, we explored the role of the glycolytic enzyme pyruvate kinase M2 (PKM2), a key regulator of the Warburg effect, in the lapatinib resistance mechanism of EAC cells.
Methods: First we established a lapatinib-resistant OE19 (LPR-OE19) cell line from OE19 EAC cells and characterized it. We then investigated the comparative cell growth inhibition and apoptotic effects of the HER2 inhibitor lapatinib and the PKM2 inhibitor shikonin, either alone or in combinations, with and without knockdown of PKM2 by siRNAs. In vitro cell growth was detected by WST-1 assay, protein expressions were detected by western blot analysis and ActivSignal assay, gene expressions were detected by qRT-PCR, cell migration capability was detected by wound scratch assay, and lactate production was detected by a lactate assay kit. To identify whether PKM2 interacts with HSP40 protein, co-immunofluorescence and immunofluorescence microscopy were used to detect their sub-cellular localization in LPR-OE19 cells.
Results: Lapatinib resistant LPR-OE19 cells showed downregulation of HSP40, both at protein and mRNA levels, whereas it showed upregulation of PKM2 only at the protein level. LPR-OE19 cells showed significantly reduced sensitivity to lapatinib induced cell growth inhibition, apoptosis, and decreased cell migration compared to parent OE19 cells. Interestingly, augmented cell growth inhibition, apoptosis, and decreased cell migration were observed in LPR-OE19 cells compared to parent OE19 cells when lapatinib was combined with shikonin. More interestingly, knockdown of PKM2 in LPR-OE19 cells abolished the reduced sensitivity of lapatinib induced cell growth inhibition and also abolished the augmented cell growth inhibition response when lapatinib and shikonin were combined. Moreover, LPR-OE19 cells showed enhanced lactate production compared to parent OE19 cells, while PKM2 knockdown in LPR-OE19 cells caused decreased lactate production. Interestingly, PKM2 and HSP40 co-localize with each other in the cell nucleus suggesting that PKM2 binds to the molecular chaperone HSP40.
Conclusions: These data suggest that combination therapy with HER2 inhibitor lapatinib and glycolytic inhibitor shikonin could be a novel treatment strategy for specific EAC.

Ophthalmology

Recognition of Ocular Syphilis: A Case Report

◆ **Ciresi, Colette**, Asdell, Stephanie, Monirian, Lydia, Salgado, Christina, Todd, Amelia

Case: A 90+ year-old female with a history of periorbital cellulitis, traumatic iritis of the right eye, and neurodegenerative dementia presented with worsening encephalopathy and recent falls. Ophthalmology was consulted for right eye pain, redness, and impaired visual acuity. Her visual acuity at presentation was 20/225 and 20/30 in the right and left eyes, respectively. Intraocular pressures were normal and pupils were reactive without a relative afferent pupillary defect. Slit lamp exam revealed periorbital edema, conjunctival injection and chemosis, and iritis, which were initially thought to be sequelae of her recent falls. Dilated exam was within normal limits. The patient was diagnosed with traumatic iritis and started on topical prednisolone acetate 4 times daily. The patient returned for follow up three weeks later with complete resolution of anterior chamber inflammation, but with persistently decreased vision of 20/150 in the right eye. Repeat dilated fundus exam revealed temporal choroidal effusion. B-scan demonstrated posterior scleral thickening and confirmed the choroidal effusion. Extensive lab work-up for rheumatological and infectious causes led to a diagnosis of ocular syphilis. Patient was treated for 10 days with IV penicillin, which successfully resolved choroidal effusion and systemic infection. At her 6-month follow-up appointment, visual acuity had improved from 20/225 on initial presentation to 20/30 in the affected eye. Unfortunately, the patient's dementia continued to progress despite adequate treatment, indicating her cognitive decline was likely unrelated to her syphilis diagnosis.
Conclusions: This case demonstrates identification and appropriate treatment for ocular syphilis in an elderly woman, emphasizing the importance of obtaining a complete sexual history regardless of age and screening for sexual abuse. Additionally, the case raises awareness of including sexually transmitted infections (STI) in the differential diagnosis of a patient presenting with an eye complaint, as chlamydia, gonorrhea, herpes, human papillomavirus infection, and HIV can also have ocular manifestations.
Clinical Significance: In 2015, the CDC issued a clinical advisory for rising rates of ocular syphilis, especially in populations of men who have sex with men and individuals with HIV, although ocular syphilis may be prevalent in any patient population as demonstrated by our case report. Ocular syphilis can be challenging to diagnose, as it can often masquerade many different inflammatory conditions and may not always be highest on the differential diagnosis in certain populations, such as the elderly. Common presentations of ocular syphilis include posterior uveitis and panuveitis which can appear at any stage of infection. Syphilitic meningitis and neurosyphilis must also be ruled out in presence of ocular syphilis. Failure to initiate prompt antibiotic treatment can lead to diminished visual acuity, optic neuropathy, and blindness.

Emergency Medicine

Physician Receptiveness of Ventilation-Perfusion Imaging in a Randomized Clinical Trial

◆ **Colton Junod**, Alice M. Mitchell

Background: Computed Tomography of the pulmonary arteries (CTPA) is the most common imaging modality for evaluating patients for suspected pulmonary embolism (PE), but carries the risk of acute kidney injury (AKI) from contrast media exposure. In appropriately selected patients, ventilation scintigraphy (VQ) imaging is a diagnostically equivalent alternative. We hypothesized that physician perceptions of diagnostic accuracy and study availability contribute to under-utilization of VQ imaging.
Methods: Patients with suspected PE at increased risk of acute kidney injury, were randomly selected to undergo VQ instead of CTPA. Patients unable to consent, patients with a history of pulmonary surgery, and those undergoing contrast-enhanced imaging for other indications were excluded. A screening chest radiograph was obtained prior to study imaging allocation. All cases were reviewed by a nuclear medicine radiologist blinded to acceptance or refusal of VQ imaging allocation. The primary outcome was defined as the rate of physician-refusal of VQ imaging. The unprompted physician-reported reason for refusal was recorded, in real-time, along with any other general responses.
Results: Following exclusions, 42 subjects were enrolled. Notably, chest radiograph findings excluded only 2 subjects. The reviewing nuclear radiologist agreed with all study-selections for VQ appropriateness and there was no instance of non-diagnostic VQ imaging. Treating physicians refused VQ imaging randomization in 48% (20/42). Physicians also believed VQ imaging lacked sufficient diagnostic accuracy in the context of active non-pulmonary malignancy in 29% (12/42) of cases. Although CT did not identify cases not seen on chest radiograph, in 12% (5/42) cases suspected pneumonia was the reason for refusal. Statements such as "VQ is inferior [for PE]," and "VQ takes too long" were characteristic of general responses from treating providers.
Conclusion: VQ imaging remains under-utilized in patients at risk of AKI. Perceived limitations to diagnostic accuracy and study availability are contributors to underutilization.

Ophthalmology

Vision Dysfunction in Circadian Clock Gene Bmal Mice

◆ **Humza Khan**, Deepa Mathew, Qianyi Luo, Ashay Bhatwadekar

Background: The circadian rhythm disruption due to shift work results in a range of disorders such as metabolic disturbances, obesity, cardiovascular diseases, and insulin resistance. Interestingly, the core clock gene Brain and Muscle ARNT-Like 1 (Bmal1), is altered in shift workers. We reasoned dysregulated Bmal will affect normal vision function. To do so, a genetically modified mouse with disrupted Bmal was assessed for visual function. We hypothesized that Bmal knockout mice will exhibit reduced retinal functions such as impaired acuity, accommodation, and tracking.
Methods: The Bmal+/- mice were inbred and genotyped to obtain wild-types (WT), Bmal+/-, and Bmal-/-. To assess the retinal function, we performed electroretinogram (ERG) recordings at the zeitgeber times (ZT) of 0, 6, 12, and 18, which correspond to 7 AM, 1 PM, 7 PM, and 1 AM, respectively, under both scotopic and photopic conditions. The optokinetic response (OKR) assessments were measured in-between ZT-3-ZT7.
Results: Consistent with previous studies, the 'a' wave and 'b' wave amplitudes of WT mice demonstrated a circadian rhythm under scotopic conditions. There was a decrease in ERG amplitude of Bmal+/-, and Bmal-/- when compared to the WT group. Under photopic conditions, the circadian peak of ERG amplitude was reversed for Bmal-/- when compared to both WT and Bmal+/- mice. The OKR assessment was decreased substantially for Bmal+/- (0.3748c/d), and Bmal-/- (0.3130c/d) as compared to the WT mice (0.4827c/d).
Conclusion: Our studies demonstrate that the loss of Bmal leads to vision dysfunction, possibly due to the impaired rod and cone function. Furthermore, using a mouse model of circadian rhythm dysfunction, we identified that individuals working on irregular shifts might be vulnerable to vision dysfunction, and our studies warrant timely testing of visual function and strategies for prevention of vision problems in shift workers.

Pediatrics

The Effect of Chronic Hypoxia on Airway Remodeling in Murine Model of Asthma

◆ **Jordan Ozolin**, Amy Gao, Page Perez, Robert Tepper

Background: Chronic hypoxia during growth and development results in adaptive responses to increase oxygen transport to tissues, such as increasing lung volume and lung diffusion. Asthma is characterized by airway hyper-reactivity, which can result from increased airway smooth muscle (ASM) and airway remodeling following airway inflammation. Chronic hypoxia may attenuate airway inflammation, airway reactivity and airway remodeling in patients with asthma. Measured by in vivo airway resistance in response to 50 mg/ml Ach, our preliminary data suggests that rats conceived and raised under chronic hypoxic conditions (15% O2) exhibit lower airway reactivity, compared to room air controls (20% O2) at baseline (0.397, 0.789 respectively) and following Ova sensitization/challenge (0.696, 1.159 respectively). We hypothesized lower airway reactivity was associated with less ASM in response to hypoxic conditions.
Methods: Sprague Dawley rats were conceived, raised and evaluated in 4 groups: hypoxia/PBS challenge (HA-PBS); hypoxia/Ova challenge (HA-Ova); normoxia/PBS challenge (RA-PBS); normoxia/Ova challenge (RA-Ova). The lung tissue (4 animals/group) was fixed, sectioned, and ASM was quantified by immunohistochemistry using imageJ software.
Results: Measured ASM (mm2) from each group was log transformed to normalize data acquired from various lumen sizes and the least square means of each group were calculated. Airways from HA-PBS animals (N= 59) tended to have the lowest ASM, and ASM progressively increased in RA-PBS (N=41), HA-Ova (N=58) and RA-Ova groups (N=38 airways) [-6.41, -6.3, -6.26, -6.17]. There was an excellent correlation between ASM and airway resistance; more ASM was associated with greater airway reactivity (Pearson correlation of 0.99).
Conclusions: Chronic hypoxia may suppress ASM development, as well as suppress the increase in ASM associated with atopic inflammation. Understanding the mechanisms that inhibit ASM growth under conditions of chronic hypoxia may provide insight into new therapies for asthma.

Ophthalmology

Retinal and Choroidal Vascular Abnormalities Contribute to the Conversion From Dry to Wet Age-Related Macular Degeneration: A Theoretical Approach

◆ **Rowe, Lucas W.**; Harris, Alon; Ciulla, Thomas A.; Chiaravialli, Greta; Verticchio Vercellin, Alice Chandra; Siesky, Brent A.; Guidoboni, Giovanna

Background: Age-related macular degeneration (AMD) is the leading cause of adult blindness in the developed world, and can be classified as one of two types: dry or wet. Abnormalities in retinal and choroidal vasculature may influence dry-to-wet conversion. This study represents a first attempt to use mathematical modeling to characterize the impact of retinal and choroidal blood flow on the oxygenation of retinal layers at various distances from the macula, in healthy individuals and AMD patients.
Methods: The macula is modeled as 7 layers: ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), photoreceptors layer (PH), retinal pigmented epithelium (RPE). Oxygen supply is provided by the vitreous, the choroid, and by three retinal capillary plexi. Oxygen profiles through the macular tissue are calculated by simulating the balance between O_2 supply, consumption and diffusion in: physiological baseline conditions; AMD conditions.
Results: Choroidal vasculature impairment affects tissue more proximal to the macular center, retinal blood flow impairment affects tissue more proximal to the macular periphery, and oxygenation of the foveal avascular zone is not affected by retinal vasculature impairment. The decrease in oxygenation due to retinal and choroidal blood flow impairment in AMD is more prominent in the RPE, PH and ONL in all three anatomical zones of the macula.
Conclusion: Our mathematical model revealed that reduced choroidal and retinal oxygenation in AMD patients mostly affects the RPE and PH layers, regardless of the distance from the macula. This finding may explain hypoxia inducible factor-1 (HIF-1) production in these layers, which leads to enhanced vascular endothelial growth factor (VEGF) production, causing neovascularization and conversion to wet AMD. Our model suggests that treatment modalities aimed at maintaining stable oxygenation in dry AMD patients may prevent conversion to wet AMD, and reduce vision loss in these patients.

Orthopaedic Surgery

The Effects of High Fat Diet, Bone Healing, and BMP-2 Treatment on Endothelial Cell Growth and Function

◆ **Seungyup Sun**, Fazal Ur Rehman Bhatti, Ushashi C. Dadwal, Olatundun D. Awosanya, Caio de Andrade Staut, Stephen K. Mendenhall, Anthony J. Perugini, III, Conner R. Valuch, Nikhil P. Tewari, Rohit U. Nagaraj, Hanisha L. Battina, Murad K. Nazzal, Rachel J. Blosser, Jiliang Li, Melissa A. Kacena

Background: Angiogenesis is a vital process during regeneration of bone tissue. The aim of this study was to investigate the angiogenic and proliferation potential of endothelial cells (ECs) isolated from lungs (LECs) and bone marrow (BMECs) from obesity-induced type 2 diabetic mice that were treated with bone morphogenetic protein-2 (BMP-2, local administration at the time of surgery) to heal a femoral segmental bone defect (SBD).
Methods: Mice were fed a high fat diet (HFD) to induce a type 2 diabetic-like phenotype while low fat diet (LFD) animals served as controls. The HFD and LFD groups were treated with either saline or BMP-2 at the time of surgery. LECs and BMECs were isolated three weeks post-surgery and were characterized by CD31 expression. Proliferation was examined by DAPI stain or crystal violet assay. Angiogenic potential was evaluated by tube formation and cell migration.
Results: The proliferation of LECs and BMECs was not altered by diet or BMP-2 treatment. HFD increased the tube formation ability of LECs. Interestingly, BMP-2 treatment at the time of surgery reduced tube formation in LECs and humeri BMECs. However, migration of BMECs from HFD mice treated with BMP-2 was increased compared to BMECs from HFD mice treated with saline. Gene expression of CD31, FLT-1, ANGPT1, and ANGPT2 were similar between humeri BMECs and LECs.
Conclusion: To date, this is the first study that depicts the systemic influence of fracture surgery and local BMP-2 treatment on the proliferation and angiogenic potential of ECs derived from the bone marrow and lungs.

Health Care System Distrust, Race, and Surrogate Decision Making Regarding Code Status

◆ **Sang Yoon Na**, James E. Slaven, Emily S. Burke, Alexia M. Torke

Background: Studies have shown African American patients are more likely to prefer aggressive life-sustaining treatments such as cardiopulmonary resuscitation (CPR) at end-of-life compared to non-Hispanic White patients. Given prior racial disparities in healthcare, low trust has been proposed to explain these preferences. We examined factors that influence surrogate decision makers' preference for Do Not Resuscitate (DNR) status for hospitalized older adults who cannot make their own medical decisions. We explored whether race is associated with surrogate preference for DNR status for a hospitalized older adult. We also examine if race is associated with distrust and if the race/code status relationship is partially explained (mediated) by distrust in the healthcare system.
Methods: Analyses were conducted using data from an observational study of patient/surrogate dyads admitted to an ICU in a Midwest metropolitan area. Distrust was assessed using the Revised Health Care System Distrust Scale. A single item asked the surrogate which status they thought was best for the patient, full code or DNR.
Results: In bivariate analysis, higher proportion of African American surrogates showed preference for full code (62.4% vs 37.6%, p=0.0001). After adjusting for trust and sociodemographic and psychological covariates, race was still significantly associated with DNR preference (aOR = 1.92; 95% CI: 1.04, 3.55; p=0.0382). Surrogate race did not show significant association with distrust in bivariate or multivariable analysis, which adjusted for sociodemographic and psychological covariates (p=0.3867).
Conclusion: Contrary to previous studies, we observed no association between surrogate race and distrust of the health care system. Differences in code status preference may be due to other factors related to race and culture. In order to ensure patients are receiving end-of-life care that is consistent with their values, more work is needed to understand the cultural complexities behind end-of-life care preference.

Natural Killer Cell Transfusion for Glioblastoma Tumor Volume Analysis via MR/PET Imaging Coregistration with Histology

Acchiardo J, Marcadis P, Smiley S, Yun YH, Hutchins GD, Veronesi MC

Abstract

Hypothesis: Immunotherapies hold great promise for the treatment of highly resistant cancers, such as glioblastoma (GBM). We hypothesized that high powered imaging modalities can be effectively combined to quantitatively assess the therapeutic efficacy of human derived natural killer (hNK) cells in an orthoptic xenografted mouse model of GBM.
Methods: Cells derived from recurrent human GBM were implanted intracranially into 10 mice. Mice in the treatment (n=5) and control (n=4) groups were given IV hNK cells and physiological saline, respectively. MRI and PET scans were performed 4 and 6 weeks after implantation. Ex vivo validation with histology was performed at week 6. Software analysis was conducted via Qimage (courtesy of Dr. Hutchins) and Indica Labs - HALO.
Results: Mean growth rates are as follows: T1 volume (μL) – 4.1 (control) vs 2.3 (hNK treated) ($p < 0.01$). T2 volume (μL) – 6.0 (control) vs 2.7 (hNK treated). PET volume (μL) – 3.1 (control) vs 2.1 (hNK treated), SUV – 5.4 (control) vs 3.0 (hNK treated).
Conclusion: Tumor volume and SUV were reduced in hNK treated mice compared to control, with a correlated lower histology TBR, suggesting MR/PET imaging is effective for in vivo assessment of therapeutic efficacy in the mouse model. Phase II of this model will include genetically engineered NK cells with greater tumor localization ability and killing capacity. Clinical trials of NK cell immunotherapy with MR/PET imaging may one day offer remission to patients suffering from an, as yet, incurable cancer.

Introduction

Glioblastoma Multiforme (GBM) is a deadly astrocytoma brain cancer with a 5-year survival rate of under 10%, comprising 17% of all brain tumors diagnosed. Even with advancements in our understanding of its molecular composition, GBM remains largely resistant to traditional treatment options, in part, because it can mutate to create an immunosuppressive extra-cellular microenvironment. Preclinical models of disease are of particular importance for establishing novel clinical treatments. Immunotherapy is a novel class of systemic cancer therapies that holds great promise in the treatment of highly resistant brain tumors such as GBM. Immunotherapy is based on activating the body's immune system to target cancer. Among immune cells, natural killer (NK) cells, in particular, play a critical role in the early host defense against cancer, which can be harnessed to become more effective cancer killing agents. In vivo neuroimaging has become an essential tool to assess such novel cancer therapies in real time, but its adaptation in the mouse model is uncommon. Combination imaging techniques provide both the high anatomical detail of MRI with the powerful quantitative detection sensitivity of PET. Additionally, PET radiotracers, such as 18F-FET, Cu-PTSM, and Cu-ETS, have been developed to assess a wide range of tumor characteristics using standard uptake value (SUV), a quantitation of initial injected dose, animal weight and signal intensity.

Methods

TT was validated via ProSense 680 Fluorescence (PF) cathepsin detection. Approximately 5 x 106 hNK cells (n=5) or saline control (n=4) were weekly injected IV into an intracranial mouse model of GBM (GB10) tumors. Therapy mice received supplemental IL-2 IP three times weekly for NK cell stimulation. MRI and PET scans were performed four and six weeks after implantation. At time of death brains were surgically removed, stored in sucrose, and histological slices were prepared at the pathology lab. Multimodal imaging of MR T1CE, T2, and 18F-FET PET was co-registered and analyzed to track tumor growth. Analysis of tumor volume and SUV was conducted using Qimage and TBR using Indica Labs – HALO software. MR/PET volumes of interest (VOI)s were generated using histogram parameters with our algorithm for rejecting background brain intensity. Histology regions of interest were hand drawn within HALO software, cell type was analyzed and TBR area was computed via proprietary algorithm. CD56 histological staining was conducted to detect NK cell localization, quantity and characteristics of immune response. Cu-ETS and Cu-PTSM PET radiotracers were administered IV, in a subset of mice, to assess metabolic activity and blood brain barrier (BBB) intactness.

Conclusion

Multimodality MR/PET imaging analysis demonstrated significantly lower T1 contrast-enhanced MRI tumor volume in the hNK treated group compared with the saline (control) treated group. hNK treatment showed a trend of reduction in tumor growth rate, SUV and variability following analysis of MRI T2 sequence and PET 18F-FET images with histological correlation of lower TBR. Histological staining showed CD56dim NK cells localized in the tumor, preferentially, and at higher concentrations in the treatment group. PET analysis suggests that brain perfusion and BBB intactness can be effectively assessed via Cu-PTSM and Cu-ETS, respectively.

Discussion

Despite positive trends, only T1CE volume data expressed significance, likely due to the inherent variability in each analysis modality and low sample size. T2 is weighted for fluid, meaning it may pick up edema surrounding tumor upon analysis, accounting for increased variability. A T2 FLAIR sequence may be considered to suppress fluid signal from CSF. PET can also be susceptible to variability due to its lower spatial resolution. This can make it difficult to accurately assess exact perimeter of tumors. Co-registration using MRI in combination with PET imaging is critical to overcoming the inherent limitations within each modality. The CD56 staining in hNK treated mice suggests that the NK cells injected were not of the CD56bright variety, theorized as a precursor to mature CD56dim/CD16+ NK cells. Moving forward, CD16 staining would be helpful in further identifying the cell types within these tumors. Decreased tumor variability in the treatment group could be explained by the hypothesis that GBM growth was made more uniform by NK cell presence. Perhaps through NK cell interruption of the extracellular matrix surrounding the tumor, GBM was unable to provide itself nutrients for proliferation. The lower sample size in this study will be supplemented with future trials to establish multimodal statistical significance in overall growth rate reduction. This and future studies would also benefit from longer NK treatment times.

Future Impact

Phase II of this animal model development and cellular therapy pipeline creation coupled with multi-modality imaging was recently funded through the Walther Oncology Embedding Program to build on the current work. Phase II will include genetically engineered NK cells with greater tumor localization ability and tumor killing capacity by Dr. Sandro Matosevic and his team at Purdue University, Lafayette. If approved for clinical trials, NK cell immunotherapy with multimodal MR/PET imaging could one day offer remission to patients suffering from an, as yet, incurable cancer.

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Gold Humanism Honor Society

The following pages contain individual essays written by students of the Gold Humanism Honor Society, a national honor society that aims to highlight compassionate patient care and humanism within the field of medicine. Many students showcase narratives that highlight interactions with patients that taught them not only how to manage disease medically, but also important lessons about the human condition - how to treat all those who seek our help with empathy and understanding. We hope that the examples that follow inspire all those who read it to provide holistic care to all our patients.

Mohammad W. Aref

She brought her husband to the ED; he wasn't feeling well. Shortly after he arrived, his heart arrested and she was rushed out of the room. We went to update her. The doctor did all the talking, I just stood by her, put my hand on her right shoulder and squeezed gently. Her husband regained a normal heart rhythm but needed to be intubated and was rushed to the cath lab. We went to update her. I didn't say a word. The doctor did all the talking; I just stood by her, put my hand on her right shoulder and squeezed gently. Her husband had 100% stenosis in his left circumflex and a massive MI. He was not arousable and was rushed to the ICU. And for the next few days on rounds, when we arrived at her husband's room and gathered around our patient, I took my position on her right side with my hand on her shoulder, didn't have a word to say, and squeezed gently. Her husband's heart, kidneys, and liver were failing, and his brain was injured, maybe permanently. We held a family meeting in hopes of better understanding his wishes, and I didn't really know where to stand. She looked at me with tears in her eyes, and smiled, ushering me to my position on her right side and reached to put my hand on her shoulder.

Months later, I was in the hospital lobby when I noticed a woman in a wheelchair smiling ecstatically at me. At first, I did not recognize her, but then I remembered my place - at her side with my hand on her shoulder. She turned her neck and looked up at her daughter who was pushing the wheelchair and said, 'that's him'. Her daughter laughed and said, 'She can't stop talking about you - the best doctor in the hospital'. I wonder if she noticed that this 'doctor' didn't write a single order, didn't perform a single procedure, and barely said a word.

I was humbled to know how simple kindness can be – a hand on her shoulder.

Michaela Campbell

"Is there anything else I can help you with ma'am?" I end every patient encounter with a similar phrase and usually hope the answer is no, because as a medical student I tend not to have answers to a lot of patients' questions. As I get ready to walk out the door, my patient responds, "Actually yes, I'm feeling pretty lonely today, and since you asked would you mind sitting and talking with me for a few minutes?" I put aside anxious thoughts of all the other patients I had to see before meeting with my attending and decided I could give her a few minutes, as listening is one thing I am qualified to do as a medical student. We talked about her experiences with polio, the painful death of her husband, and her children and grandchildren that are often too busy to visit her. Although it's like we talked for hours, I was only in the room for an additional 15 minutes and still had plenty of time to see my other patients. But with that short conversation, I developed a strong understanding for my patient as an entire person, and she felt like the healthcare team truly cared about her. This basic interaction once again reminded me how important humanism in medicine is. People should feel like they are being treated as humans – not just as a disease. Taking a few minutes to form a connection helps patients feel heard and gives them greater trust and confidence in their care team. Finally, this encounter helped me realize that although there are many things I can't do as a medical student, I can still be a valuable asset in one of the most important aspects of medicine: compassionate and humanistic care.

Jennifer Choe

I met a patient during my VA Internal Medicine rotation. He was a 63-year-old male who came into the ED with a severely necrotic left leg secondary to peripheral vascular disease. He had been on antibiotics for months but finally came into the ED because he could no longer tolerate the pain. Upon first meeting me, he made it clear he did not want an amputation and that he wished to only have his pain controlled with the help of palliative care. This was baffling to me because he was otherwise relatively healthy and most likely would have a long life expectancy if we were to remove the infection source. I argued with him in the beginning and we even brought Psychiatry on board. As we got to know each other, he opened up about his life and how hard and lonely it had been to be the sole caregiver of his wife who had suffered a hypoxic brain injury. He had not been able to take care of himself and now he was terrified of possibly being brought back after a cardiac arrest with a similar outcome as his wife. He was strict DNR and did not want to risk going under anesthesia. He was tired and wanted to be comfortable. I did not agree with his decision but he taught me that ultimately as a physician you need to respect the patient's wishes. All you can do is be there for them and do what you can do to make them feel physically and psychologically comfortable during a very difficult time in their lives. I felt ashamed I had judged him initially for allowing his leg to get this bad before seeking help or that I just assumed he was giving up. After I was done with my service I visited him to eat M&Ms and watch TV with him a few more times before he was discharged with hospice. He taught me that we have no idea what people have been through in their lives and that if we give them the opportunity to tell you their life story you can come to understand and respect their decisions.

Kyle Davis

As a medical student it often feels difficult to find meaningful ways to contribute to the care of patients. You can get trapped into trying to find "medical problems" that you can address that have been ignored by other members of the team. But luckily, as a student you have one thing that other healthcare providers may lack, and that is time. Time to spend that extra twenty minutes to explain the treatment plan, time to learn more about their family, or time to just give the patient someone to talk with to lift their spirts.

One of the most impactful patient interactions that I experienced during my clinical rotations involved a young boy hospitalized for a cystic fibrosis exacerbation. He was not one of my assigned patients but through the week I would hear about him during rounds and would say hello from the doorway of his room. Most mornings he was alone because his mother was taking care of her other children at home. He looked uncomfortable as he sat in bed playing video games gasping for breaths through his BiPAP nasal mask. I wanted to help this patient but what really could I offer that has not been addressed already by the resident and attending. One day on rounds the resident mentioned that the patient was begging her to play video games with him. Immediately, I regretted that I had not thought of doing this days earlier, as it was something that only required extra time. Later that day, me another medical student entered his room and challenged him to a round of Mario Kart. His eyes sparked open and he began to smile. He was ecstatic and it felt amazing to provide him a little joy during his long hospital stay.

Obviously, I probably won't be able to play video games with all my patients in the future, but I will do my best to look past just the "medical problems" at hand and try find simple ways to lift their spirts.

Maritza Gómez

Taking a patient's history is a necessity in medicine, and for me, it is also an opportunity to gain insight into the lives of my patients to help better understand them. One patient, in particular, exemplified this more meaningfully than I ever expected. S.D., a 64-year-old Hispanic male with systemic amyloidosis, was likely too complex a patient for a student on her first rotation. However, as the daughter of immigrant parents I understood intimately how language barriers interfere with medical care. For this reason, I felt called to support him throughout his extensive stay by being someone who could advocate for his needs in his native language. While listening to his history, I learned that he had three children and that he was an avid reader. I formed a relationship with him and his family and, when they were not there, I called to update them on the status of their dad, as that is the kind of treatment I would like my own family to receive.

Serving him helped me reconnect with my love for medicine, as I felt that I made a strong connection with him. He was the kind of patient that was always remembered by medical teams because he always had a smile on him. Once his condition started deteriorating, he was transferred to another team. However, I continued to visit him as he was always filled with gratitude when I came. We used to converse about books, listen to music and sometimes I would read to him.

When his FiO2 maxed on the bipap machine, I informed his family that, unfortunately, he was nearing his final days. Sadly, he became my first patient to pass away, but he lives on in my memory and in the impact he had on who I aspire to be as a healer. I am convinced, now more than ever, that achieving an understanding of our patients' lives is crucial to delivering competent and compassionate care.

Katherine Griffin

I met Ana early into a ten-month stay with Floating Doctors, an organization providing weekly clinics to the indigenous population of northern Panama. Ana lived in Valle Escondido, a small village in the islands of northern Panama with no electricity, no clean water and a 30-minute cayuco paddle away from the nearest city. Even further was the children's hospital in David, a three-hour taxi ride away. Further yet was Panama City, the only place in the country able to fix Ana's congenital heart defect, a 7mm patent ductus arteriosus (PDA). Ana's mom, a 21-year-old mother of 4, had no job and no way to get her child to David for imaging, let alone to Panama City for surgery. One day at a clinic in Valle Escondido, I saw a little girl sitting on the sidelines of the soccer field. It was Ana, looking longingly out to play with her peers. She then told me of her "broken heart" which she felt by placing a hand over her heart; a sign that I now recognize as a palpable thrill, a sign of a significant heart murmur. I reviewed her records and noticed the murmur documented at every visit, but no treatment plan had been discussed. I soon learned about some interventional cardiologists coming to Panama City to repair congenital heart defects pro bono. Months went by as I continued to fight and advocate for Ana. After meticulously coordinating food, transportation and housing, I was able to accompany Ana and her mother to Panama City for surgery. After riding all night on a bus, we walked into the hospital and checked in for surgery. We sat eagerly in pre-op while whirls of people checked on us. After Ana returned from the OR, her mom placed her hand lightly on her daughter's chest, looked at me with tears in her eyes and said, "It's gone. Thank you." And so, I say to my future self, my future colleagues, and my future patients: keep persevering. Keep fighting to overcome each and every seemingly insurmountable barrier and keep advocating for those who can't.

Emily Hentz

'This next patient is an elderly woman, here for follow up on her blood pressure,' I was informed before seeing her at the family medicine clinic. An all too familiar chief concern in primary care, I went in and began my standard screening questions. A few minutes into my interview, her responses to my light probing regarding depression and anxiety prompted further questions as my concern for her mental health increased. This interview unearthed her life story: a child abandoned by her parents, sexually abused at a young age, then thrust into an abusive marriage, an immigrant struggling with limited support in a foreign country, her only son passed away at a young age due to medical conditions, and now having difficulties taking care of her aging husband on her own. By the end of her social history we were both tearful, and yet she was offering me a tissue.

Apart from her story being quite poignant, it left a sense of awe at how well the clinic and my preceptor have done in aiding patients in this community. She specifically noted that her motivation to keep herself healthy has stemmed from this clinic. "Aqui hay amor," she boasted, referring to the love and support she received from the staff at the clinic amidst the loneliness and lack of support that has permeated her life.

This is the kind of physician I aspire to be. An extra ten minutes spent genuinely listening to a patient's background can create the trust needed for a patient to be motivated in their own self-care. I hope to continue to acknowledge and validate my patients' experiences before working with them to address their physical needs. Building strong, lasting relationships that enable me to empower patients to improve their health is what I look forward to as a future physician.

Guadalupe Jimenez

Throughout my clerkships, one family in particular reminded me of why I decided to change my career and become a physician. My patient was 7 years old with intussusception as a result of HSP. Her father spoke Burmese and was unable to communicate with me or any of the staff. The patient was stoic but brave. She spoke with the surgeon and they informed her that there was a chance that they would have to get surgery. The surgeon used the translating services to communicate with her father. After the surgeon left, I was curious on their understanding, so I applied the teach-back method. I realized that even though the translating services were utilized, her father didn't have a great understanding of the potential gravity of the situation. This hurt me because I knew that he was in fear, he was scared for his daughter's health. I know from personal experience that he has made taken extraordinary measures to ensure that his daughter grows up in an environment free from unnecessary threats to her well-being. Families come to country hoping to escape war, violence, poverty etc. They want what's best for their families but often find themselves helpless in certain situations. Recognizing that this was the story of my family, it touched my heart and I remembered why I entered medicine. I want to advocate for families like them until the day I retire. It's often more time consuming to have to use translating services, but it's necessary. I would lovingly encourage everyone, do your best to ensure your patient is receiving the same information as all of your other English speaking patients. Always keep in mind that they are fearful, and the best way to fight fear is with information.

Sandra Jones

Patients deserve a vote of confidence in the same way one would encourage a teammate, coworker, or loved one. One of my patients had survived a terrible MVC and regained consciousness. Everything hurt, she was unable to move, and she was afraid. Each day my colleagues and I told her our medical plans to keep her as informed as possible, performed thorough exams to catch everything we could, and went on our way to let her retain at least a measure of privacy. And yet every day it was evident she was miserable. One afternoon, I decided to stop by her room and saw her mom telling her that she can do this, that she has made a miraculous recovery, and showering her with encouragement as she worked with physical therapy. I specifically remember how the mom told the patient "I'm so proud of you." As soon as she heard this, brightness flooded her eyes and a smile spread across her face. That next day I saw her listening to music and even making jokes with her care team for the first time in her 40+ day hospital admission. She was working harder than ever with physical therapy and seeking more insight into her care. Though part of an amalgamation of reasons why she was improving, it was clear that the moment she and her mother shared was imperative to her improvement. I had no idea that pausing the medicine to lift her spirits could mean so much for her recovery. This realization was magnified when I recognized how little time my colleagues and I had spent acknowledging her emotional state. Caring for her taught me about the invaluable role of encouragement, even in the modern era of advanced surgical techniques and life preserving technology she was dependent on. This moment helped me see that medicine cannot work its best if it's not paired with a whole lot of positive human reinforcement.

Mathew K. Marsee

"How am I supposed to care full time for my husband with end-stage dementia AND fight my own cancer at the same time?!" she said to me during my first week on the general surgery rotation. I was only a month into my second year in medical school when the general surgeon I was following sat down with a woman in her late sixties to break the news that she has metastatic breast cancer. This kind, gentle woman had come into clinic two weeks prior with a massive necrotic mass growing off of her left breast. I'm going to tell you how this interaction changed the way that I look at a physician's role as a healthcare "provider". How our role as educators is arguably as important to our patients' outcomes as are our diagnostic or therapeutic skills.

Our patient told us that she "knew it was bad", but that she put off seeing a doctor because she didn't "have the time or the money to take care of this right now with everything going on with [her] husbands' dementia".

Following that visit, the surgeon told me that the hospital has a mobile mammography truck that holds yearly events relatively close to our patients' home; and that prices are based on patient income. "Are you kidding me?!" I thought. There is a resource that could've caught this cancer earlier and potentially the life of this patient (and by default her husband who depends on her care); and it's both convenient AND affordable?!

Nicholas Elias Kalafatis

I was once rotating on internal medicine and during my inpatient rounds, the physician I was with was absolutely brilliant. His only downfall, I would say, was that he often had difficulty communicating with patients about their diagnosis in layman's terms. One time in particular stood out to me because the patient turned to me during the physician's summary with a look of confusion and proceeded to ask me to describe what is going on. I felt embarrassed for the doctor who was trying to explain to the patient what was going on with their health but on the same note understand that for the patient, this is a difficult time in their lives and they do not understand all of the medical terminology that we so effortlessly use on a daily basis. This memory has taught me that my role as a physician is not only to treat disease but also to teach disease to my patients. I love to educate my fellow peers or under-classmates on topics, and I feel like I have a calling for teaching as well and hope to teach someday in the future. Moments like this where you get to educate a patient on what is going on with their body feel exhilarating for me because understanding and learning is something that I feel everyone can appreciate and enjoy.

Joshua Mifflin

I used to shy away from human suffering. Not just physical avoidance, but mental blocking, numbing myself subconsciously instinctually. As a CNA in a LTAC hospital prior to medical school, I did not understand it. I saw it, interacted with it, but certainly did not feel it. That began to change as my experience in medicine grew.

In medicine you are surrounded not just by patients but their stories. It is truly a blessing to be in our profession. The opportunities to learn and grow from those we treat are endless. I am reflecting on a recent patient: a 50 year-old man who presented to the ED having suffered a stroke with a medication list you might expect from a man a couple decades senior with a busy medical history.

When I explained to him what the imaging showed, it was clear that it was weighing on him. The man was assuredly suffering already. His diabetes had taken half of his foot, and his functionality had been on a steady decline at a time he desperately needed it to take care of his debilitated mother. The next day on rounds, we learned he had spent years with depression and suicidal thoughts. He began lashing out on staff becoming verbally abusive as he attempted to grapple with the implications of his new prognosis. Nursing continued to struggle and emergency psychiatric detainment seemed unavoidable.

I went and listened to him. Years of dealing with undeserved suffering poured out of him as I learned about his life. I confided in my fiancé that evening on my way home telling her about his outbursts and his story. I told her I wish I had known what to say, what to do to help him get through it. I thought I'd failed.

Cally Miller

Bob was an 80-year-old gentleman who I admitted to the hospital with pneumonia. He had end stage COPD and the pneumonia had really knocked him down. His wife Suzy was present with him at the hospital. They were kind, personable people and I enjoyed talking with them. One morning, in a conversation, Suzy told me that she had throat cancer 2 years before, and her husband Bob had taken care of her during that time. She was so strong, could speak well, and was doing great. I never would have known she'd had throat cancer if she hadn't told me. They continued to tell me the story of how they had cared for one another in difficult times…and all the help that they had met along the way: people who had offered to house them in Indianapolis for 2 months in an apartment so she could attend treatment, doctors who believed in recovery, and even how Bob pushing Suzy around in a wheelchair all over University Hospital had helped improve his lung function. To hear their story was such an inspiration. And then they continued by thanking me. They said that they felt that medical professionals never got enough appreciation, and that they felt so happy with the care they were receiving at the hospital where I was rotating at that time. They also took time to encourage me and it was a major blessing to me. This was the first time in my medical career that a patient had thanked me for care I was providing, and it was both a humbling and reassuring experience. I will always remember Bob and Suzy. Sometimes we are there for patients and feel like we are not appreciated, but just taking extra time to chat with them makes a big difference. It's a reminder that if we continue to see our patients as people—rather than just another disease entity such as COPD or diabetes—both the patient and we ourselves can be blessed in ways that we could never imagine.

Amit Nag

On my first day of inpatient internal medicine, I was assigned to a patient who would end up being on our service for longer than we expected. He was admitted due to anasarca and taught me at least two things: what does anasarca mean (after a brief google search on that first day, I learned it meant generalized swelling around the entire body) and how our interactions on a human level aid our ability to teach and heal. The service happened to be slow when I started, and so I was allowed that which all doctors want more of with their patients: time. In my early morning pre-rounds or in the afternoons when he had an upcoming procedure, I was able to talk with him and get to know about his life and how this disease affected him. Like how he had a dog named Trucker at home that loved to go on walks, but who had to stay inside because his edema made him short of breath within seconds. Through the stories he told me, I was able to connect with him beyond his diagnosis and lab values, and he took it to heart when I told him that he would need to cut down on eating his favorite snack: raw tomatoes with salt. Despite that bad news, I could provide him with some hope that even though he couldn't be discharged safely that day or the next, in a few days' time, he would be able to take Trucker out on that walk. I respected him more and more as we talked, and in turn he trusted me and the counsel I provided. And one day, when he was worried that the increased dose of Lasix we were giving him would hurt his kidneys, I was able to allay his fears and educate him as to the reasoning behind our plan. He taught me that our patients have lives outside of their care, and that we can provide better care when we know more about them as people.

Paige Schultheis

During my internal medicine rotation, I had an opportunity to form a unique connection with a patient on the Heme/Onc service. This patient was an aspiring singer, mother of two, and someone newly diagnosed with acute myeloid leukemia (AML). Despite her diagnosis of a high-risk leukemia, she was the person you saw doing 70 laps around the floor and greeting everyone with a smile. She was extremely optimistic and positive always.

She and I clicked. This was a patient who I was visiting multiple times a day just to chat. We listened to her music, talked about my upcoming exams, and of course, discussed her care daily. To my surprise, during my morning rounds one morning, she ended up confiding her fears in me and broke down in tears. In the moment, we hugged and she cried. I didn't say anything, but I was there.

This experience provided me with a first; the first patient that I truly connected with. This relationship showed me the kind of connection I want to build with as many patients as I can in my future career. It showed me that forming that connection is what can provide resilience and dedication in your care. As much as these relationships can fuel myself, I believe forming these connections will also help me understand my patient's goals in their care as well.

Madalyn Vonderohe

On my first day of my Pediatrics rotation, my attending said something that has stuck with me to this day. She told us that, anecdotally, she believes patients with medical students on their care team receive better, more holistic care because resident physicians often have to spend more time taking care of their computers rather than their patients. As incompetent and clueless as I have felt this year, I have tried to keep that sentiment with me and be the best advocate for my patients as I can be, as their voices often slip through the cracks between over-burdened residents.

This story, though, is about one who refused to let her patient's care suffer, despite discovering that the medical system had already failed him. This patient had been previously healthy, a grandfather, father, husband, brother beloved by his entire family. He loved to be active, talking walks with his dog daily, visiting with the neighbors and entertaining the children of his apartment complex. You would have no idea, though, looking at him in the ICU, mere days away from his passing. What started out as simple cellulitis from a diabetic foot ulcer turned into fulminant bacteremia with massive end-organ damage, and we couldn't seem to figure out why.

My resident refused to let him go without figuring out what happened. She dug through his chart, spoke to physicians, nurses, family, staying at the hospital beyond any of her colleagues in order to put the pieces together. Ultimately, through all of her digging and her persistence, she discovered that due to a miscommunication between practitioners, the patient was not initially placed on antibiotics when the cellulitis was diagnosed, allowing the infection to spread to the bloodstream. This delay in care ultimately led to the likely preventable death of this patient, the loss of a grandfather, father, husband, and brother.

While her determination and investigation into what happened to this patient could not prevent his death, it will hopefully prevent something similar from happening again in the hands of the same facility. Witnessing this all unfold taught me the lesson that you are never too busy to give your patient the best care they can get, and to constantly strive to improve the system for your future patients.

Raghav Vadhul

As a citizen of a developed nation, I often find myself taking for granted the luxuries that I am privileged to have at my disposal. One of these luxuries, which should perhaps be considered a necessity, is my easy access to vision care. I have worn glasses since I was in middle school and would be practically blind without them. However, it is commonplace for people in the developing world to live their whole lives without access to this service. I witnessed firsthand how severely lack of access to vision care affects patients and how dramatically the work of a few compassionate physicians can change these patients' lives for the better.

I met Mr. R in Cheyyar, India the summer after first year when I was volunteering as a Global Impact Fellow. Mr. R was a farmer who had worked his whole life in the fields and had developed severe bilateral cataracts as a result. His vision was so poor that he could not even see a hand waving directly in front of his face. Because of Cheyyar's remote location and his financial situation, he had never seen a doctor that could have helped him. Mr. R could have easily been forgotten and abandoned by society were it not for the compassionate physicians that decided to make it their own mission to help him and others like him. These physicians took days off from their own clinics to travel and provide free vision screens and cataracts surgeries for patients like Mr. R. We served everyone from local politicians to the homeless, and in a society where social status often defines how you are treated by others, these physicians demonstrated genuine humanism by putting the patients' humanity before some social construct of worth.

Clearly, these physicians had no personal gains from performing these services; in fact, they likely lost capital from missing clinic days. However, they understood the greater impact of serving their community and helped me understand what my pledge to "practice my profession with conscience and dignity" looks like in practice.

Kirsten Zborek

In our first two years of medical school we routinely talk about giving bad news. This usually takes place in a classroom, in a textbook format, without real patients, and pretend bad news. However, observing real bad news delivered to real people doesn't look or feel like what we practice. I've observed physicians giving diagnoses, unfavorable lab results, or poor outcomes. Sometimes it goes well, with both the patient and physician agreeing on treatments and understanding their prognosis. Other times it doesn't. During my third-year rotations, I can recall one event that went particularly poorly. We were seeing a patient in the Emergency Room for a seizure. Unbeknownst to the patient, his hemoglobin A1C was 10%. We did not believe his newly diagnosed diabetes was the cause of his seizure. On our way to see the patient we let the attending know the patient did not yet know about the diabetes diagnosis. Maybe it had slipped her mind by the time we got to the room, but she began the conversation talking about "your diabetes". Not only was the patient in shock and disbelief, but so was I. These few words would change how the patient lived his life and my heart ached for him. We dropped this bad news on him with little explanation or empathy and left the pieces for another physician to pick up. When the patient further questioned what his new diabetes diagnosis meant my attending said, "Your primary doctor will help you", not realizing he did not have a primary physician. I left that encounter confused and saddened. As I reflect on this experience it's easy to pinpoint what went poorly. In contrast, I've found it more difficult to identify what goes well in positive interactions. One lesson I have taken away from my third year clerkships is that physicians who continue to show every patient compassion and remain sensitive to the burden their words may carry undoubtably built a better relationship with their patients.

Celestina Okoye

The first two years of medical school was a whirlwind of being in the books and constantly stressing about each upcoming exam. I often looked forward to the end of second year and finally being able to see patients. When third year arrived and my Pediatrics rotation started, I was excited to finally have more patient interaction; however, this emotion was entangled with nervousness around adapting to a new environment. Towards the end of my month on inpatient pediatrics, I was assigned to an 18-year-old girl. I introduced myself to her and her father who was in the room and began to take an initial history. She had been diagnosed with lupus a few years ago and had frequent flare-ups that required hospitalization. In the afternoons, I would have time to go and check on her and, in this time, I learned a lot more about her. She often talked about her dreams of becoming a cardiothoracic surgeon. We also talked about her prom coming up and the dress she was going to wear that her father made himself and we looked together for matching shoes. Her father was so proud of her. He talked about how worried he was that her flare-ups would keep her from accomplishing her dreams, but he admired her determination and resilience. When it was time for her to be discharged, her father asked to speak with me outside of the room. He thanked me for making his daughter feel "normal" and taking the time out talk about other things besides her lupus. I told him how much I appreciated his kind words and I knew this would leave a lasting impression on me. This experience reminded me of my belief that at the core of every human is the desire to create meaningful bonds. Along with building these bonds comes compassion for one another. If we continue to remember that in the stressors of becoming physicians who will be taking care of many sick patients, we will be able to continue when times become tough.

Mackenzie MacGrath

On my medicine Sub-I, I helped take care of a man named Mr. D. He was admitted for reported rapid onset ascites and jaundice. No one knew what was wrong, but after multiple rounds of testing he was thought to have alcoholic cirrhosis. His presentation was unusual, and his vitals and labs were not consistent with that etiology. I didn't believe what everyone else thought.

I had good rapport with Mr. D, and a large portion of my time at the hospital was dedicated to his care. After a long day on call, my resident asked me to go check on him before heading home around 2230. The next morning as I pre-rounded at 0600, he asked me if I had even gone home - because I was the last person he saw before going to bed and the first person he saw that morning.

The last thing I said to Mr. D was that I had a day off, but I would see him on Monday. Over the weekend, he was transferred to another hospital. I was a little surprised but very relieved as this hospital was the best place for him. Then the COVID-19 pandemic hit, and medical students were removed from the clinical environment. In those initial days off, I frequently thought of Mr. D and was very curious about his outcome. When I texted my resident for updates, I was given the shocking news that he had passed. I was devastated. I have experienced death before, but the loss of a patient was different. I still don't quite have the right words to describe all the emotions that flood my heart, but I feel humbled that I helped with his care. Mr. D will be a patient that I will remember for a very long time.

◆ **Shae Jensen**

No one had told her, but she was dying - heart failure at 31 years old. Years of IV drug use that resulted in endocarditis, now leaving her with a failing heart. Her legs was swelling, and her lungs repeatedly filled with fluid. She kept leaving against medical advice, presumably to indulge her detrimental addiction. We either assumed she must've known she was dying, or we didn't care if she did, both possibilities breaking my heart. No one told her, but she was dying. And without a continuous course of intravenous antibiotics and heart valve replacement surgery, her months were numbered.

I met her on the first day of my internal medicine rotation. She graciously invited me to sit with her and shared about what seemed to weigh most heavily on her heart - her newest daughter she hasn't met yet. She had delivered her daughter prematurely 2 weeks prior due to life threatening pregnancy complications. While my patient wrestled against the last days of her life in and out of the hospital, her newest daughter fought for her first days in the NICU across the street. I asked permission to discuss her health. She knew that her heart had an infection, but she did not know that her state was critical and her heart was failing. No one had told her, but she was dying. My white coat felt even shorter than it was as I realized that educating and empowering her with information about her health could include sharing about the severity and fatality of her condition. As a medical student, I didn't know how to perform surgeries or order complex therapies, but I had the time to talk. And so we talked.

We drew pictures and talked through her disease, and as she asked more questions she began to understand the pathway by which her IV drug use led to tricuspid valve failure and the irreversibility of her disease state. Although this conversation was scary and tearful for both of us, it empowered her to be invested in her health journey and pathway to recovery. My patient taught me about the importance of learning our patients' stories, building relationships, and being on a team with our patients. She taught me about the power of empowering our patients through education. I am thankful my patient shared her journey with me.

"Whoever offered that Sabonis contract should be fired."

Such talk may be found in a sports bar in Indiana, where Pacers players are often the center of attention. However, I was not expecting to find a critic of Domantas Sabonis' contract extension in an inpatient room at Eskenazi hospital.

During my internal medicine rotation at Eskenazi, I was lucky to be invited to watch a Pacers game with one of our patients. She was awaiting workup for a mass that was causing her significant fatigue and weight loss. Through our conversations, I learned that not only was basketball a way for her to escape the monotony of the hospital schedule, but it was also something that gave her joy and energy despite her condition. So, after I was dismissed for the day, I made my way to her room to share happiness in our mutual interest. To my surprise, I walked into a room that looked more like Bankers Life Fieldhouse than a hospital room, one that was packed full of her grandchildren.

In that moment, I saw evidence that no matter the diagnosis, patients should not be defined by their illness. Seeing her eyes brighten and face so animated when talking about the Pacers with us proved how far reaching loving relationships can be. It also reminded me that medicine is more than just interpreting lab values or findings on a physical exam; rather, it is the relationships that we build and moments like watching Pacers basketball with others that make it a profession worth serving. As a developing physician, I hope to keep this experience in mind and build lasting, holistic relationships with my future patients. I aspire to always see the person behind the patient, understanding that along with their physical health comes emotional and psychological wellbeing that must also be nurtured.

Mr. F did not want to stay in the hospital; he wanted to go home to his farm on the coast. Mr. F's daughter disagreed. Mr. F had not been on medication for a single day of his 90+ years of life until one month prior to meeting me, and he did not want anything new. Mr. F's daughter was open to medical management. Mr. F only knew he was having a stroke because he couldn't read his sheet music while playing his violin. Mr. F's daughter wanted him to make it to his upcoming birthday where his ten children and many grandchildren were planning a performance using all their musical talents, which had started with Mr. F and his wife. Mr. F, a humble and strong man, cried when he told me that his wife had died in a hospital, far away from the farm where they had raised their ten children; Mr. F didn't want that for himself. Mr. F's daughter cried when she told me how scared she was that if her father went back to the farm, no one would find him quick enough if he got sick. I wanted to cry when I experienced their tears. I didn't have a good answer for either of them; as I listened to the story of Mr. F's life, I could understand why treatments to prolong his life weren't valuable to him if he couldn't live that life in the only place he knew as home. I could also understand Mr. F's daughter's desire to take care of her father who had given her so much. When we discharged Mr. F, there still was no clear plan for where he would go long term. I've thought about him often though; I've hoped that he made it to the musical performance and hoped that he is resting at his farm. I've also thought about the lesson he gave me to remember why we do medicine—not just to fix bodies and prolong the days of life, but to help prolong the kind of days that people love to live.

I've had many inspiring experiences with patient's and patient families and am so privileged and honored to have been allowed to be a part of their care. One incidence stands out to me. It was during my Family Medicine clinic. The patient had recently lost her job and was worried whether she was able to afford her appointment that day and her medications that month. Her multiple chronic conditions leave her often immobilized due to pain. In addition to her financial and physical health concerns, she had recently started being more active to help with her grandchildren as the children's father had been recently incarcerated due to domestic violence against her daughter. Needless to say, she was feeling overwhelmed, tears streaming down her face. And although we provided her comprehensive management of her chronic conditions and additional community resources regarding her other social considerations, it seemed that my preceptor could sense that something else was needed. She knew the patient well and offered to say a prayer for her and her family. In that small moment in which we prayed in this tiny exam room, I could sense, even if just a little, there was a weight lifted off the patient's shoulders. The prayer not only acknowledged the patient's struggles, but also offered hope that like many bad times, this too shall pass. This showed me the importance of building a relationship with patients and how often times the little things outside of "medicine" are the most important parts. It is the "art of medicine."

The first time I met KA, the small 3 year-old Mexican boy was terrified at the sight of any physician. He was crying and screaming and all that was running through my head was how can we help you. His mom was trying to calm him down but nothing seemed to work. She seemed very shy and embarrassed (but I do not mean this in a negative way) at her son's behavior. Over the next few days, KA became known as the "cryer" and the patient that no one wanted to go see, but this inspired me to get to know him and his incredible mom, who was with him 24/7 despite having 3 other children at home. Slowly KA started to warm up to me. Every time I saw him all I could think of was how resilient he was, he had already undergone chemotherapy and an organ transplant in almost the same amount of time that I have been in medical school. The little champ had a great sense of humor and a sly personality. We found out a couple of days into his stay that his crying episodes were due to intussusception, and he was treated appropriately. On my last day of the rotation I knew I could not leave without saying goodbye. When I entered his room, I knew that I was not only saying bye to him but to his entire family whom I got to know well. For the past two years, I have run the Monumental Marathon to give my medal away to a true champion, a fighter. This year it only felt right to give it to KA. I can still perfectly picture his face when he first saw the medal; he could not believe it belonged to him. The medal was bigger than his palm, and he would not let it go.

Ever since the day I said bye to you, K, I think of you. I think of all the potential you have in you, and I just hope that one day you realize that you have made a huge impact on my life. You were more than a patient to me—you became my motivation. I will continue to run and get to know all the "difficult" patients, but most of all refrain from labeling someone as "difficult" but instead take the time to know them as a human.

CJ was admitted again as the painful expansion of her abdomen and yellowing of her complexion bore evidence to fluid that kept accumulating. This pattern had repeated itself over the past weeks, with paracentesis only providing temporary relief. Each hospitalization stabilized her until the encephalopathy resolved. She needed the definitive fix of a liver transplant yet didn't have a high enough MELD score to qualify. Additionally, she had recently become uninsured, and without drastic intervention, she would not live to reach 65 to qualify for Medicare. CJ had no family in the area, her closest son a flight away. She knew the gravity of her situation but never complained. As I went each morning to check on her before our neurology team rounds, it was bittersweet. She expressed her gratitude for the consistency of our short morning visits, but I felt frustration at what little I could do in the big picture. Near the end of the week, our team had an afternoon where we had finished seeing all our consults, so I went back to see CJ. We sat for half an hour, talking about her family, hobbies, projects she had at home—anything besides treatment options and medical care. When I eventually had to leave, she thanked me for taking the time to come sit and listen. Even without having any new answers for her, I left that day feeling that those 30 minutes were the most meaningful care I had been able to provide all week. In the daily rhythm of rounds, consults, orders, and charting, it can be easy to lose sight of the shared need for human interaction, the need to be seen beyond the roles we inhabit as patient or physician. That encounter was a reminder to strive to see my patients as the individuals they are, for their lives outside of the space in which we interact

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One of the prevailing pieces of advice that I heard before heading overseas to work at the Moi University Teaching Hospital was to be prepared for people to have conditions that could be treated in the United States, but not in Kenya, and for some of them to die because of it. I had months to think about this, and by the time I was getting on my flight in Chicago to leave, I thought I would be prepared. I wasn't prepared.

While on the female adult ward, it wasn't uncommon for us to have multiple patients with conditions that stemmed from an underlying chronic lung disease. Whether that be right heart failure, a superimposing secondary pneumonia, or a straightforward COPD exacerbation, we treated it all, and most people recovered. One of my first days on service, we had a patient come in with a relatively uncomplicated COPD exacerbation. We treated her with steroids, inhalers, and azithromycin, and initially she looked a lot better. Normally I wouldn't give this case much of a second thought. In the United States, they often would get better, and if they didn't we could transition them to BiPAP support as a bridge until they did improve. However, we didn't have BiPAP there, and she didn't improve. Over the coming hours she progressively went into worse and worse hypercarbic respiratory failure, and we weren't able to transition her over to ICU level care because of a lack of beds. Unfortunately, she passed away, and I felt terrible for letting something so straightforward become the cause of her loss of life.

When reflecting on this, there wasn't anything else that could have been done based on the situation that was present. We simply just needed supplies that weren't available to us. However, this experience has impacted my current path as a developing physician. It was a humbling experience to realize that even with all the knowledge in the world, health outcomes are still so dependent on the things we have and the barriers to care that are present in an area. I am committed to advocating for those faced with these types of disparities, and I hope that I can be an instrument for preventing these deaths in the future.

Mr. V is a father, a grandfather, a lover of nature documentaries, and a huge fan of Coca-Cola, who happens to have end stage renal disease at the relatively young age of 54. I had the privilege of being a part of his care team when he was admitted to our medicine service with anemia and, what we thought was, an elusive GI bleed. He spent two weeks on our inpatient service undergoing invasive procedures to diagnose the bleed, but we could never find it. All the while, he was getting blood transfusion after blood transfusion and maintaining his weekly dialysis schedule. Mr. V was also what most healthcare professionals would call a difficult, or non-compliant, patient. He frequently refused medications and blood draws from the nurses, opted out of speaking with the medicine team on morning rounds, and even denied visits from his family members. I did not blame him, because I would be grumpy too if I had spent weeks in a hospital without answers. One day, after three straight mornings of him refusing to speak to me when I pre-rounded in the morning, I asked him what had been the most difficult part about this hospitalization. He replied, "Being scared." I asked him what was frightening him, thinking that it would be the life-threatening anemia, but he looked at me, rolled his eyes, and said, "Needles, I am deathly afraid of needles." I reflected over his time in the hospital recognizing that almost every aspect of his treatment had required being stuck with a needle. He told me that to combat this during his dialysis appointments his daughter usually comes with and lets him squeeze her hand as the needle goes in. From that point on, our team's care plan focused on minimizing needle sticks, and I was given my job as the designated hand squeezer for the remainder of his hospitalization. It was incredible to see how us taking Mr. V's fears, priorities, and preferences into consideration transformed him from "difficult patient" to the kind father, grandfather, nature documentary lover, Coca-Cola fan, and patient that he was.

During my inpatient pediatrics rotation, I picked up a young patient who had just immigrated to the US with her mother. She had gotten ill during her time in a detention center and was having serious trouble breathing by the time she arrived in the hospital. There was an obvious language barrier, culture shock, and lack of trust affecting the patient's mother. We were able to treat her daughter quickly and while she was initially transferred to the PICU, she was able to go home within a few days. This patient interaction is one of the most impactful patient interactions I have experienced. Witnessing a patient in our community who had such a clear tie to far-reaching global health was unexpected for me. From this interaction I was able to see first-hand how easily a young child can go from healthy to gravely ill simply from being held in a location without readily available access to health care. Being on the team treating this patient reinvigorated my passion for addressing health care inequities both in our local community and abroad. Working with this family challenged me to understand what my role will be in the future treating patients who are affected by the political climate in this country. It's clearly a topic that many disagree on and I learned an important lesson in balancing my role as a physician and my role as an activist in our local community and our country.

There was something different on my resident's face. I could tell as soon as I walked into our team room that morning. I had seen A LOT of difficult diagnoses in my first week of the Heme/Onc wards but immediately knew this morning was different. What are the odds that two little girls, the same age, would come in with similar leukemia diagnoses on the same night? Our team geared up for rounds, knowing even though we were about to give very treatable diagnoses to these families, it still wouldn't be easy. The first room was difficult: crying parents, distraught feelings, and pure agony. This poor family had justifiably lost all sense of control and hope in this moment. I expected more of the same as we approach the second room and I began to feel sick to my stomach. I'll never forget what this mother said, as tears slowly rolled down both parents' faces, "No matter what happens we'll get through it, day by day, as a family." Her calm manner instantly had an effect on myself and the entire team. How could she be so calm staring at the mountain in front of her? Didn't she know how her family and daughter's life was soon going to change? I spent the rest of that rotation and the many months since then thinking about the stark contrast I saw that day. The way we approach any patient interact can be reflected back at us. So as I continue to grow through medical school I strive to bring the calm demeanor of this mother to every encounter knowing that even the same diagnosis is never the exact same in two different patients. Now as I approach residency, I hope that when my time comes to care for patients on my own I will be ready to gently and meaningfully guide my patients through their disease while adapting to every individual I have the opportunity to care for.

Serving one another is vital for the flourishment of an individual and community. Medicine has helped me to recognize this truth. It is where I feel most alive and serving in this way further drives my passion to live by this truth. One such instance was on my Palliative Care rotation. My staff provided wonderful guidance but gave us autonomy when navigating difficult conversations. My first instance of delivering horrible news of malignant cancer with a prognosis of weeks to live was to a hardworking man who was estranged from his son. Work was so vital to his identity that he was still fielding calls from his crew while he was in the hospital in significant pain. This initial delivery of bad news became something I did daily, as he dwelled in the denial portion of the grieving process for a whole week. Every day, I spent at least an hour talking about his construction work, how much he missed his son, his stepdaughter that took care of him, and how Speedway has the best creamer, but Starbucks has better coffee. However, he would not tell his family his diagnosis, claiming that he would call later, on his own time. Eventually, I was able to call his family with him, and informed them of the extent of his cancer. The news seemed to finally hit him then that he was going to die soon, and he started to cry. Not too long after, he passed away. After debriefing with my staff, it struck me that this was my first instance of caring for an individual to their death, rather than toward the hope of healing. As physicians, one can be continuously working toward the next cure, but many times, the answer on how to best serve a patient is to be present, and work toward a peaceful death.

New on the wards, I made my way to the room of my first patient whose complaint was shortness of breath. Your answers were short. You didn't make eye contact with me once. With a history of untreated HIV, you were diagnosed with a disseminated fungal infection. Day after day, you fought the wicked side effects of the systemic therapy you were on. I watched you battle depression and yearn for family, friends, and familiarity. No smiles. Why didn't they seek treatment sooner? Questions like this came up every day on rounds. Then the shortness of breath improved. Your mood perked up. You started gaining weight. I saw you smile for the first time. We started having daily conversations in the afternoon. You were homeless for a period of time after you learned of your HIV diagnosis. The medicines back that weren't nearly as easy to take daily. You battled addiction and depression and lost most of your family along the way. However, playing cards always made you feel at home. You would always find time to do that. On my last day of service, I came into your room with an Uno deck in my hands. The smile the broke out on your face will forever be embroidered in my memory. It was during this last interaction that you told me you were ready to start taking your daily medications. I beamed with joy at the new-found responsibility you had taken in your health. With that, I told you it had been a pleasure taking of you and that I was so happy to see your improving health and your smile. As physicians, we can lose sight on why our patients don't take the appropriate steps to ensure their health. It's easy and takes very little time to project judgements on our patients. However, it's much more rewarding, enlightening, and compassionate when we take extra time to ask ourselves why our patients do what they do. With this little bit of extra time and effort, we are able to help our patients far beyond our clinic spaces or hospital rooms.

My 1st rotation as a third-year medical student was internal medicine, and as a neophyte clinician, I fast realized that the greatest thing that I could offer was my time, a realization which resulted in many long conversations with the patients on our service. And through one of these conversations, I found that despite his diagnoses of heart failure, renal failure, bilateral lower extremity lymphedema, and a non-healing foot ulcer, 60-year-old Mr. Roberts (pseudonym) was most bothered by rectal bleeding. We consulted gastroenterology, who suspected hemorrhoids, and from their note, I learned that: 1. A previous colonoscopy had failed to remove the entirety of a colonic polyp, 2. There were two endoscopic options – one would allow for polyp removal but not hemorrhoid banding, while the other would allow for hemorrhoid banding but not polyp removal – and 3. Gastroenterology had recommended polyp removal, to which Mr. Roberts had agreed. However, when I pre-rounded on him, Mr. Roberts was unaware that the procedure probably would not treat the bleeding. This experience taught me that our problem lists (i.e., with the residual polyp being most important) are often at odds with our patients' (i.e., with rectal bleeding being most important). I am in no position to judge the gastroenterology team for its decision, but ever since, I have tried to be more aware of how my problem lists align – or do not align – with my patients'.

When I was on my IM overnight call shift, I met a gentle, smiling elderly woman—Ms. D—who had been complaining of recent abdominal distress. A few days later, when I was back on the day shift, I saw that Ms. D was on our census with a small bowel obstruction. I requested to take her on as my patient, since we already knew each other. She had an extensive medical history but was always cheerful and brightened up when I came by to talk, even when my questions were painstaking and repetitive.

Over time, however, I found out that her family members weren't able to visit every day, so I started stopping by her room to chat every day after being dismissed, even after switching to other services. Even her family came to be familiar with me and was always appreciative that I came to visit when they couldn't

Several months later, I happened to hear two radiologists talking to each other about a patient that had experienced two major strokes in the past three days. I went over to learn about the case, but my heart sank when I saw the name on the CT—it was Ms. D

When I went to her room, Ms. D's daughter introduced me to the family members I hadn't yet met, and explained what had happened in the past few days. Ms. D could no longer eat or speak, was half paralyzed, and would rarely respond to stimuli. She offered me a seat next to Ms. D's bed; I sat there for a few minutes, held Ms. D's hand, and told her how much it had meant to me to be able to be a part of her life, and how glad I was to see her again. Until that moment, I hadn't known whether she was awake or blissfully unaware, but she gave my hand a long squeeze, and I squeezed back.

That squeeze meant everything to me. I realized how profoundly we had influenced each other's lives, and the invaluable power of human connection in medicine.

Some of my most impactful experiences with patients has been during my times volunteering at the free student outreach clinic. One poignant encounter I had was with a patient I met my second year, whom I'll call Caleb. Caleb, like many of the neighbors we treat was going through a harder season. He had bad glaucoma which caused him to go blind in his left eye and was going to cost him his right eye without intervention. He needed some glaucoma meds and possibly a surgery. It was his first time at the clinic and as a second year I was blessed to have more free time to talk with him and hear his story. It was so simple. He had a stable job in Illinois with insurance but made one bad choice which causes him to be in jail for a couple years. While in jail his left eye went blind and he was started on medicine which helped the right. When he got out he left his job to move to Indianapolis to be with his dying mother. Since he left his job, he lost his insurance. Now he can't afford the $8 of medications he needs to prevent complete violence. What struck me was how similar we could be. One bad choice, one sick family member, one medical problem—and then I could be homeless and about to go blind. It was a less in the assumptions I make of patients. Caleb is a reminder that when a patient is late, or is not compliant, or makes some "unwise" choices in my eyes, to remember that I am only two steps away from poverty, or illness, or need of grace. All of us are—no matter how far we have come. So I need to keep humility and compassion while caring for future neighbors like Caleb.

Addendum: Caleb is doing well on his medications as of March 2020 and got a new job and a PCP through Eskenazi.

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.

Qualitative Analysis of Syringe Services Program: Using Stories to Foster Changes in Public Health Crisis

◆ **Nafisch A**

Addiction has impacted populations for centuries, and with the emerging field of narrative medicine, clinicians can address individuals' health and illness accounts in greater depth. By listening to people's stories and interpretations, qualitative researchers and health care professionals can, based on conversations with key participants involved in the situation, foster changes in medical and public health issues, like the opioid crisis in Indiana.

To determine how to most effectively move forward in combatting the challenges that Scott County and Indiana as a whole currently face with opioid addiction and HIV and hepatitis C outbreaks, fifteen interviews were conducted and coded via the qualitative data analysis program, NVivo 10, for recurring themes related to the implementation of syringe services programs. Law enforcement, first responders, and local health department employees were interviewed to discuss their experiences with the programs and working directly with clients dealing with opioid addiction.

Conducting qualitative studies focusing on the community in Scott County allowed researchers to work closely with public health officials and other key figures to attempt to determine how to preserve and refine the current solution of syringe services programs. By asking questions, reviewing responses, and thoroughly discussing themes with a group of researchers from distinctive backgrounds, interviewees' stories are more effectively heard and understood. Examining data obtained from individuals who play significant roles in working with community members impacted by drug abuse and HIV outbreak cases and analyzing a previous study done with community members enrolled in syringe services programs led to new recommendations and treatments to come to light.

Complex Diagnosis of Tuberculous Meningitis

◆ **Roesler A**, Christodoulides A, Sandler R, Petrucciani A, Allen D

A 33-year-old woman, 14 weeks pregnant, presented to the emergency room with a four day history of headache with chills, fever, night sweats, nausea, and vomiting. She had several risk factors for TB, including immigrating from Mexico, a weakened immune system, and a recent pregnancy. Meningitis was suspected, however a lumbar puncture was unable to be performed due to patient discomfort. Empiric antibiotics were given and the patient was discharged home after symptoms improved a day later. Following discharge, the patient experienced a spontaneous abortion the next day that was thought to be unrelated to the illness. One week later, she returned to the emergency room with similar symptoms of headache, fever, nausea, and vomiting. During this visit, a lumbar puncture was performed and cerebral spinal fluid analysis revealed aseptic meningitis. Stain and culture were negative but the T-spot returned positive. The health department was contacted and the patient was started on rifampin, isoniazid, pyrazinamide, and ethambutol. As of January, the patient is responding well to therapy.

Pulmonary TB has drastically declined in the United States, however the rate of meningeal TB has not. Early detection is pivotal as 15-40% of cases prove fatal, despite effective treatment. In Indiana alone, there were 116 cases of tuberculosis in 2018, with 16.4% being extrapulmonary. Pregnant women are at significant risk, with tuberculosis being an important contributor to maternal mortality and one of the top three leading causes of death for women aged 15-45 globally.

Disseminated TB has the ability to present in a myriad of manners depending on organ systems being afflicted, making initial diagnosis a challenge. With this being said, early diagnosis and treatment is pivotal to improved patient outcomes as the timeliness of clinical action has been shown to drastically improve patient outcomes.

Is Sedentary Behavior Associated with Dysglycemia in Youth with Obesity?

◆ **Sotomayor AA**, El-Mikati H, Yazel-Smith K, Hannon T

Background: The childhood obesity epidemic is linked with an increase in dysglycemia and type 2 diabetes (T2D) amongst youth. Adolescence is associated with decreased levels of physical activity, however, there is a paucity of research investigating physical activity measures and dysglycemia in youth. We hypothesize that decreased physical activity and/or increased sitting time is positively correlated with dysglycemia.
Methods: Study participants were youth aged 10-21y with a BMI >85th percentile for age and gender. Accelerometers (activPAL) and the FELS Physical Activity Questionnaire (FELS PAQ) were used to assess objective and self-reported physical activity levels. Glucose tolerance was assessed with 2-hour oral glucose tolerance tests (OGTT). Independent t-tests were used to compare physical activity levels for participants with normal glucose tolerance (NGT) and dysglycemia. Correlation analysis was performed to evaluate relationships between measures of physical activity and OGTT measures.
Results: Participants with NGT (N=27) and dysglycemia (N=26) had comparable demographics; age, race, and ethnicity. Hemoglobin A1c (HbA1c) ($p = 0.002$), average fasting glucose ($p<0.00$), indices of insulin resistance (HOMA-IR) ($p=.023$), insulin secretion (disposition index, DI, a marker of risk for T2D) ($p=.008$), 2-hour-OGTT measures for glucose ($p=.004$) and insulin ($p=.002$) differed between groups. There were not group differences for objective or self-reported measures of physical activity. For the entire cohort, sitting time was positively associated with OGTT 2hr glucose ($r=.38$, $p=.03$). However, a subgroup analysis showed that the association between sitting time and OGTT 2hr glucose was significant in the dysglycemia group only ($r = .64$, $p=.006$, vs $r = .016$, $p=.95$ for NGT group). Self-reported measures of activity (Likert scores) and OGTT measures for insulin and glucose were positively correlated.
Conclusion: Increased sitting time is associated with impaired glucose tolerance in youth with obesity at risk for T2D.

Low Oxygen Regulates Phenotypic Properties of Hematopoietic Stem Cells

◆ **Karlapudi A**, Bhagwat M, Pate S, Basile C, Dausinas P, Slack J, O'Leary H

Hematopietic stem cells (HSCs) reside in bone marrow in specialized low oxygen (O_2, 1-4%) niches and give rise to all cells of the immune system. However, previous HSC studies have been performed with cells collected in non-physiologic ambient air (O_2, ~20%). Past publications from our lab have shown that air exposure decreases stem cell number and their ability to engraft. Therefore, we investigated biomarker alterations in HSCs in native low O_2 conditions to understand their phenotype, function, and signaling patterns. One of these biomarkers was dipeptidylpeptidase 4 (DPP4), a serine protease expressed on hematopoietic cells that also has scaffolding functions and regulates, signaling, homing, and engraftment. We hypothesized that expression and activity of DPP4 in HSCs would be modulated by surrounding oxygen levels.

Thus, we isolated populations of HSCS from the bone marrow of C57BL/6 mice, exposed these cells to either normal or air or low oxygen conditions, and then treated these two populations with DPA and an antibody panel. We then collected data using flow cytometry, ImageStream, and a DPP4 activity assay. Results showed that DPP4 enzymatic activity was significantly decreased in HSC populations that were exposed to low oxygen conditions. However, the percent of $DPP4^+$ cells was significantly increased in cells exposed to low oxygen as well. These data suggest that DPP4, a major regulator of HSCs, is modulated by oxygen levels in ambient air. Therefore, DPP4 may serve as a clinical target to mimic the protective effects of low oxygen on HSCs. Further investigations of collaborative mechanistic pathways modulating DPP4 expression and activity may open new avenues in enhancing HSC transplantation.

Platelet Cryopreservation: A Means of Generating a Standardized In-Vitro Human Blood Clot

◆ **Christodoulides A** and Alves NJ

Background: Numerous models, both in-vitro and in-vivo, exist for the analysis of blood-clotting pharmacodynamics. However, reliance on animal models, fresh blood, or lack of a complete component profile translates to little standardization/reproducibility of clotting parameters. Given the above limitations, the goal of our study was to generate a reproducible, physiologic human blood clot through cryopreservation of platelets. We hypothesized that the cryopreserved platelets would have a prolonged ability to generate reproducible clots from the same blood draw over time.
Methods: Initial efforts focused on understanding the metabolic effects of storing platelets, plasma, and red blood cells (RBCs) at either 25 or 4˚C over a period of 25-days. Glucose consumption was utilized as a proxy for metabolic activity and assessed using a glucose-hexokinase assay. Secondly: RBCs, platelets, and plasma were stored under their optimal storage conditions to retain functionality over time. RBCs at -4˚C+CPDA1, plasma at -20˚C, and platelets cryopreserved at -80˚C. Stored blood components were assessed over 13 weeks following recombination via Thromboelastographic (TEG) kinetic clotting readouts and compared to Whole Blood+CPDA1 samples stored at 4˚C. Blood samples were provided by healthy volunteers (n=5).
Results: Utilization of glucose by RBCs and platelets was significantly increased during storage at 25 versus 4˚C, with RBCs maintaining very consistent glucose consumption rates compared to platelets. More importantly, storage of platelets at -80˚C was shown to preserve clotting function for up to 14-weeks in comparison to WB that only maintained functionality for 2-weeks.
Conclusion: We were able to generate a reproducible synthetic human blood clot after 14 weeks of separated blood storage, as determined by TEG. Although not all parameters were preserved, we were able to maintain relative differences, ensuring consistent coagulability even with cryopreserved platelets. This marks a major stride toward the ultimate goal of generating a platform for pharmaceutical testing.

Utility of SPECT-CT in Localization of Normocalcemic Primary Hyperparathyroidism

◆ **Loncharich AJ**, Huffman EM, Tann M, McDow AD

Background: Normocalcemic primary hyperparathyroidism (nPHPT) is characterized by normal serum calcium levels in the setting of elevated parathyroid hormone, which is unattributable to secondary causes. Prior studies have examined localization accuracy using ultrasonography, scintigraphy, and four-dimensional computed tomography (4DCT), but little is known about the utility of SPECT-CT in this cohort. The aim of this study was to investigate the utility of SPECT-CT in nPHPT patients.
Methods: We performed a retrospective analysis of patients receiving preoperative parathyroid localization at a single institution between 2015-2018. Exclusion criteria included patients with renal failure, vitamin D deficiency, malabsorptive disorders, liver disease, hypercalciuria, and certain medications. All patients underwent pre-operative localization with SPECT-CT, which entailed early and late planar images of neck and mediastinum following administration of Tc-99m sestamibi, SPECT, and CT with and without contrast. All patients were evaluated by an otolaryngologist or endocrine surgeon before surgery. Parathyroidectomy was performed with intraoperative PTH monitoring and pathologic confirmation of disease.
Results: A total of 783 patients were analyzed with 39 patients meeting inclusion criteria. The mean age of the patient cohort was 63.6+/-11 years and 87.2% were female. The mean preoperative calcium, PTH, and Vitamin D were 10.3+/-0.2 mg/dL, 102.6+/-45.7 pg/mL, and 48.5+/-13.7 ng/mL, respectively. Of the patients undergoing pre-operative bone mineral density scan, 43.3% and 53.3% had osteopenia and osteoporosis, respectively. Kidney stones were present in 25.6% of the cohort. SPECT-CT revealed a single gland in 69.2% and multiglandular disease (MGD) in 7.7% of patients. Pathology revealed 61.5% had a single adenoma and 38.5% had MGD. SPECT-CT determined the correct laterality of disease for 53.8% of patients.
Conclusion: SPECT-CT accurately lateralized disease in over half of patients with normocalcemic primary hyperparathyroidism. Compared to prior studies, SPECT-CT is a superior method of parathyroid localization than both ultrasonography and scintigraphy, and is comparable to 4DCT.

L-Carnitine Deficiency Unmasked After Roux-en-y Gastric Bypass Surgery

◆ **Pikus A**, Patel P, Carlos WG

Clinical Significance: Levocarnitine deficiency is an inherited metabolic disorder consisting of a defect in transport of long chain fatty acids into the mitochondria leading to a buildup of lipids in multiple organs. Patients after gastric bypass are especially susceptible to nutritional deficiencies which may unmask such diseases. Gastric bypass-related hyperammonemia is a known complication with presentation ranging from weeks to years post op and carries 50% mortality, most commonly seen in females.
Clinical Case Summary: A 56 year old female with a history of Roux-en-Y gastric bypass presented for a worsening rash. She reported 10 days of a painful sloughing rash in her lower extremities, hands, abdomen, and vulvar/sacral areas. She was suspected to have cellulitis, given IV clindamycin and discharged home with cephalexin. She returned due to rapid spreading of her rash, diarrhea, dysphagia, visual changes, and dysuria. Physical exam was notable for tachycardia, right eye exudate and conjunctival injection, large areas of desquamation, and 2+ pitting edema. Initial workup for SJS was negative. She required MICU transfer due to cardiogenic shock and respiratory distress. Labs were significant for hyperammonemia (>250) and zinc/copper deficiency. She received lactulose with no improvement and was started on continuous veno-venous hemofiltration. She continued to be encephalopathic concerning for a urea cycle enzyme deficiency but the amino acid profile was not consistent with this. Genetics workup was more consistent with a L-Carnitine deficiency.
Conclusions: This case illustrates the importance of considering a variety of metabolic deficiencies that can fruition after a gastric bypass surgery. Moreover, this case brings awareness to the complex and oftentimes delayed presentation of L-Carnitine deficiency.

Expect the Unexpected: An Emergent Identification of a Cornual Ectopic Pregnancy

◆ **Tenbarge M**, Fraser A, Hand B, Shepler C, Underwood A, Thomas C, Benson H

A 36-year-old G5P4004 at 7w4d via LMP presented to OB triage with right sided abdominal pain and vomiting for several hours. She denied vaginal bleeding or passage of tissue. She had no history of prior ectopic pregnancies or abdominopelvic surgeries. BP was 83/49 and HR 80. Physical exam revealed exquisite tenderness to palpation in bilateral lower quadrants with involuntary guarding. Ultrasound demonstrated a left-sided cornual pregnancy measuring 10 weeks gestation with free fluid noted. Due to hemodynamic instability and peritoneal signs, she was emergently taken to the OR for an exploratory laparotomy. Approximately 800 mL of blood was noted upon opening and a left-sided cornual ectopic was confirmed. A left salpingectomy and wedge resection were performed without complication.

Cornual ectopic pregnancies are rare, comprising 2% of all ectopics, and are at high risk of hemorrhagic rupture. Risk factors include prior ectopic, IVF, and history of abdominopelvic surgery. Others include smoking, endometriosis, history of infertility, and history of Chlamydial infection.

Treatment approaches include surgery, methotrexate, or expectant management. Methotrexate is preferred because it is noninvasive and has comparable efficacy, safety, and fertility outcomes as surgery. Surgery is necessary in cases of rupture or large size. Studies appear to show that salpingectomy and salpingostomy lead to similar future fertility outcomes. Approximately ⅓ of women are candidates for methotrexate, while the other ⅔ require surgery.

In terms of future fertility, those with invasive uterine surgeries are at a higher risk for uterine rupture during subsequent pregnancies, a slightly higher risk of delivering preterm, and are more likely to deliver via cesarean section. Women who have had previous ectopics will also be at an increased risk for future ectopic pregnancies. Early identification and emergent intervention were paramount in this case and should help guide patient education on when to seek medical evaluation.

Early Clinical Predictors for Disease Progression and Severity in Novel Coronavirus SARS-CoV-2 to Guide Patient Triage and Management

◆ **Grisoli A**, Fraser A, Turchi AM, VanDeman HR, Koscielski MF, Riordan ND, Zimmer DF, Fraser ME

The SARS-CoV-2 pandemic has tested the limits of healthcare response systems on a global scale. A novel and rapidly spreading virus creates immediate need for data to predict clinical course and necessary interventions to allow hospital systems and providers to prepare and respond to the pandemic. Prolonged clinical course is common in COVID-19 patients. This has resulted in patients being discharged from emergency departments only to return in more severe disease states. A wide range of clinical severity across a large patient population creates difficulty for clinicians to identify which subsets may benefit from intervention, continued monitoring, hospitalization, or intensive care interventions. Providers require an effective set of criteria to accurately predict which patients will progress in illness to levels requiring inpatient support, ICU level care, or intubation followed by prolonged ventilation. With retrospective chart review of available patient data from Memorial Hospital in South Bend, Indiana, we have analyzed presenting signs, symptoms, quantified analysis of chest radiographs, and existing clinical prediction scoring systems to correlate with patient outcomes. These data may guide screening order sets to more accurately triage patients according to future need and allow for approximation of disease progression for individuals. These results will be vital to more efficiently utilize the available medical resources while minimizing unnecessary resources for patients with more mild progression and optimistic prognosis, throughout the course of this pandemic.

Dazed and Confused: Overlap Presentation of ADEM and CAPS

◆ **Jacobs A**, Bajpai S, Burns C, Tat K, Peterson R

Case: 4-year-old female with periodic fever syndrome presented to emergency department febrile to 103-105F for three days with preceding bilateral leg pain, characteristic of her periodic fevers. However, she did not respond to periodic fever treatment, remaining febrile with emesis, diarrhea and concern for visual hallucinations. Lumbar puncture showed lymphocytic pleocytosis. Empiric meningitis treatment was begun and stopped once ruled out. Hallucinations and altered mental status persisted. MRI showed multifocal hyperintense signals consistent with Acute Disseminated Encephalomyelitis (ADEM). Her ADEM diagnosis was complicated by a concomitant positive NLRP3 gene mutation consistent with Cryopyrin-Associated Periodic Fever Syndrome (CAPS).
Conclusion: CAPS is an autoinflammatory disorder in which pediatric patients recurrently present with fever, malaise, rash and arthralgia due to excessive production of IL-1beta. ADEM is a monophasic autoimmune demyelinating disease of the central nervous system associated with heightened expression of IL-1beta and TNF-alpha in response to infection or genetic proclivity. These inflammatory markers are toxic to myelin causing fever, headache and nausea, as well as neurologic symptoms.
Clinical significance: Both ADEM and CAPS cause severe immune-mediated responses due to overexpression of IL-1beta. Initial presentation of high fever and leg pain in a child with CAPS strongly suggests the onset of a fever flare. However, worsening GI and neurologic symptoms with refractory fever warrant a wider differential and prompt workup of other etiologies. ADEM must be on the differential for pediatric patients with acutely altered mental status and symptoms of periodic fever syndrome. This case poses a possible synergistic association between ADEM and CAPS due to immune dysregulation. Underlying CAPS and increased IL-1beta may have predisposed the patient to developing ADEM or exacerbated the systemic response.

Evaluation of Lever-Actuated Resonance Assistance (LARA) Wheelchair Device for Stroke Rehabilitation

◆ **Sedaghat A**, Harvey RL

For those with upper extremity impairment post-stroke, the road to recovery can be daunting. There is evidence that the lower extremity is faster to train and can regain function better than the upper extremity due to the fact that there are more resources available for the retraining of the lower limb. Originally developed at University of California Irvine, the Lever-Actuated Resonance Assistance (LARA) was created to solve these issues. A LARA device uses a lever drive and arm support to provide proper arm positioning and ease of use, as well as mechanical resonance with elastic bands to provide increased ease of mobility as compared to the traditional push rim wheelchair. LARA can be attached to a manual wheelchair and allow patients to rehabilitate their weakened extremity through stationary exercise, self-powered overground propulsion, or through a motor-based electronic interface that allows patients to use their arms to control a video game using the LARA wheelchair lever drives. In this study, the effects of the LARA wheelchair were investigated using post-stroke arm movement recovery with improvement in functioning as the primary outcome, as determined by the Upper Extremity Fugl-Meyer Assessment. Six individuals with a stoke within 30 days of enrollment were recruited from the inpatient Brain Innovation Center at the Shirley Ryan Abilitylab in Chicago, Illinois. Baseline Fugl-Meyer assessments were performed and subsequently compared to post-clinical Fugl-Meyer values after 3 weeks of therapy with LARA. Among these participants, the average increase in UE Fugl-Meyer scores was 4.3 ± 7.2 (95% CI, 4.27-4.3), with current literature citing a clinically significant increase in UE Fugl-Meyer score to be 4.25. It was thus determined that clinically significant improvement was seen among these participants overall. However, meaningful statistical conclusions cannot be drawn from the data at this time given the extremely small sample size.

Evaluation of Ross Aortic Valve Replacement on Patients Over the Age of 50

◆ **Gilani A**; Patel P, Brown J, Herrmann J

Background: The Ross procedure has traditionally been performed in younger patients due to lack of indefinite anticoagulation and long-term reintervention required of mechanical, xenograft, and allograft aortic valve replacement (AVR), respectively. This case series serves as an evaluation of follow-ups from all patients over the age of 50 who have undergone the Ross Procedure at Indiana University School of Medicine and seeks to understand the efficacy of utilizing pulmonary autograft (Ross) in older patients.
Methods: From 1995-2019, 71 patients over the age of 50 underwent the Ross Procedure at Indiana University School of Medicine. A retrospective chart review including pre-operative diagnoses, surgical notes, and longitudinal follow-ups were all evaluated in order to understand the long-term efficacy of the Ross procedure in this patient population.
Results: Patients in this review receiving the Ross Procedure were between the ages of 50-68, with a mean age of 56.9 years. Among the 71 patients, 58 [81.7%] presented pre-operatively with aortic stenosis while 13 [18.3%] presented with aortic insufficiency. Of the former 58 patients, 35 also presented with concomitant aortic regurgitation ranging from either mild [17], moderate, [11], or severe [7]. Patients had a median length-of-stay (LOS) of 5 days, with a mean of 7.7 days. There were no peri-operative mortalities; however, there were six instances of late mortality post-Ross ranging from two months to 16 years. There was also one instance of early mortality due to cardiac tamponade. Of 71 total patients, 63 (88.7%) experienced lifetime freedom from any valvular reintervention. Of those requiring reintervention, the average time to reintervention was 3.94 years, while 10-year freedom from reintervention was 90%. There were no mortalities associated with reintervention in any of the patients in this study.
Conclusions: The Ross Procedure is a viable alternative to mechanical and allograft AVR in individuals over the age 50, effectively alleviating the need for lifelong anticoagulation associated with mechanical AVR, as well as the consistent reintervention required with allograft AVR.

The Safety of Rituximab for the Treatment of Autoimmune Blistering Diseases

◆ **Mohammed A**, Li W, Rahnama-Moghadam S

Background: The anti-CD20 antibody rituximab has been shown to improve response rates in patients with autoimmune blistering diseases. However, the safety profile of rituximab is unclear. We aimed to systematically evaluate reports of complications.
Objective: To evaluate rituximab's safety for the treatment of autoimmune blistering diseases compared to other immunosuppressive agents.
Methods: The PRISMA checklist guided the reporting of the data. We searched Ovid MEDLINE(R), PubMed, EMBASE, Cochrane Library, World Health Organization's Global Index Medicus, EBSCO CINAHL Complete , Elsevier Scopus, the Web of Science Core Collection, and grey literature databases between 22 February 2019 and 10 July 2019 concentrating on autoimmune blistering diseases including pemphigus vulgaris, pemphigus vegetan, mucous membrane pemphigoid (cicatricial pemphigoid), bullous pemphigoid, and linear IgA.
Results: The literature search identified 4,567 articles. After screening titles and abstracts against the inclusion and exclusion criteria and assessing full texts, 95 articles were finally included in a narrative synthesis. 66 articles were cohort studies and case series which reported adverse affects in 253 patients over a denominator of 1548 patients with autoimmune blistering diseases (16.3%). Adverse events included sepsis, pneumocytis carini, osteomyelitis, phlegmon, cytomegalovirus, alveolitis, cellulitis, community acquired pneumonia, citrobacter, herpes simplex, herpes zoster, neutropenia, hypogammaglobulinemia, brain abscess, and infective endocarditis.
Conclusions: The available data suggests that despite the safety of rituximab for autoimmune blistering diseases, its use may be associated with significant adverse effects. Thus, close monitoring of patients treated with rituximab is recommended, along with prophylaxis as necessary.

A Prototype ECG for Neonatal Resuscitation

◆ **Woloshuk A**, Sivaprakasam A, Patel N, Warrick A, Witten A, Brennan L, Guckien Z, Diggins N, Garcia L, Wang L, Acchiardo J, Merrell J

Introduction: Evaluation of neonates based on cry, muscle tone, and heart rate is essential in triage of resuscitation efforts. In particular, the neonatal heart rate is used to determine the next steps in management. Auscultation or pulse oximetry can be used to assess heart rate, but these methods are often imprecise. ECG remains the gold standard of heart rate assessment . However, a barrier to ECG use during critical and time-sensitive actions is the fact that lead placement currently requires time, expertise, and space. The 2015 Neonatal Resuscitation Program (NRP) suggests that improved technology for rapid ECG assessment may result in better resuscitation outcomes [1].
Methods: Two surface electrodes were used to calculate potential differences between either the wrists, shoulders, or chest. The electrode potential difference was amplified and pre-filtered in a custom circuit prototype composed of an instrumental amplifier, a band-pass filter, and a notch filter. This signal was then sent to a computer which used a custom algorithm to further filter noise, create a threshold, and compute heart rate. A housing unit was constructed using computer-aided design (CAD) software to prototype the neonatal heart rate monitor. The housing protects the device power supply and internal hardware, while providing the clinician with easy access to the electric leads.
Results / Conclusions: The prototype neonatal heart rate monitor consists of a housing, ECG circuit, and postprocessing algorithm. Data collection from three locations on an adult volunteer suggests the signal collection and processing provides enough information to determine heart rate. Future design considerations involve reducing the size of the circuitry, refining the peak detection algorithm, and performing validation on ECG signals from neonates. Future implementation of this device has the potential to provide hassle-free, fast, and accurate heart rate monitoring in the neonatal resuscitation workflow.

Assessment of Bone Healing Agents for Promoting Bone Regeneration in Spaceflight

◆ **Sun S**, Zamarioli A, Dadwal UC, Childress PJ, Chakraborty N, Gautam A, Hammamieh R, Kacena MA

Background: When faced with difficult-to-heal bone injuries, orthopedic surgeons may use biological agents to stimulate healing. Bone morphogenetic protein-2 (BMP-2) and thrombopoietin (TPO), an FDA-approved agent and a novel therapeutic alternative respectively, can be used in these cases to stimulate osteogenesis. Additionally, with the growing interest in space exploration and colonization, these agents may be used to treat fractures in astronauts. This study aims to elucidate how the absence of gravity alters the mechanisms and actions of these agents.
Methods: 60 C57BL/6 male mice underwent a 2-mm femoral segmental bone defect (SBD) surgery and were treated with either saline, BMP-2, or TPO. These mice were further divided into groups that were either housed on Earth at the Kennedy Space Center (Ground) or in space at the International Space Station (Flight). After 4 weeks, bone regeneration in the femurs was assessed by micro-computed tomography (μCT).
Results: BMP-2 treatment induced successful callus formation and bone bridging in both Ground and Flight groups, but usage in flight resulted in lower bone density ($p=0.08$), fewer trabeculae ($p=0.03$), and higher trabeculae separation ($p=0.04$). Comparatively, TPO treatment induced better bone bridging in the Flight group than in the Ground group, with usage in flight resulting in higher bone density ($p=0.05$) and trabeculae connectivity ($p=0.001$).
Conclusions: BMP-2 has remarkable bone healing properties, but its mechanism of action is dependent on gravity. Although TPO heals bone more slowly than BMP-2, its mechanism of action does not depend on gravity and new bone is of higher quality. BMP-2 treatment also caused either death or distress (resulting in euthanasia) in 50% of the spaceflight mice, suggesting a possible negative interaction. Understanding this phenomenon further is important for providing safe and efficacious fracture treatments for those living in space for long-term periods.

Irreversible Gastrointestinal Failure in Necrotizing Pancreatitis Treated with Abdominal Multivisceral Transplant

◆ **Bajpai S**, Hacker A, Monirian LM, Saldivar R, Zyromski NJ, Maatman TK

Background: Necrotizing pancreatitis (NP) develops in 10-20% of acute pancreatitis patients and results in a profound locoregional and systemic inflammatory response. Occasionally, NP causes catastrophic abdominal visceral failure. Irreversible gastrointestinal (GI) failure is increasingly treated with multivisceral transplant (MVT); however, MVT has not previously been described in the NP population. We hypothesized that patients developing GI failure secondary to NP may be successfully treated by abdominal multivisceral transplant.
Methods: A retrospective review of patients developing irreversible GI failure from NP treated with abdominal MVT between 2005-2018.
In a case report of 647 NP patients, three patients developed irreversible GI failure and were treated with MVT. Two patients were male, and one patient was female. The median age at onset of NP was 49 years. Etiology of NP was biliary (N = 2) or alcohol (N = 1). In each case, infected necrosis was treated with repeated open pancreatic debridement and multiple percutaneous drains. Etiology of intraabdominal organ failure included enterocutaneous fistula and multiple small bowel resections in two patients and superior mesenteric vein thrombosis resulting in intestinal ischemia and total enterectomy in one patient. All patients developed short-gut syndrome with total parenteral nutrition induced liver fibrosis. Abdominal MVT was performed a median of 3.3 years after onset of NP and included stomach, small intestine, pancreas, and liver (N = 2) or small intestine, pancreas, and liver (N = 1). Median survival after MVT was 3.9 years. Two patients died during follow-up after MVT; one patient died of metastatic lung cancer 6.6 years after MVT and one patient died of angiosarcoma of the transplant liver 3.9 years after MVT. One patient is alive without complication 6.6 years after MVT.
Conclusion: Irreversible gastrointestinal failure is a rare complication of necrotizing pancreatitis. In this desperate circumstance, a lifesaving therapy in select patients is multivisceral transplant.

A Potential Avenue to Atherosclerotic Cardiovascular Disease: An Analysis of the Effect of Genetically-Induced Hypercholesterolemia on Zebrafish

◆ **Bowens J**, Macrae C, Kithcart A

Atherosclerosis is the leading cause of death in the U.S., killing one American every forty seconds, and is a medical nightmare to many. The current understanding is that hypercholesterolemia may play a role. Research has suggested that genetic mutations in low-density lipoprotein receptor (LDLR), apolipoprotein-B (APOB), and apolipoprotein-CII (APOC2) correlate positively with the development of atherosclerosis. On the other hand, alterations in proprotein convertase subtilisin/kexin type 9 (PCSK9), interleukin-1B, and angiopoietin like-3 (ANGPTL3) have correlated negatively. For these reasons, this project seeks to explore novel mechanisms that may link hypercholesterolemia with atherosclerosis.

We utilized the CRISPR-Cas9 system to create null mutants in LDLR, APOB, and APOC2. Guide RNAs were designed and injected into zebrafish embryos at the one cell stage. These fish were then screened using a fluorescent microscope to confirm injection one day after fertilization. The fish were then incubated until the seventh day after fertilization, at which point they were graduated into adult tanks where they were fed under a controlled or high-cholesterol diet. DNA was isolated from fish fin clips and amplified with PCR to confirm the presence of mutation. Cardiovascular-related phenotypes were assessed at several points.

We show that CRISPR-Cas9 technology can be applied to create zebrafish mutants. We found that embryos injected with LDLR and APOC2 CRISPRs often display embryologic deficiencies and were unable to hatch from their respective chorions, even after showing initial signs of life. Enhanced angiogenesis and high levels of cholesterol deposition were found in the dorsal aorta and the caudal vein of APOB mutants under both regular and high cholesterol diet. This was synonymous with wildtype zebrafish fed a high cholesterol diet. Uninjected fish did not display any clear sign of hypercholesterolemia.

Based off this data, it is fair to conclude that LDLR and APOC2 CRISPRs may lead to embryologic development deficiencies in zebrafish. APOB and LDLR mutants display similar characteristics as fish fed a high cholesterol diet. Overall, it was found that genetic manipulation can be used to mimic diet-mediated hypercholesterolemia in zebrafish. This will be useful in the future to study new mechanisms of atherosclerosis and the genetics causes of hypercholesterolemia.

A Rare Case of Pseudomonas Mendocina Sepsis

◆ **Northquist W**, Howley L.

Background: Pseudomonas mendocina is a gram negative, aerobic bacteria which rarely causes infection in humans; there have been 14 reported cases of infection worldwide, with only two from the United States. A range of infection types have been caused by P. mendocina, including endocarditis, meningitis and wound infections. Different antibiotics have been used to treat the infections, and patients survived the infection with treatment. In all cases, a source of the infection was unable to be identified. However, previous case reports have speculated regarding the possibility of inoculation through the skin as a potential source.
Case: A 60 year old male with history of alcoholic cirrhosis, chronic heart failure and recurrent lower extremity cellulitis presented with 1 day of fever to 103.2, shortness of air and increasing drainage and pain from LLE wound. He was admitted to the hospital with septic shock likely from a left leg cellulitis as the source of infection, and was started empirically on IV Vancomycin and IV Piperacillin-Tazobactam. On hospital day 3, the admission blood cultures were positive for P. mendocina. He was transitioned to oral Levofloxacin on day 4 and completed a 14 day total antibiotic course with resolution of the infection.
Discussion: Pseudomonas mendocina very rarely causes infection in humans. The infection discussed here presented with acute fever, which rapidly responded to antibiotic treatment. P. mendocina is susceptible to a multitude of antibiotics. Consistent with previous reports, this patient had significant co-morbidities, suggesting that patients with co-morbidities may be at increased risk. Previous reports have also suggested the possibility that the bacteria may be introduced through the skin. The fact that this patient with P. mendocina bacteremia had a chronic lower extremity wound provides additional support to the idea that the bacteria can cause sepsis via introduction through the skin.

Characterization of Medical Malpractice Lawsuits Relating to Dermatologic Emergencies in the Inpatient and Emergency Setting

◆ **Rumancik B**; Keele BJ; Rahnama-Moghadam S

Introduction: Characterization of malpractice lawsuits can help improve patient safety and reduce medical liability. Little information is available regarding dermatologists' potential to alleviate legal burdens facing hospitals and physicians in the hospital setting.
Objective: We sought to characterize malpractice lawsuits filed against physicians or hospitals for dermatologic emergencies in the inpatient or emergency setting.
Methods: In September 2019, we conducted a search for malpractice lawsuits using a national legal research database, Lexis Advance®. To be included, the lawsuit must describe a plaintiff claim originating from an inpatient or emergency department occurrence directly related to a dermatologic emergency.
Results: From the years 1987 to 2018, 158 lawsuits met inclusion criteria. Sixty-five lawsuits resulted in plaintiff verdicts or settlements for a total monetary recovery of $221,032,728. Ninety-three lawsuits resulted in defendant verdicts or outcomes with no reported monetary recovery. Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) was the most common diagnosis with 73 cases. Total monetary recovery from the 27 SJS/TEN plaintiff verdicts or settlements was $153,367,500. Delayed diagnosis, misdiagnosis, or failure to diagnose was the cause of 77% of the lawsuits included in this study. Wrongful death was the injury for 48% of the lawsuits that defined an injury. Of identified physician specialties, emergency medicine was named most commonly (n = 37); however, 54 lawsuits originating from an inpatient setting named the hospital exclusively or did not explicitly identify the specialties involved. Dermatologists were never identified as defendants. Only 7 cases described dermatology involvement in the care of the plaintiff.
Conclusion: This study underlines the value inpatient dermatology has in protecting hospital systems and non-dermatologists from legal and financial harm in addition to protecting patients.

Stunning (and Yet Unnecessary) Diagnostic Imaging of an Aspirated Foreign Body - Case Report and Clinical Images

◆ **Marsee M**, Collins S

Introduction: Pediatric foreign body aspiration is a common cause of emergency room visits. Despite the high sensitivity and specificity of a thorough history and physical exam, such cases often involve expensive and invasive procedures including bronchoscopy and/or clinical imaging as part of the diagnostic process. In cases where the aspirated foreign body is located in the upper airway, and can be visualized using direct laryngoscopy, such expensive and invasive procedures may be wasteful, unnecessary, and even harmful.
Case Report: A 5 year old was brought to the emergency department in moderate distress with complaints of difficulty breathing. Her parents reported that she had swallowed a toy doll approximately 15 minutes earlier. Besides mild difficulty breathing, a thorough history and physical revealed no signs of any immediate threat to life or acute decompensation. Using direct laryngoscopy, the emergency physician was able to visualize the feet of the toy doll hooked on the child's arytenoids, with the body extending down into the child's trachea. The physician decided not to attempt intubation due to the location of the foreign body. The physician then ordered several imaging tests and a consultation to the on call gastroenterologist who performed esophagoscopy. All three imaging modalities confirmed what was previously found on direct laryngoscopy: a toy doll in the child's upper trachea. Ultimately, the on-call otolaryngologist was consulted, was able to visualize the toy using direct laryngoscopy, and removed the toy using a pair of children's size larynx foreign body removal forceps.
Conclusion: Aspiration of a foreign body in a child can be an anxiety-provoking experience. However, unless the child presents with immediate threat to life, clinicians should use careful judgement when considering expensive, harmful, and possibly unnecessary diagnostic imaging.

Neonatal Lupus with Left Bundle Branch Block and Cardiomyopathy

◆ **Rumancik B**, Haggstrom AN, Ebenroth ES

A 4-week-old female, born to a mother with anti-Sjögren's-syndrome type A/Ro (anti-SSA/Ro) and anti-Sjögren's-syndrome type B/La (anti-SSB/La) autoantibodies, presented with a 2-week-long rash consistent with neonatal lupus (NL). Screening fetal echocardiograms showed no abnormalities. After discovery of her rash, a screening electrocardiogram revealed left bundle branch block (LBBB) and echocardiography found severely dilated cardiomyopathy with a 25% ejection fraction and a thin echogenic dyskinetic ventricular septum. Serum testing revealed elevated antinuclear, anti-SSA/Ro, and anti-SSB/La antibody titers. Other than the rash, she was asymptomatic and treated with medical management for heart failure. At 3 months of age she was admitted for intermittent tachypnea. Cardiac catheterization revealed patent coronary arteries, and endomyocardial biopsy showed no abnormalities. During catheterization she developed pulseless electrical activity requiring extracorporeal membrane oxygenation (ECMO). While on ECMO, she was treated with biventricular pacemaker placement, plasmapheresis, and intravenous immunoglobulin (IVIG). ECMO was weaned off after 7 days, and she was discharged with improved systolic function (30% ejection fraction). Outpatient follow up at 8 months of age revealed narrower LBBB paced rhythm, normal left ventricular volume, 70% ejection fraction, and age appropriate weight and height percentiles.

Cardiac structural abnormalities, most often associated with histologic inflammatory signs, are well-described in NL. This patient's thin, dyskinetic ventricular septum is an abnormality not previously reported in NL. This patient's lack of histologic inflammatory signs contributes to growing evidence of a possible "late-onset" subtype of NL-related cardiomyopathy. "Late-onset" cardiomyopathy may be due to an ongoing postnatal autoimmune process, as was concerning for our patient given her negative fetal cardiac screenings. Given the possible postnatal immune process, IVIG and corticosteroid regimens have been attempted in other case reports. Our case provides further anecdotal evidence for IVIG, plasmapheresis, and biventricular pacemaker use in NL-related cardiomyopathy. Lastly, LBBB is a manifestation rarely reported in association with NL.

Asthma in Indiana: Using a Community Health Matrix to Determine Asthma Health Factors for Indiana Counties

◆ **Burrell M**, Casey R, Savaiano D

Background: Asthma and its appropriate treatment are public health issues in Indiana that Indiana Joint Asthma Coalition (InJAC), a partnership within CTSI, is attempting to address. This is done through state-wide coalition building, which unifies efforts regarding asthma health and education and promotes interprofessional collaboration. Because time and resources are limited, InJAC must choose the areas that would benefit most from their focused work. A matrix was developed to establish the 10 counties with poorest asthma health and high vulnerability to social determinants to aid in this choice. We hypothesize that the 10 counties with the highest vulnerability to social determinants of health will have the worst asthma health.
Methods: Asthma health outcomes, contributing asthma-related variables, and social determinants of health were identified in all 92 counties in Indiana. Counties were compared by composite z scores to determine the top 10 counties with the poorest health statistics for asthma and social determinants. In addition, qualitative data will be used to identify local health coalitions that have the capacity and desire to work with InJAC to improve asthma treatment. InJAC will begin sessions with these counties to determine if long-term, sustainable, health promotions are feasible.
Results: The top 10 counites that were identified as having the poorest asthma health and factors were Lake, Grant, Madison, Marion, Huntington, Vanderburgh, Howard, La Porte, Blackford, and Noble. The top 10 counties with highest vulnerability to social determinants were Owen, Ripley, Daviess, La Grange, Fayette, Wayne, Elkhart, Newton, Switzerland, and Marion.
Potential Impact: The data from this matrix will help direct InJAC to the areas of Indiana with the greatest need for asthma coalition efforts. This will be done through improvement on education, awareness, and quality of care based on the Indiana State Asthma Plan.

Causes of Infant Mortality in Indiana, 2013-2017

◆ **Cummiskey CA**

Background: Indiana has a high infant mortality rate compared to the rest of the country, which is driven in part by stark racial disparities. There is a lack of reported data on causes of infant death in Indiana.
Methods: Indiana causes of deaths were analyzed using data from ISDH mortality and natality data sets from years 2013-2017. National data was analyzed from comparable data from the CDC WONDER Online Database. All deaths for individuals less than 1 year of age were included. Cause of death was determined by standardized underlying cause of death. Rates of death were determined by taking total number of infant deaths and dividing by the total number of live births in the same time period. Mortality rates for each cause of death were compared between Indiana and the United States, and within Indiana by single race.
Results: Indiana had significantly higher than national infant mortality rates for 7 of the top 15 causes of infant death, including all of the top 4 causes of infant death. Indiana had significantly lower than national average infant mortality rates for 2 of the top 15 causes of infant death. Within Indiana, Non-Hispanic (NH) black infants had an increased relative risk compared to NH white infants for 9 of the top 14 causes of infant death.
Discussion: Indiana has higher infant mortality rates compared to national for diverse causes of death. This poor overall infant mortality rate is driven by stark disparities between NH white and NH black infant mortality rates. NH black infants have worse mortality rates in most of the causes of death analyzed. Efforts to improve Indiana's infant mortality as a whole and should take an approach that addresses all of the diverse causes of death and that specifically addresses the disparities that disproportionately affect NH black infants.

An Orthoplastics Approach to Complex Soft Tissue Defects Around the Hip

◆ **Speybroeck J**

Objective: Hip soft tissue defects, dead space and degloving injuries are rare, but challenging cases. Exposed bone and/or hardware require coverage with high rates of wound complications and infection. Various reported treatment algorithms exist without a defined gold standard. An orthoplastics approach can be successful to management of these defects at institutions lacking adjunctive soft tissue experts.
Methods: We retrospectively reviewed two patients (1 traumatic, 1 recurrent abscess) with complex lateral hip soft tissue defects requiring coverage after multiple surgical debridements. Intraoperative laser angiography using the SPY Elite system (Stryker, Kalamazoo, MI) confirmed the perfusion of the proposed adjacent soft tissue flap following intravascular injection of indocyanine. Keystone perforator island flaps (KPIF) were designed for a flap-to-defect ratio 1.5 to 1 by incorporating pedicle perforating vessels and surrounding fasciocutaneous tissue. Flaps were mobilized by previously described principles. De-epithelization of the more medial flap edge was used to decrease dead space over exposed hardware or bone. Closure was accomplished over multiple deep suction drains with monofilament inverted suture for the deep dermal layer and nylon suture for the epidermis. Laser angiography was used again after closure to assess perfusion of flap edges. Appropriate antibiotic coverage was used without purposeful prophylaxis.
Results: Both wounds healed without dehiscence, infection, or need for secondary intervention. At one year follow-up, satisfactory soft tissue integrity, osseous healing and functional status were observed in both cases.
Conclusion: Intra-operative laser angiography perfusion assessment can help guide local tissue rearrangement by KPIF to provide durable coverage of complex soft tissue defects around the hip. With experience and discretion this technique can be applied by the orthopedic trauma surgeon who may not have robust plastic surgical services readily available.

A 6 Month Retrospective Analysis of the Clinical Results of Arthroscopic Rotator Cuff Repairs Between Standard Population and Diabetes Group

◆ **McKeeman J**, Sassmannshausen G

Rotator cuff tear is a common shoulder injury typically resulting from overuse or trauma. Diabetes is a possible risk factor for rotator cuff tears although current research has been inconclusive. This study explores the outcomes of rotator cuff repair surgery in a population with a history of Type II diabetes and a standard population. From July 2017 to December 2017, Dr. Sassmannshausen performed 43 rotator cuff repair surgeries. This clinical study demonstrates consistent success in the rotator cuff repair as well as establishes that there is no significant difference in the outcome of rotator cuff surgery in patients with a history of diabetes when compared to the standard population. This was achieved through data collection through voluntary survey following the surgery. Patients filled out three separate surveys; the Simple Shoulder Test, the UCLA shoulder test, and the ASES shoulder test. These tests give insight into the success rate of surgery by revealing patient percent recovery in specific objective and subjective categories, as well as an overall average score for each test. This particular analysis compares the standard population to patients with a history of diabetes. From the data gathered, it was concluded that none of the tests had statistical difference between the diabetes population and the standard at a level of $p<.05$. The data set is relatively small at 20 patients and continued research is being done to draw more solid conclusions, but from the data gathered in this study it can be concluded that Dr. Greg Sassmannshausen's rotator cuff repair surgeries are consistently successful between both groups.

Folliculotropic Mycosis Fungoides in a Peculiar Distribution

◆ **Okoye C**, Hooper P, Hoffman K

Introduction: Folliculotropic mycosis fungoides (FMF) is a variant of cutaneous T-cell lymphoma. FMF is unique in its tropism for the follicular epithelium¬. The infiltrate is mostly seen in the follicular epithelium with less cases showing epidermal involvement. This correlates with the predilection to localize to areas where pilosebaceous units are greatest which includes the head, neck and upper torso. It also accounts for the wide spectrum of clinical presentations seen with FMF.
Case Presentation: We describe a case of a 72-year-old male who presented with a 10-year-history of pink, scaly, pruritic patches and plaques scattered over the scalp, cheeks, and nose. Lesions were also present on the back, abdomen, bilateral hips, and thighs, but were morphologically different as they appeared as erythematous papules coalescing into plaques. He had a presumed diagnosis of psoriasis made many years prior. Histopathological analysis of the right frontal scalp revealed an atypical T-lymphocyte infiltrate with focal folliculotropism, concerning for mycosis fungoides. Sections demonstrated a relatively dense superficial to mid dermal perivascular infiltrate of small to medium sized lymphocytes with rare mixed large cells. Immunohistochemical staining showed that the infiltrate was composed of predominant CD3-positive T lymphocytes. A diagnosis of folliculotropic mycosis fungoides was confirmed.
Discussion: Due to variable presentation and histopathologic findings the diagnosis can be difficult. These presentations include follicular based patches and plaques, keratosis-pilaris like lesions, acneiform eruptions, and alopecia. One study showed an average mean time of 2.84 years between onset of rash and diagnosis. With a delay in diagnosis, a delay in proper treatment ensues. We highlight the importance of placing FMF in the differential diagnosis in patients presenting with those various presentations as mentioned above even with a deviant presentation that includes lesions on the extremities.

Disseminated Blastomycosis in an Immunocompetent Female

◆ **Okoye C**, Vinson W, Hoffman K

Introduction: Blastomycosis is caused by Blastomyces dermatitidis, a dimorphic fungus that can be found in soil and is endemic to North America, particularly the Mississippi and Ohio river valleys, Great Lakes region, and southeastern states. The lungs are typically the first site of infection, via inhalation of organisms; however, extrapulmonary dissemination to the skin, central nervous, and bone can occur. Cutaneous involvement commonly occurs in disseminated disease.
Case Presentation: We report a case of a 35-year-old African American female admitted with a six-week history of subcutaneous tender nodules. The first nodule appeared on her left clavicle. She subsequently developed similar lesions on her mid lower back, breasts, legs, and lastly, her face. The lesions were painful on palpation and would occasionally drain yellow to brown thick fluid. She had been seen in the emergency department on two separate occasions and received courses of clindamycin and augmentin as well as incision and drainage with no improvement. No cultures were collected at the time. Upon admission, the patient was found to have positive Blastomyces antigen. Chest CT demonstrated multiple consolidations and a CT scan of the neck demonstrated an enhancing mass overlying the left clavicle. FNA of the mass overlying the left clavicle showed a granulomatous inflammation with suppuration for which fungal culture was positive for Blastomyces. A punch biopsy of a lesion on the cheek showed intraepidermal microabscesses containing the walled fungal spore suggestive of blastomycosis. GMS stain demonstrated broad-based budding, consistent with blastomycosis. She denied any history of being immunocompromised and HIV testing was negative.

The knowledge that Blastomyces spp. can disseminate in both the immunocompromised and the immunocompetent is imperative. For physicians in endemic areas, characteristics such as simultaneous pulmonary and cutaneous infection should raise clinical suspicion. Diagnosis of blastomycosis involves the use of culture and non-culture diagnostic methods.

Oral Facial Digital Syndrome Type 1 with Features of Nevus Comedonicus Syndrome in a Fourteen-Month Old Female

◆ **Bittar N**, Okoye C, Mannam H, Skillman S

Introduction: Oral-facial-digital syndromes (OFDS) represent a heterogenous group of rare neurodevelopmental disorders associated with malformations of the face, oral cavity, and digits. Here we present a case of OFDS type 1 with features of nevus comedonicus syndrome in a fourteen-month old female.
Case Presentation: A 14-month-old girl presented to the dermatology clinic with her mother for concern of "spots" on her daughter's face since birth. On physical exam, the patient had hypertelorism, a depressed nasal bridge, natal teeth, and a bifid tongue. Additionally, multiple white pin-point cysts on her central forehead, nose, medial cheeks, and chin. Scaly pink patches were present on her scalp, arms and legs. Numerous closed comedones and prominent pores were in her left axilla. Further laboratory studies revealed low hemoglobin of 12.9 and slightly elevated creatinine 0.55. Genetic studies revealed a likely pathogenic variant in OFD1 gene. An MRI showed agenesis of the corpus callosum. A renal ultrasound demonstrated no significant findings, and a foot X-ray revealed a duplicated right 1st metatarsal. Based on the physical exam findings, in conjunction with the laboratory, genetic, and imaging results, the diagnosis of OFDS type 1 was made. The patient is being followed by Neurology, Ophthalmology, Pulmonology, Orthopedics, and Dentistry, who noted additional findings of optic nerve hypoplasia and moderate sleep apnea.
Discussion: Of the OFDS group, type 1 is most commonly associated with cutaneous findings, as in this patient. OFDS type 1 patients can develop a wide range of neurological, ophthalmologic, renal, and skeletal abnormalities. This patient's particular presentation shows overlap with another rare condition, known as nevus comedonicus syndrome, which is the presence of nevus comedonicus with extracutaneous findings of the bones, eyes, and brain. The relationship between the OFD1 gene and nevus comedonicus syndrome is unclear but may offer an avenue for future research.

Dyskeratosis Congenita Presenting as Hypopigmentation and Nail Dystrophy in Siblings

◆ **Bittar N**, Okoye C, Broussard-Steinberg C, Haggstrom A

Introduction: Dyskeratosis Congenita (DC) is a rare telomere disorder with an incidence of approximately 1 in 1 million. DC has a large spectrum of mucocutaneous features and is associated with high risk of hematologic and solid malignancies as well as bone marrow failure. The classic triad of reticular skin pigmentation, dysplastic nails, and oral leukoplakia is diagnostic of DC. Here we present two unique cases of DC in siblings.
Case Presentation: Two siblings, a 9-year-old male and six-year-old female, presented to the dermatology clinic with nail and skin changes of several years duration. There is no known family history of skin conditions, nail disorders, or similar symptoms. On physical exam, both patients show variable reticulate hypopigmentation involving the neck, arms, wrists, palms and fingertips. Nail thinning, splitting, and dystrophy were also noted in both patients. Dermatoglyphics were intact in both patients and there were no mucosal lesions or plaques present. A complete blood count (CBC) was within normal limits for the male and mild leukopenia without neutropenia for the female. Further testing included telomere length quantification testing which revealed very short telomeres in comparison to age and sex matched controls. Based on these findings, the diagnosis of Dyskeratosis congenita was made.
Discussion: Dyskeratosis Congenita patients are at a high risk for multiple systemic complications from an increased incidence of malignancies to avascular necrosis of the hips and shoulders, to liver disease, pulmonary fibrosis and stenosis of the lacrimal ducts, esophagus and urethra. DC is thought to be due to genetic mutations in genes regulating telomere production. For these reasons it is critical to recognize the triad of cutaneous findings as early as possible in order for the appropriate follow-up assessments to be made. Routine monitoring of blood counts and bone marrow is key to monitor progression of cytopenias.

Does a Robotic Approach to Adrenalectomy Improve Outcomes?

◆ **Regele EJ**, Steward JE, Sundaram CP

Introduction: A minimally invasive approach has become the standard of care for most cases requiring adrenalectomy. Both laparoscopic and robotic methods are currently used. We compare outcomes of these two surgical techniques for adrenalectomy.
Methods: A retrospective review of minimally invasive adrenalectomy cases conducted from 2009 to 2020 at a single academic institution was completed after Institutional Review Board approval. The daVinci Surgical system was used for the robotic procedures. Outcomes evaluated for comparison included length of hospital stay, operative time, readmission rate, and complications. The Clavien-Dindo Classification system was used to categorize complications. Independent samples T-tests and Pearson Chi-square analyses were used to assess for statistical significance.
Results: Of 138 patients included in the study, 82 underwent laparoscopic adrenalectomy and 56 underwent robotic adrenalectomy. The mean length of hospital stay for the laparoscopic and robotic groups was 2.05 (SD = 1.63) and 2.21 (SD = 1.33), respectively. The mean operative time in minutes was 119 (SD = 34) in the laparoscopic group and 145 (SD = 36) in the robotic group. In the laparoscopic group, five patients had a Grade ≥II complication. There were nine patients in the robotic group that had a Grade ≥II complication. Readmissions in the laparoscopic and robotic groups were eight and six, respectively. Operative time in the laparoscopic group was significantly shorter than in the robotic group ($p=0.001$). There was no statistical significance between the laparoscopic and robotic groups in terms of length of stay ($p = 0.52$), complication rate ($p = 0.06$), and readmission rate ($p = 0.85$).
Conclusions: The laparoscopic approach to adrenalectomy was significantly faster than the robotic approach. However, there was no statistical difference in length of hospital stay, complication rate, or readmission rate between the two groups.

The Impact of Palliative Care on End-of-Life Characteristics in Pediatric Hematopoietic Cell Transplant

◆ **Achiko FA**, Levine DR, Wilcox R

Hematopoietic cell transplantation (HCT) is an intensive, curative, therapeutic procedure offered to patients with high risk-malignancies and non-malignant illnesses. Transplant recipients are, however, at risk of increased morbidity and mortality. Pediatric oncology patients (POP), despite therapeutic interventions, experience traumatic characteristics that impair their quality of life (QOL), especially at the end-of-life (EOL). While recent studies show that POPs benefit from early palliative care (PC), research on the outcomes of integration of PC in pediatric transplant patients EOL care is scarce. We sought to identify differences in EOL characteristics of pediatric HCT patients based on PC involvement. Retrospectively, we reviewed electronic medical records of all HCT patients at St. Jude Children's Research Hospital (SJCRH), who unfortunately died between March 2008 and October 2017 (n=160). Charts were mined for specific variables of interest that included patient demographics, clinical and EOL characteristics, PC consultations, and symptom recognition. Data was organized using excel and analyzed using descriptive statistics. Of 160 deceased HCT patients, 114 (71.3%) had PC team involvement, and 46 (28.8%) did not. There was no difference between the two patient groups concerning demographics and the cause of death. The average time between the last transplant received, and death was 309 days ([IQR], 9-2,834) in the PC group, and 232 days ([IQR], 13-1,1444) in the non-PC (NPC) group. PC consultation occurred approximately 190 days ([IQR], 0 to 3,760) post-transplantation, with the most commonly discussed goal of care in these consultations being the goal of cure (56%). The symptom burden at EOL was high for all HCT patients; however, the PC group had increased recognition of every symptom assessed. Patients on the PC team were more likely to have documentation on resuscitation elections (PC, 65%; NPC, 28%), less likely to have cardiac resuscitation (CPR) attempted (PC, 10%; NPC, 17%) and less likely to be intubated in the last 24 hours of life (PC, 28%; NPC 44%). With matters concerning EOL care patterns such as location of death, compared to NPC, PC patients were more likely to die at home (PC, 18%; NPC, 15%) or inpatient settings (PC, 30%; NPC, 24%) and least likely to die in intensive care units (PC, 34%; NPC, 46%). Patients who had PC involvement were also more likely to have hospice involvement (PC, 20%; NPC, 7%). Incorporating PC in pediatric HCT does not lead to shorter life spans for patients. It may enhance patient outcomes, and EOL experiences through early discussions and documentation on EOL care preferences, decreased exploration of extreme interventional focused care, increased symptom recognition, and increased hospice support.

Combined Mitral Papillary Muscle Avulsion with Pericardial Rupture and Cardiac Herniation due to Blunt Thoracic Trauma-Induced. Difficult and Delayed Diagnoses

◆ **Shariff F**, McCauley R, Steinberg M, Patel J, Thompson M, Lesh C, Walsh M, Evans E

Clinical Significance: We describe the first case of combined pericardial tear with cardiac herniation and ruptured mitral papillary muscles following Blunt Thoracic Trauma (BTT). Surgeons must be vigilant for cardiac and pericardial injury post-BTT even without traditionally suggestive clinical, physical, and radiological findings.
Case: A 40-year-old female presented to the ED following a high speed MVC. On exam, HR 107, RR 30, BP 141/108, and oxygen saturation of 92% RA. Cardiovascular exam revealed no murmurs, gallops, rubs, or JVD. EKG demonstrated no significant findings. Chest CT revealed fractured left ribs 2-7, sternum, mediastinal hematoma, left pneumothorax, grade III splenic laceration, and left pleural effusion. Transthoracic echocardiography was normal. Three days later, the patient developed rapidly worsening SOB and bilateral opacification on CXR consistent with acute cardiogenic pulmonary edema confirmed by CT. There was a new 3/6 holosystolic heart murmur heard best at the apex with crackles two-thirds of the way up the lung fields bilaterally. A transesophageal echocardiography (TEE) demonstrated a normal-sized LA, severe 4+ mitral regurgitation, anteromedial mitral papillary muscle avulsion, normal ventricular function, and no pericardial effusion. Cardiac catheterization confirmed these diagnoses and an intra-aortic balloon pump was placed. Patient underwent a sternotomy and surgery for mitral valve replacement. Findings included (1) full-thickness pericardium rupture from apex to the left atrium with pronounced cardiac herniation leftward, (2) anterior mitral papillary muscle avulsion, abnormally positioned riding up towards the mitral valve apparatus (3) large septal hematoma, and (4) mid-sternal fracture. A 25 Hancock II porcine prosthesis was placed and the pericardial tear repaired. The patient tolerated this procedure well and was discharged to a rehabilitation facility with uneventful recovery.
Conclusions: The holosystolic murmur with coinciding pulmonary edema guided the clinician to the diagnosis of mitral papillary muscle avulsion using TEE leading to the intraoperative diagnosis of pericardial rupture and cardiac herniation.

Shock and Awe: Surprise Medical Bills and Seeking Care

◆ **Schultheis P**, Haddad A, Chiang J, Khan M, Rohr-Kirchgraber T

Case: 61yo woman presented with palpitations and dyspnea. After observation and general workup, she was diagnosed with new-onset atrial fibrillation and treated. She returned a year later with similar symptoms and was observed overnight with a negative workup, including a nuclear stress test. The visits accumulated over $24,000 of healthcare costs, of which insurance covered $10,000. She agreed to a $200/month interest-free payment plan for the remaining $14,000. The hospital sent $6,500 to collections, requiring a $2,100 immediate payment to protect her credit score. She has since restructured her debt and delayed her retirement to ensure payment; another hospitalization at the time would have resulted in bankruptcy.
Conclusions: A surprise medical bill affects 1 out of 6 insured, hospitalized patients and occurs when patients have care that is uncovered or done by an out-of-network physician. The patient is unaware of the cost upfront and is left to pay. Surprise billing is an increasingly urgent national political issue as the financial risk surrounding hospitalization plays a systemic role in delayed medical care and negative health outcomes.
Clinical Significance: The medical and financial health of women are inextricably linked. Surprise medical billing drives patients away from physicians to avoid financial ruin. This delay in care poses a risk for advanced disease and poor prognosis. A recent study in JAMA Oncology found non-Hispanic black, American Indian, and Hispanic women are among those at highest risk for late-stage breast cancer diagnosis secondary to being uninsured. Late-stage diagnosis increases time away from work due to increased prevalence of treatment-related illness, further impacting her ability to afford appropriate care. Increased physician literacy on this matter will improve the physician-patient relationship through empathic care and, hopefully, increased physician advocacy around surprise medical billing.

Obesity Decreases the Contribution of Kv Channels to Hypoxic Coronary Vasodilation

◆ **Clark HE**, Baker HE, Goodwill AG, Blaettner BS, Kozlowski MC, Tune JD

Background: Our group previously demonstrated that reductions in the functional expression of voltage-dependent Kv channels contribute to impaired metabolic control of coronary blood flow in the setting of obesity. This study tested the hypothesis that obesity diminishes the contribution of Kv channels to coronary vasodilation in response to hypoxemia.
Methods: Control lean (n = 7) and obese (n = 5) swine were anesthetized and the heart exposed via left lateral thoracotomy. Coronary blood flow was measured in response to hypoxemia, before and after inhibition of Kv channels by 4-aminopyridine (4-AP; 0.3 mg/kg, iv), by a flow probe placed about the left anterior descending coronary artery. Hypoxemia was induced by progressive increases in the amount of nitrogen introduced into the ventilator. Arterial blood samples were obtained at each reduction in arterial oxygenation via a catheter placed in the femoral artery.
Results: Blood pressure decreased from ~88 ± 5 mmHg to ~68 ± 6 mmHg (P = 0.01) as arterial PO_2 was reduced below 50 mmHg in both lean and obese swine (P = 0.51). In lean swine, coronary flow progressively increased from ~0.6 to >3.0 ml/min/g as arterial PO_2 was reduced. This response was decreased by ~40% in obese swine and by ~30% in lean swine treated with 4-AP. Administration of 4-AP had no effect on coronary flow in obese swine.
Conclusion: These data support that Kv channels contribute to increases in coronary flow in response to hypoxemia in lean swine and that reductions in Kv channel function contribute to impaired hypoxic coronary vasodilation in obese swine. We propose that therapeutic targeting of obesity associated pathways (angiotensin-aldosterone system) known to influence K+ channel expression could improve coronary microvascular function and cardiovascular outcomes in subjects with obesity.

Predictors of Patient Satisfaction Following Primary Total Knee Arthroplasty: Results from a Traditional Statistical Model and a Machine Learning Algorithm

◆ **Farooq H**, Deckard ER, Ziemba-Davis M, Madsen A, Meneghini RM

Background: It is well-documented in the orthopedic literature that 1 in 5 patients are dissatisfied following total knee arthroplasty (TKA). However, multiple statistical models have failed to explain the causes of dissatisfaction. Further, payors are interested in using patient-reported satisfaction scores to adjust surgeon reimbursement rates without a full understanding of the influencing parameters. The purpose of this study was to more comprehensively identify predictors of satisfaction and compare results using both a statistical model and a machine learning (ML) algorithm.
Methods: A retrospective review of consecutive TKAs performed by two surgeons was conducted. Identical perioperative protocols were utilized by both surgeons. Patients were grouped as satisfied or unsatisfied based on self-reported satisfaction scores. Fifteen variables were correlated with satisfaction using binary logistic regression (BLR) and stochastic gradient boosted ML models.
Results: 1,325 consecutive TKAs were performed. After exclusions, 897 TKAs were available with minimum one-year follow-up. 85.3% of patients were satisfied. Older age generation and performing surgeon were predictors of satisfaction in both models. The ML model also retained CR/CS implant; lack of inflammatory conditions, preoperative narcotic use, depression and lumbar spine pain; female sex, and a preserved PCL as predictors of satisfaction which allowed for a significantly higher area under the ROC curve compared to the BLR model (0.81 vs. 0.60).
Conclusion: Findings indicate patient satisfaction may be multifactorial with some factors beyond the scope of a surgeon's control. Further study is warranted to investigate predictors of patient satisfaction particularly with awareness of differences in results between traditional statistical models and ML algorithms.

Thumb Metacarpophalangeal Hyperextension in an Arthritic Population

◆ **Acott TR**, Farooq H, Merrell GA, Peck KM, Sparks D, Smetana BS

Purpose: To study the correlation between passive MP hyperextension, dynamic MP position, and pinch strength in patients with concurrent CMC arthritis.
Methods: Cross-sectional analysis of patients with thumb CMC arthritis was performed. Measurements of passive thumb MP hyperextension and dynamic thumb MP position during lateral key pinch, jar grasp, and cap grasp were collected. Additionally, pinch strength and level of pain at rest and during pinch activity using a VAS scale were recorded. Subgroup analysis was performed for patients with passive MP hyperextension <30 and ≥30 degrees.
Results: Thirty-three patients were enrolled in our observational study. Average passive MP hyperextension was 28 degrees (range 55 flexion – 88 hyperextension). A poor correlation was appreciated between passive MP hyperextension and MP position during dynamic activities. No difference was seen between the two subgroups (<30 and ≥30 degrees passive hyperextension) when comparing average MP joint position during dynamic key pinch and dynamic jar grasp. However, there was a significant difference between the two subgroups when comparing average MP joint position during dynamic cap grasp, though both positions were in flexion (m=24° and m=9°). Poor correlation was also seen between MP position during dynamic pinch activity and pinch strength. Furthermore, no difference in pinch strength was seen between patients with and without dynamic control (dynamic MP position £0). Finally, there was no difference seen in pinch strength between patients with passive MP joint hyperextension <30 vs ≥30 degrees.
Conclusions: Passive MP hyperextension had little correlation with both dynamic MP position and pinch strength. Majority of patients in our study functionally position their thumb MP in position of flexion, despite an average passive hyperextension of 28 degrees. Passive MP hyperextension may not be the optimal parameter to indicate the need for MP stabilization in patients undergoing treatment for CMC arthritis.

Efficacy of a Single Image-Guided Corticosteroid Injection for Glenohumeral Arthritis

◆ **Metzger CM**, Farooq H, Merrell GA, Kaplan FT, Greenberg JA, Crosby NE, Peck KM, Hoyer RW

Background: It remains unclear how severity of radiographic GHOA, OSS, and VAS scores impact the effect and longevity of single, image-guided corticosteroid injections. We hypothesize that patients with more severe radiographic GHOA and poor baseline shoulder function would require earlier secondary intervention with repeat injection or surgery.
Methods: Patients with GHOA who received a single, image-guided corticosteroid injection for primary intervention were enrolled. Phone interviews were conducted to record OSS and VAS scores at baseline and months 1, 2, 3, 4, 6, 9, 12. Endpoints were designated when patients required second injection, surgery, or reached month 12. Patients were grouped by respective baseline OSS (mild, moderate/severe) and Samilson-Prieto classification (mild, moderate, severe) for analysis.
Results: 64.7% of the mild group and 50% of the moderate/severe group completed 12 months without secondary intervention. No significant difference was seen in overall survival between these groups. 87.5%, 46.2%, and 62.5% of the mild, moderate, and severe classes, respectively, completed 12 months without secondary intervention. No significant difference was seen in survival between these classes. OSS and VAS scores at each follow-up were compared to baseline. Increase in OSS from baseline to month 1 was significantly higher in the moderate/severe group than the mild group. As an entire cohort, significant difference was seen between baseline and months 1-4 for OSS and between baseline and months 1-4, 6,9, and 12 for VAS, both above MCID.
Discussion: We established, patients with more severe shoulder dysfunction may experience a statistically significant greater symptomatic relief compared to patients with milder dysfunction. Additionally, we demonstrated that following a single injection, patients may experience statistically and clinically relevant improvements in shoulder function up to 4 months post-injection. Lastly, following a single injection, patients may experience statistically and clinically relevant improvements in VAS pain scores up to 1 year.

Unilateral Expandable Interbody Cage Placement in Minimally Invasive Midline Fusion

◆ **Sharma I**, Krzyskowski M, Khanna N

Introduction: Minimally invasive midline approach utilizing cortical screws has grown in popularity due to its familiar anatomy, limited dissection, and associated decreased morbidity. This approach is well-suited for bilateral "inline" cage placement after bilateral facetectomies. Many surgeons prefer to utilize a single cage, TLIF, for midline fusions to optimize time, decrease exposure, and lower costs. This novel study assessed cage position for a unilateral cage utilizing the minimally invasive midline approach.
Methods: Retrospective chart and radiograph review was performed on 25 consecutive patients who underwent a midline lumbar fusion utilizing a single expandable interbody cage. Post-operative radiographs were examined to determine cage position relative to the vertebral bodies. Cage positioning was graded A, B, or C based on its midline position relative to the medial, middle, or lateral third of the superior vertebral body.
Results: Surgeries were performed by a fellowship-trained orthopedic spine surgeon. 25 patients (48% male; 26 cages, n=26) underwent a lumbar fusion utilizing a single, expandable interbody cage using a midline approach. 24 patients had one-level fusions, while 1 patient had a two-level fusion. 18 devices were graded "A"; 8 devices were graded "B". None received a grade of "C."
Conclusion: Ideal cage position for midline lumbar fusion is the middle-third of the superior vertebral body to allow for symmetric distraction and load sharing. This can be difficult to accomplish when utilizing a single cage, as it can be difficult to maintain the necessary 30-45-degree insertion angle in order to position the cage. With technical modifications to disc preparation, retractor considerations, and facetectomy we can obtain the necessary angles for cage placement without the need to increase exposure. The cage position was further optimized through radiographic imaging prior to the expansion of the lordotic oblique cage, highlighting another advantage to the expandable technology with this procedure.

A 6 Month Retrospective Analysis of the Clinical Results of Arthroscopic Rotator Cuff Repairs Between Standard Population and Smoker Group

◆ **McKeeman J**, Sassmannshausen G

Rotator cuff tear is a common shoulder injury typically resulting from overuse or trauma. Smoking status is a known risk factor for rotator cuff tears and this study explores the outcomes of rotator cuff repair surgery in a population with a history of smoking and a standard population. From July 2017 to December 2017, Dr. Sassmannshausen performed 43 rotator cuff repair surgeries. This clinical study demonstrates consistent success in the rotator cuff repair as well as establishes that there is no significant difference in the outcome of rotator cuff surgery in patients with a history of smoking when compared to the standard population. This was achieved through data collection through voluntary survey following the surgery. Patients filled out three separate surveys; the Simple Shoulder Test, the UCLA shoulder test, and the ASES shoulder test. These tests give insight into the success rate of surgery by revealing patient percent recovery in specific objective and subjective categories, as well as an overall average score for each test. This particular analysis compares the standard population to patients with a history of smoking. From the data gathered, it was concluded that none of the tests had statistical difference between the smoking population and the standard at a level of $p<.05$. The closest to a significant difference was the simple shoulder test at a level of .056. The data set is relatively small at 20 patients and continued research is being done to draw more solid conclusions, but from the data gathered in this study it can be concluded that Dr. Greg Sassmannshausen's rotator cuff repair surgeries are consistently successful between both groups.

Angioedema Associated With Clozapine and Olanzapine

◆ **Bittar NM**, Bittar JM, Fretwell H

Background: Drug induced angioedema is a rare cutaneous drug reaction that has primarily been associated with betalactam antibiotics and anti-inflammatory drugs. However, angioedema associated with antipsychotics is a much more rare side effect, with only a few reported cases. To date, there are only three reports in the literature of angioedema associated with clozapine or olanzapine.
Objective: This report serves to add to the literature on the association of clozapine and olanzapine with angioedema.
Results: A 69 year old male with a history of schizophrenia presented to the emergency department on 9/30/2016 for altered mental status. Medical workup was unremarkable and he was transferred to inpatient psychiatry service. Patient was being managed by outpatient psychiatry for schizophrenia with clozapine 450 mg total daily dose for many years, however stated he had not been taking his medications. His other medications included sertraline 50 mg, buspirone 10 mg, and buproprion 150 mg. Upon admission, his sertraline and buproprion were held and he was restarted on buspirone 150 mg, and clozapine 25 mg BID for 3 days with a plan to increase by 25 mg every 3 days until back to 450 mg total daily dose. He developed facial and bilateral arm swelling on 10/14/2016. Clozapine was discontinued and diphenhydramine was initiated. Internal medicine team was consulted. CBC was notable for eosinophilia at a level of 1.1. Physical exam significant for induration of both arms and desquamation, mild erythema of the upper chest, no urticaria. He was diagnosed with allergic form of angioedema and his diphenhydramine was changed to hydroxyzine. After discontinuation of clozapine, his angioedema resolved however his psychosis worsened. The patient was subsequently started on olanzapine on 10/23/2016 and developed facial angioedema with eosinophilia two days later on 10/25/2016. Olanzapine was discontinued, haloperidol was initiated and his facial edema resolved. The patient is still being followed by outpatient psychiatry and has not had a recurrence of the angioedema since discontinuing the olanzapine and clozapine.
Conclusions: This case report adds to the literature on the adverse effects of clozapine and olanzapine and suggests the need for physicians to be aware of the possible side effect of angioedema secondary to clozapine and olanzapine use when treating patients with psychotic disorders.

Dermatofibrosarcoma Protruberans Treated with Mohs Micrographic Surgery: Risk Factors, Tumor Characteristics, and Treatment Outcomes

◆ **Bittar, Julie M.**; Xiao, Honglin; Garcia-Dehbozorgi, Sara; Bittar, Noor M.; Somani, Ally-Khan B.

Introduction: Dermatofibrosarcoma Protrubrens (DFSP) is a rare, low-grade neoplasm that occurs in the dermis and subcutaneous tissue with the propensity for subclinical spread. Diagnosis is difficult given the early clinical signs are nonspecific. Treatment for this tumor varies widely with both surgical and non-surgical treatment options and recurrence rates in published literature are highly variable.
Objective: To evaluate the risk factors, tumor characteristics and local recurrence rate after MMS for DFSP.
Methods: This IRB approved retrospective cohort study identified fourteen patients with the diagnosis of primary DFSP treated with MMS at our institution between 2010 and 2019. We defined local recurrence as biopsy proven DFSP arising with the scar of MMS. Tumor characteristics were obtained through chart review. Follow up data was based on review of electronic medical records and telephone calls to patients.
Results: Fourteen patients consented to participate in this study. Our cohort had a mean age of 38 years (median: 36 years, range: 28-50 years), was comprised of 57% males (8/14) and 43% females (6/14). The most common site of DFSP was the trunk (50%, 7/14), followed by the head/neck (21%, 3/14), lower extremity (14%, 2/14), and upper extremity (14%, 2/14). The mean preoperative tumor size was 3.32 x 2.21 cm and mean postoperative size 7.59 cm x 6.17 cm. Tumors were treated with a mean of 2.93 stages. On review of pathology: 100% of tumors stained positive for CD34, 7% (1/14) showed fibrosarcomatous change, 14% (2/14) had 17:22 translocations, and 14% (2/14) showed PDGFB rearrangements. Assessment of patient postoperative management showed that 36% (5/14) followed up with oncology. No patients (0/14) experienced a local recurrence with a mean follow up time of 17.9 months (median: 13.5 months, range: 1-57 months).
Conclusion: This retrospective study provides support for the use of MMS for treatment of primary DFSP given its very low local recurrence rate (0/14 patients). The 17:22 and PDGFB rearrangements seen in a subset of our cohort may indicate that patients with these genetic translocations may be at higher risk for developing DFSP. Postoperative referral to oncology for observation and follow up may be indicated given DFSP's propensity for subclinical spread.

Utilization of Thromboelastography with Platelet Mapping to Guide Perioperative Management of Intravenous Immunoglobulin, Steroids, and Blood Component Therapy in a Patient with Immune Thrombocytopenia Purpura Requiring Emergency Coronary Artery Bypass Grafting

◆ **Hatch J**, Marsee M, Speybroeck J, Grisoli A

The perioperative management of patients with immune thrombocytopenic purpura (ITP) who require intravenous immunoglobulin (IVIG), steroids, and blood component therapy (BCT) is a challenging clinical scenario which requires an understanding of the delicate balance between hypercoagulability and hypocoagulability in the perioperative setting. This is especially true for those patients undergoing coronary artery bypass grafting (CABG). Common coagulation tests (CCT) do not adequately predict hemostatic integrity of patients undergoing CABG and modified thromboelastography with platelet mapping (TEG/PM) has been shown to reduce BCT as well as provide better survival for patients undergoing this surgery. We present a patient with immune thrombocytopenic purpura (ITP) who received 48 hours of low osmolality IVIG with successful raising of his platelet counts to safe levels which allowed for successful CABG without platelet transfusion and without complications related to the well described post-IVIG hypercoagulable state.

Viscoelastic Testing in Orthopaedics and Trauma: Past, Present, and Future

◆ **Hatch J**, Speybroeck J, Marsee M, Grisoli A

Viscoelastic tests (VETs), such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM), are practical, cost-effective assays that provide a comprehensive evaluation of whole blood coagulation. VETs have several advantages over conventional coagulation assays, including activated partial thromboplastin time (aPTT) and prothrombin time (PT)/International Ratio Normal (INR), which depict only the coagulation cascade's initial fluid phase (the ability to initiate clot formation). VETs are gaining popularity among non-orthopaedic trauma physicians as an assessment of comprehensive coagulopathy from clot formation through clot stability versus fibrinolysis, and as an adjunct to guide blood component therapy resuscitation. Additionally, VETs are useful in monitoring post-operative coagulation status, predicting the risk of venous thromboembolism, and evaluating the clinical inhibition for patients on anticoagulants and antiplatelet agents. Despite these applications, the discussion of VETs remains sparse in orthopaedic literature. This review familiarizes orthopaedic surgeons with the usefulness of VETs in orthopaedic trauma and elective surgeries and highlights emerging research into orthopaedic specific applications of VETs.

Posterior Tibial Slope in Patients Undergoing Anterior Cruciate Ligament Reconstruction (ACL) with Patellar Tendon Autograft: Analysis of Subsequent ACL Graft Rear or Contralateral ACL Tear

◆ **Shelbourne KD**, Benner RW, Jones JA, Gray T

Objectives: To examine the relationship of posterior tibial slope and rate of graft tear or contralateral anterior cruciate ligament (ACL) tear among patients undergoing primary or revision ACL reconstruction with patellar tendon autograft.
Methods: From June 2001 to 2015, 2,796 patients received primary or revision ACL reconstruction with patellar tendon autograft (PTG) and were followed prospectively to determine rate of graft tear and contralateral ACL tear. Minimum follow-up for study inclusion was 4 years. Posterior tibial slope (PTS) was measured preoperatively on digital lateral view radiographs with knee flexion between 30° and 45°. Intersecting lines were drawn along the medial tibial plateau and the posterior tibia; the value of the acute angle at the lines' intersection was then subtracted from 90° to obtain the PTS. This procedure was carried out by a clinical assistant with interrater reliability of 0.89. Chi-square analysis, Pearson correlation, and t-tests were used to determine relationships between rate of graft tear or contralateral ACL tear and PTS, age, and sex among primary and revision surgery groups. A threshold of PTS ≥10° was used for analysis.
Results: The mean age of patients was 24.3±10.2 years for patients undergoing primary ACL reconstruction (n=2472) and 24.3±8.8 years for revision ACL reconstruction (n=324). The mean follow-up time was 11.6 ± 4.0 years. The rate of primary graft tear was 5.1% (n=126), and primary contralateral ACL tear rate was 4.9% (n=121). The rate of revision graft tear was 5.9% (n=19), and revision contralateral tear rate was 1.9% (n=6). Among primary reconstructions, the mean surgery age of patients who experienced graft tear (19.2 ± 6.3 years) or contralateral tear (21.5 ± 9.5 years) were significantly younger (P<.001, P=.0011, respectively) than patients who did not suffer a subsequent tear (24.7 ± 10.3 years). The mean PTS among primary graft tears was 5.4 ± 3.1°, which was statistically significantly higher than the mean of 4.8 ± 2.9° for patients without tear (P=.041). The mean PTS was 4.9 ± 3.3° for patients with contralateral tears, which was not statistically significant different than other groups. Furthermore, primary reconstruction patients with PTS≥10° had a significantly higher rate of graft tear (9.6%) than patients with PTS ≤9° (4.7%) (P=0.004), but not a higher rate of contralateral tear. Among patients undergoing revision surgery, there were no statistically significant differences between graft tear, contralateral tear, and no tear groups with relation to age, PTS, or PTS ≥10°. Among all patients (primary or revision group), there was no difference in PTS between sexes (P=0.278), nor was surgery age significantly correlated to PTS (R=0.0226).
Conclusion: Higher PTS appears to be correlated to higher rates of ACL graft tear in patients undergoing primary ACL reconstruction with PTG, particularly when PTS is greater than 10°. However, rate of graft tear remains low (5.1% overall, 9.6% with PTS≥10°). Furthermore, for patients undergoing revision surgery, there is no significant association between PTS and rate of subsequent tear. Therefore, caution should be exercised when considering more radical interventions, such as osteotomy, to prevent retear in patients with high PTS.

Utilization of Extracorporeal Membrane Oxygenation for Pulmonary Toxicity Caused by Inhaled Synthetic Cannabinoid. A Harbinger of Future Complications Associated with Inhaled Cannabinoid Products

◆ **Speybroeck J**, McCauley R, Hatch J, Betts A, Mark N, Keenan M, Jones J

Emergencies related to synthetic cannabinoids (SC) have increased recently in the United States. The legalization of marijuana in states such as Nevada, Maine, Colorado, and California has increased accessibility of SC leading to the presentation of medical complications related to SC. The most common adverse presentations of SC use include nausea, vomiting, anxiety, psychosis, paranoia, and agitation. In addition, there are case series and case reports of stroke, hypertension, cardiac toxicity, and encephalopathy related to SC inhalation. Specifically, there has been a recent increase in reports of respiratory pathology such as acute respiratory distress syndrome (ARDS), diffuse alveolar hemorrhage (DAH), and chronic pulmonary findings associated with inhaled SC use. The acute and chronic findings of direct pulmonary toxicity do not include the depression of respiratory drive caused by SC. In addition to SC induced respiratory depression, there has been a recent increase in cases due to direct pulmonary toxicity not related to aspiration or infection. In all the reported cases, alveolar hemorrhages developed within 48 hours after SC inhalation suggesting a temporal relation.

Direct pulmonary injury by SC leading to the development of ARDS and DAH requiring endotracheal intubation has been reported infrequently. Failure to successfully treat respiratory insufficiency, ARDS, and DAH caused by SC with endotracheal intubation and mechanical ventilation is even more rare. The utilization of Extracorporeal membrane oxygenation (ECMO) to treat such a patient has been reported on only one occasion in abstract form. In this first full case report we describe a 21-year-old woman who developed interstitial pneumonitis which required endotracheal intubation and immediate utilization of ECMO in order to ensure proper gas exchange.

How Do Preoperative Patient Characteristics Affect Clinical Outcomes for Partial Nephrectomy?

◆ **Krishnan N**, Zappia J, Steward, JE, Sundaram CP, Boris RS

Introduction: Few studies have investigated how preoperative patient and tumor characteristics affect clinical outcomes for patients undergoing robotic-assisted laparoscopic partial nephrectomy (RLPN). The objective of this study is to evaluate how these characteristics influence operative time, estimated blood loss (EBL), and length of hospital stay (LOS).
Methods: We conducted a retrospective review of a prospectively collected cohort of patients who underwent RLPN by two experienced robotic surgeons between 2013 and 2019. Preoperative patient and tumor characteristics were collected. The cohort was divided into tertiles based on operative time (the 25th percentile and faster, the 25th to 50th percentile, and the 50th percentile and slower). Univariate analysis was performed to compare the patient characteristics among the tertiles. A multivariable linear regression model was developed to examine the impact of these factors on EBL and LOS.
Results: A total of 410 patients who underwent RLPN were included in the study. On univariate analyses, tumor dimension, perirenal fat thickness, LOS, and EBL were all significantly related to longer operative time (Table 1). On multivariate analysis, tumor dimension significantly affected EBL in the fastest 25th percentile group, and RENAL Nephrometry Score significantly impacted EBL in the greater than 50th percentile group (Table 2 and 3). There were no other preoperative characteristics that significantly affected EBL or LOS among the tertiles. Conclusions: Tumor dimension and perirenal fat thickness have a significant influence on operative time. Longer operative time is associated with increased EBL and LOS. Overall, in the hands of an experienced robotic surgeon, preoperative patient and tumor characteristics have minimal impact on EBL and LOS.

All that Hurts isn't Appendicitis: A Case of Cecal Volvulus in Pregnancy

◆ **Burgett KM**, Pandita P, Smith C, Waller S, Menchaca A

Clinical Significance: Acute abdomen in pregnancy (AAP) represents a diverse range of etiologies, including obstetrical and non-obstetrical causes. Regardless of the etiology, management of AAP first begins with accessing the patient's hemodynamic stability. Hemodynamically unstable patients require fluid resuscitation and emergent exploratory surgery. On the other hand, hemodynamically stable patients may be classified as either urgent or non-urgent based on signs of sepsis, peritonitis, or deteriorating signs. Urgent cases warrant surgical intervention. Non-urgent patients are assessed via physical exam, lab work, and/or imaging to determine the most likely etiology, and if appropriate may trial conservative therapy first.
Case: A 24-year-old G3P2 female at 18 weeks gestation presented to the ED with severe right lower quadrant abdominal pain that was exquisitely tender to palpation. Abdominal ultrasound and MRI to rule out appendicitis were both inconclusive. She was taken to the OR for exploratory laparoscopy and possible appendectomy. However, intra-operatively she was found to have a cecal volvulus. Endoscopic detorsion was therefore performed. The cecum was examined and showed no signs of ischemia. Given the high risk of further intervention, definitive repair with resection or cecopexy was deferred until after pregnancy.
Conclusions: This case demonstrates the importance of prompt decision making when confronted with the acute abdomen in pregnancy. Normal physiologic and anatomic changes of pregnancy may make a diagnosis difficult, and physicians may be hesitant to operate on a pregnant patient. However, the use of decision-making algorithms based on hemodynamic stability and urgency may aid physicians in their decision of when to operate on a pregnant patient.

The Effects of Propofol of the Human Blood Brain Barrier

◆ **Lewis KA**, Hughes JM, Canfield SG

Background: Recently, the safety of repeated and lengthy anesthesia in young children has been called into question. Previous studies have shown propofol, an anesthetic, can diminish blood-brain barrier (BBB) properties. However, the underlying cellular mechanisms are relatively unknown. The BBB is critical in ensuring that potentially harmful circulating factors are impermeable to the brain. Previous animal studies models have shown that propofol increases the levels of matrix metalloproteinases (MMPs), which have independently been shown to degrade the extracellular matrix and breakdown tight junctions, a critical component of the BBB. Hypothesis: Propofol exposure to a human induced pluripotent stem cell (iPSC)-derived BBB model increases MMP activity ultimately contributing to a leaky barrier phenotype.
Methods: This study utilized human iPSCs differentiated into brain microvascular endothelial cells (BMECs), the barrier forming cell type of the BBB. iPSC-derived BMECS were exposed to propofol (50μM) for three hours and barrier properties were monitored. Barrier tightness was monitored using trans-endothelial electrical resistance (TEER) and sodium fluorescein permeability assays. Tight junction localization was determined with immunocytochemistry. MMP activity was determined with SensoLyteâ assay kits. To determine the role of MMPs, a broad spectrum MMP inhibitor, GM6001, was utilized and barrier properties were monitored.
Results: Propofol treatment significantly reduced TEER and increased sodium fluorescein permeability, indicative of a leaky barrier. Propofol treatment increased levels of MMP-2 activity but not MMP-9 when compared to non-treated BMECs. Inhibition of MMPs by GM6001 prior to propofol treatment appeared to partially restore barrier integrity as monitored by sodium fluorescein permeability.
Conclusion: These results indicate that increased MMP-2 activity levels could be in part responsible for diminished BBB properties. Inhibition of MMPs protected barrier integrity from propofol treatment. A further understanding of the underlying mechanisms of anesthetic-induced damage can potentially improve anesthesia safety.

Boerhaave Syndrome: an Emphasis on Early Detection and Intervention

◆ **Comer L**, Campbell N, Bozell H, Ivaturi S, Bona A

A 93-year-old male presented to the ED with fever, abdominal pain, and hematemesis. He was previously treated for pneumonia and had no history of alcohol use or liver disease. He denied chest and back pain. Physical exam was unrevealing. CXR showed a left lung opacity and pleural effusion, but no mediastinal air. CT with IV contrast exhibited a large hiatal hernia with air foci within the intrathoracic gastric wall, and presence of a posterior mediastinal mass. Further CT with oral contrast confirmed a paraesophageal hiatal hernia with perforation but showed no extravasation of oral contrast.

The leading diagnosis for this patient was Boerhaave syndrome (BS) secondary to perforation within a hiatal hernia. Treatment included broad spectrum IV antibiotics. There was no stent-requiring esophageal tear identified on Esophagogastroduodenoscopy. His condition gradually improved and he was discharged with a proton pump inhibitor, IV meropenem, and a G-J tube.

We present this case of BS, a rare phenomenon of esophageal perforation with diverse presentations and a high mortality of 40% if untreated. The pathophysiology of BS includes elevated intra-abdominal pressure progressing to transmural tears in the esophageal-gastric junction. Presentation depends on the location of the tear. Cervical tears typically present with pain radiating to the back, dysphagia, crepitus, and infection while thoracic tears can present with pneumothorax, pleural effusion, empyema, and/or mediastinum crepitus. Differential diagnoses typically include: aortic dissection, acute pancreatitis, MI, and pneumothorax. Imaging studies can help confirm BS through CXR/CT showing air in soft tissues and widening of the mediastinum as well as esophagogram with water-soluble oral contrast for location of the tear. Early antibiotic and surgical intervention are critical to prevent fatal infection. Given its rare prevalence and high mortality without time-sensitive treatment, providers must remember to consider this dangerous differential for hematemesis and/or chest pain.

Brain Metastasis Epidemiology Over a 20-year Period at a Tertiary Care Institution in Indiana

◆ **Lorentz S**, McVeigh L, Williams A, Smith T, Monaco G, Shah M

Introduction: In comparison to the past twenty years, patients with metastatic cancer have multiple treatment options available today. As a result, many patients are now living longer with cancers that were previously associated with extremely poor prognoses. Prolonged survival rates have increased the percentage of cancer patients with brain metastases. However, it is unknown if the primary tumor epidemiology is changing. Such information could contribute towards research efforts in brain metastasis prognosis and treatment.
Methods: The neuropathology database at Indiana University, the state's only National Cancer Institute-designated institution, was queried from the years 1997 – 2017; brain metastasis samples were recorded along with demographic, treatment, and survival data in conjunction with available primary sample pathology. Pediatric data and spinal metastases were excluded.
Results: Diagnosis of brain metastasis at our institution is increasing, occurring almost 2 years after diagnosis of primary cancer, including patients with brain metastases on initial cancer diagnosis. Median survival after brain metastasis diagnosis is 9.3 months, which is consistent with other population data. Synchronous brain metastases presentations were 292 out of 688, a high percentage of 42.3%. The five cancers that preferentially metastasize to the brain (breast, lung, melanoma, renal, and gastrointestinal) are unchanged; lung cancer is commonest (29.5% of cases). Relative to national averages previously reported, melanoma has surpassed breast cancer in our area.
Conclusions: This epidemiologic study of brain metastases is the first to include Indiana data. The observation of patients whose initial cancer presentation includes synchronous brain metastases may reflect the health of the region. Since advances in oncology have increased survival, the risk for developing brain metastases has increased. With this knowledge, efforts should continue to focus on the main cancer subtypes with a particular emphasis on lung cancer treatment and screening for brain metastases.

Diameter Dependence of Dual-Wavelength Retinal Oximetry

◆ **Rowe LW**, Arciero J, Harris A, Siesky BA; Verticchio-Vercellin AC, Mathew S; Beach JM

Purpose: Retinal vessel oxygen saturation obtained by dual-wavelength oximetry shows a dependence on vessel diameter with measured saturation increased in smaller vessels. This is considered an artifact of measurement as hemodynamic considerations cannot explain it. This study aims at understanding the artifact as a consequence of vessel light transmission and reflectance from retinal tissue.
Methods: Retinal oximetry data were compared with outcomes from a model of tissue reflectance (Kubelka Munk, KM). KM considers only double-pass transmission (transmission to and from retina behind vessel) and back-scatter by lumenal blood. KM predicts that vessel reflectance, and ultimately measured saturation, follows a nonlinear (hyperbolic) relationship with vessel diameter. Light intensity returned from first and higher-order vessels (Iv) and from adjacent retina was extracted (Oxymap Analyzer) from dual-wavelength oximetry images. Vessel reflectance (Rv) was defined by the relationship Rv = Iv / I0, where illumination intensity I0 was determined such that for large vessel diameter (>150 mm), vessel reflectance matched the theoretical reflectance predicted by KM.
Results: At the oximetry measurement wavelength (600 nm), there was close agreement across the sampled diameter range (20-200 mm) between KM reflectance and experimental arteriolar and venular reflectance. At reference wavelength (570 nm), for diameters below 90 mm, the experimental reflectance from both vessel types exceeded by as much as 1.4x the model prediction.
Conclusions: Agreement between oximetry data and KM supports the role of double-pass transmission as a source of diameter sensitivity. As diameter decreases, reflectance behind the vessel becomes important, increasing Iv which ultimately raises measured saturation. Smaller diameter also allows single-pass transmission through the vessel which is a departure from the KM model. At low absorption (600 nm) the contribution is weak since there is nearly equal light return inside and outside vessels. At high absorption (570 nm), single-pass transmission raises vessel reflectance above the model prediction.

Insulin Receptor Substrate 1 (IRS-1) Regulates Circadian Rhythm of Retinal Period 2

◆ **Arif M**, Mathew D, Luo Q, Bhatwadekar AD

Background: The mammalian circadian rhythm regulates many physiological processes. The circadian rhythm at a molecular level is controlled via a complex set of clock proteins, such as Period1 (Per1), Period2 (Per2), CLOCK, and BMAL, among others, interlock and form autoregulatory feedback loops that oscillate. It has been found that even many peripheral tissues such as retina, liver, pancreas also exhibit their own circadian rhythms. Dysregulated circadian rhythm has been implicated in the development of a variety of diseases, including diabetes. IRS-1 is a critical downstream regulator of insulin's action. We explored the hypothesis that inhibition of IRS-1 using a pharmacological inhibitor SecinH3 would alter the biorhythm of clock protein Per2 in the retina.
Method: Using mPer2Luciferase knockin mice, we utilized isolated cultured retinas and used 100uM SecinH3 to inhibit IRS-1 and mimic the diabetic condition of impaired insulin signaling. We performed real-time bioluminescent recording of circadian rhythms using a Lumicycle luminometer. We also created a cDNA library from treated harvested retinas and measured mRNA expression of specific clock genes by quantitative PCR.
Results: Our results demonstrate that IRS-1 inhibition by 100uM SecinH3 created a prominent increase in the period lengths and induced an apparent phase shift when compared to control. Gene expression studies also showed a difference in expression profiles of clock genes Per1 and Cry1.
Conclusion: Our findings demonstrate the impact of insulin signaling in retinal circadian rhythm and provide another temporal dimension to view ocular complications of diabetes, such as diabetic retinopathy. Ultimately, further studies and a closer understanding of the roles of molecular clocks and insulin signaling may help to develop novel therapeutics for treating some of the harmful effects of diabetes.

Qualitative Analysis of Children with Mobility Disabilities and their Caregivers in Gulu District of Post-Conflict Northern Uganda

◆ **Etling MA**, Amony J, Muyinda H, Ogwang M.

In Uganda, approximately 12% of children, or 2.5 million individuals under the age of 18, have a disability. While disability prevalence varies across Uganda, it is highest in the northern region which has experienced decades of civil strife. In 2014, the United Nations Children's Fund (UNICEF) identified children with disabilities living in Uganda as a vulnerable population in situational analysis, however limited qualitative data was gathered from the northern region.

This study aims to gain a deeper understanding of the barriers experienced by children with mobility disabilities and their caregivers in Gulu district. In total, 50 semi-structured interviews were conducted with caregivers living in 16 villages within Paicho division and Bardege division. Using a community-based approach, families were identified by the village chairman (LC1). Caregivers included 31 mothers (accompanied by 4 fathers), 2 step-mothers, 11 fathers, 3 grandmothers, 1 grandfather, 1 aunt, and 1 sister. Caregivers were primarily Acholi, Christian, and working as peasant farmers, casual laborers, or operating small businesses. Additionally, 24 semi-structured interviews were conducted with key informants, including teachers, government officials, medical professionals, and traditional healers.

Using thematic analysis, the following were determined to be the primary barriers: limited understanding of disability, financial constraints, negative attitudes, lack of paternal support, limited supportive and rehabilitative services, and lack of accessibility. Due to abandonment, death, or remarriage, some children were living with relatives or in institutions, rather than with their birth parents. Overall, caregivers were most concerned about the child's health, education, and future independence.

At the conclusion of the study, caregivers and key informants were invited to a workshop where the results were disseminated. The workshop included activities on education, empowerment, and community. This gave caregivers the opportunity to get build relationships and to learn about how to access resources in the community from key informants.

Effects of the Coronavirus Disease 2019 Pandemic on the Functioning of a Student-Run Free Clinic

◆ **Aksu E**, Read M, Gensel A, Smock C, Barber M, Khan M, Pandita P, Aref M

Background: The COVID-19 pandemic has affected primary care across the country. The pandemic poses a unique challenge for the Indiana University Student Outreach Clinic (IUSOC), a student-led free clinic on Indianapolis' near-east side, where students from health professions, law, and social work partner to serve patients. Student-run clinics depend on students to function, and with nation-wide cessation of student participation in healthcare, this multidisciplinary clinic has been limited to faculty-run urgent medical consults and medication refills. The objective of this study is to measure the impact of clinic closure due to COVID-19 on patient care at the IUSOC.
Methods: Patient care data from January 2019 to March 2020 was compared to data since the closure of most clinic services on March 15, 2020.
Results: The IUSOC cared for 727 patients in 2019 (average of 24 encounters per clinic day) and 246 patients in 2020 (average of 31 encounters per clinic day) before closure due to COVID. In March 2020, the clinic cared for 62 patients in the first 2 weeks before clinic closure and only 3 after clinic closure. The IUSOC cares for 249 patients with hypertension and 131 patients with diabetes. In this time period, 21.2% of HbA1c measurements were above 9.0%, requiring close follow up. Since clinic closure, an average of 11 appointments were cancelled per clinic day. With ongoing data analysis, our presentation will include further analysis of effects on chronic disease management.
Conclusions: The closure of the IUSOC due to the COVID-19 pandemic has halted patient care, leaving an already vulnerable population alone with their chronic and acute concerns. The IUSOC team is working on creative ways to maintain patient care through clinic closure and without student volunteers. Understanding the impact of closure on patient care will prove essential to the continuity of care at IUSOC.

The Effect of Ocular and Leg Dominance on Single-Leg Balance

◆ **Dimmett MM**, Needle AR, Liu K

Background: Maintaining balance requires multiple systems to work together to assess somatosensory input and make corrective motor outputs. Comparisons in stability measures can be influenced by unintentional effects of ocular and leg dominance. There are mixed results in the effect of leg dominance on stability. No differences have been reported between eye dominance conditions. The purpose of this study was to examine the interaction of ocular and leg dominance on stability.
Methods: This cross-sectional study included 49 subjects (M:8, F:41, age: 20.1±1.6yrs, height: 169.8±8.2cm, mass: 66.9±10.3kg). The experiment consisted of three 20-second static stance trials of eight conditions for a total of 24 randomized trials on a force plate. Conditions included standing on a single leg (dominant/non-dominant) with both eyes-open (BO), both eyes-closed (BC), dominant eye-open (DO), and non-dominant eye-open (NO). Average time-to-boundary (TTB) minima in the anteroposterior (AP) and mediolateral (ML) directions were calculated and a 2x4 ANOVA was used to analyze the interaction of ocular and leg dominance on TTB.
Results: The ML component of TTB-minima showed no significant interaction ($F=0.892$, $p=0.447$), but had significant effect of eye ($F=188.829$, $p<0.001$) and leg ($F=10.745$, $p=0.002$) conditions. The BO condition had significantly better TTB-minima and the BC condition had significantly worse TTB-minima than any other eye conditions. The non-dominant leg had significantly better TTB-minima than the dominant leg. The AP component showed no significant interaction ($F=0.603$, $p=0.614$) or significant effect of leg condition ($F=0.101$, $p=0.752$), but had a significant effect of eye condition ($F=82.602$, $p<0.001$) with the BO condition significantly better TTB-minima than any other eye condition.
Conclusion: Single-leg balance on the non-dominant leg with both eyes-open was the most stable condition. The TTB-minima showed more instability in the ML direction compared to the AP direction. Since the foot is longer than it is wide, more ML adjustments must be made to maintain stability.

The Importance of the Newborn Screen in Detection of Congenital Hypothyroidism in Females

◆ **Nunge R**, Rose M, Husain M, Bittar J, Zimmerman M

Clinical Significance: Congenital hypothyroidism has an incidence of 1:2000 in the United States, and females are twice as likely to be diagnosed. Thyroid hormones are necessary for physical and neurological development, especially brain development. The prognosis for congenital hypothyroidism is excellent as long as medication is started early (as in this patient's case). The severity of neurodevelopmental defects is related to the severity of the case, as well as how long the hypothyroidism is left untreated. The longer an infant goes without treatment, the more severe the deficit is, as demonstrated by lower IQ values. This case illustrates the need for comprehensive newborn screening for thyroid deficits. Newborn screening is a public health program whose recommendations vary by state, region, and country.
Case: A nine-day-old female infant presented to the pediatric endocrinology clinic to establish care for congenital hypothyroidism. She was born vaginally at 36 weeks and 6 days, without complications to a 15-year-old mother with no past medical history or family history of chronic illnesses, including thyroid disease. At birth, she weighed 5 lb 10 oz, and was 19" long. Newborn screen showed TSH >1000 mcU/mL (reference 0.72-4.77) and free T4 of 0.3 ng/dL (reference 0.9-1.7). Exam revealed slightly indented anterior fontanelle, overriding sutures and a palpable posterior fontanelle. She had no palpable thyroid. Thyroid ultrasound showed no thyroid tissue in the neck. She was started on 37.5 mcg (16 mcg/kg) daily of levothyroxine. At two-month follow-up, TSH had decreased to 17 mcU/mL and free T4 1.1 ng/dL. Accordingly, her levothyroxine dose was increased to 44 mcg. Two months later, her TSH was 25 mcU/mL and free T4 1.2 ng/dL. She will require lifelong thyroid supplementation and close follow-up.
Conclusions: Newborn screening for thyroid defects is crucial to detect congenital hypothyroidism and prevent lifelong neurocognitive deficits and developmental delay.

Predictors of Use of Spreader Grafts in Patients Undergoing Nasal Valve Repair

◆ **Marsee MK**, Newman S, Novinger LJ, Nesemeier R, Shipchandler TZ

Introduction: Spreader grafts are commonly used in nasal valve repair. Preoperative history/physical exam findings associated with use of spreader grafts have not been fully characterized. The purpose of this study was to describe the most common preoperative symptoms and exam findings of nasal airway obstruction.
Methods: Single academic center retrospective study of patients who have undergone surgery by facial plastics trained otolaryngologists for nasal airway obstruction. Adult patients with nasal airway obstruction undergoing septoplasty and/or nasal valve repair performed by facial plastics fellowship trained faculty from 2015 to 2019 were included. Clinic and operative note review was performed, data was stored in a RedCap Database, and statistics were completed with GraphPad Prism.
Results: Of 176 patients included, 51.7% were male, mean age was 46 years (SD 15.48), and 27 patients received spreader grafts. Spreader graft patients were significantly more likely to complain of purulent nasal discharge preoperatively ($P<.0131$), and trended toward xerostomia ($P<.1410$). Preoperative signs/symptoms recorded but statistically insignificant were: cranial nerve dysfunction, external bony/cartilaginous deformity, xerostomia, obligate mouth breathing, difficulty sleeping, objective or subjective improvement with modified Cottle maneuver, foreign body sensation, chronic sinus pressure/pain, anterior rhinorrhea, nasal tumor, sneezing, throat itching, headache, and age at the time of surgery.
Conclusion: In this patient population, patients receiving spreader grafts were significantly more likely to have purulent nasal discharge. Few preoperative characteristics were significant predictors spreader graft use in nasal valve repair surgery.

Novel Repair of a Traumatic Flank Hernia

◆ **Bhagat ND**, Tadevich JT, Drucker NA, Stanton-Maxey K, Laughlin M, Mossler LP

Background: Traumatic flank hernias often precipitate as a result of high-speed blunt force traumas, such as high-speed motor vehicle accidents. Open repairs may prove challenging due to abdominal oblique muscle avulsion from the iliac crest as a result of the trauma, resulting in unstable anchoring for the hernia mesh. In these instances, anchoring of the hernia mesh to the iliac crest may be a more suitable treatment solution with regards to patient safety and outcome.
Case: A 47-year-old male was admitted to a Level 1 trauma center after involvement in a motor vehicle collision. Among other injuries, patient presented with left sided traumatic abdominal hernia. Upon readmission 1 month later, laparotomy was performed for treatment of the hernia with concern for strangulation. Postoperatively, the traumatic flank hernia was stable over the next approximately 17 months, however the patient then experienced recurrent flank bulging consistent with progressively enlarging recurrent hernia over the course of 4 months prior to presenting to clinic. Final repair of the traumatic flank hernia was successfully completed approximately 22 months post-trauma. Open repair with mesh anchored to the iliac bone was utilized in order to lower risk of recurrence and because the oblique musculature was unable to be brought down to the iliac bone to re-establish normal anatomy given the size of the defect. There has been no hernia recurrence 5-months post operatively.
Discussion: Traumatic flank hernia injury can be complicated by abdominal wall musculature avulsion from the iliac crest, and traditional traumatic flank hernia repair relies on anchoring of hernia mesh to these abdominal muscles, so avulsion can reduce effective treatment options. As seen in this patient, anchoring to bony structures such as the iliac crest are a suitable option in these cases, resulting in more effective traumatic flank hernia repair.

A Case of Vancomycin-Induced Thrombocytopenia

◆ **Hadley A**, Bell M, Gates K, Prakash A, Gandhi D

Case: 80-year-old female was admitted for bullous pemphigoid exacerbation. Her course was complicated by acute thrombocytopenia with a decrease from 341k to 55k over a 24-hour period five days after initial presentation. She was started on vancomycin on admission due to concern for infection. Drug-induced thrombocytopenia was suspected. Her serum was found to be positive for anti-vancomycin antibodies. Platelet counts reached a nadir of critically low levels down to 6k but improved with removal of vancomycin, platelet transfusions, intravenous immune globulin (IVIG), and steroids. Platelet count improved to 91k prior to discharge.
Conclusions: Drug induced thrombocytopenia (DITP) is an immune-mediated reaction to drug exposure that generates drug-dependent antibodies, resulting in platelet destruction. It often presents as sudden, severe thrombocytopenia. Certain drugs such as quinine and NSAIDs are more commonly implicated; in the case of our patient vancomycin was thought to be the culprit. While the exact mechanism is unknown, it is thought to be mediated by anti-vancomycin antibodies that promote platelet clearance.
Clinical Significance: DITP is a serious condition that requires prompt diagnosis and treatment to avoid complications such as fatal hemorrhage. It is often overlooked due to confounding factors such as sepsis, splenic sequestration, and heparin administration. DITP should be considered in patients with severe thrombocytopenia five to ten days after exposure to a new drug, making a thorough medical review essential. Immediately remove the suspected offending agent and if the patient is at high risk of hemorrhage, platelet transfusions, IVIG, and corticosteroids can be considered. Counsel the patient to avoid the drug going forward. DITP is a clinical diagnosis made through exclusion and correlation, for confirmation drug-dependent antibodies can be considered. It is important that clinicians recognize drug induced thrombocytopenia.

Fundamentals of COVID-19: Virtual Student-led Curriculum Design for Third and Fourth-Year Medical Students

◆ **Bailey K**, Baker J, Brenner A, Brown C, Chiu M, Francis B, Galante E, Gerena R, Gomez M, Luna Hinojosa M, Huang C, Khan I, Roll R, Ko P, Allen B, Bauer M, Mensz J, Corson-Knowles D

Introduction: In early March 2020, the Association of American Medical Colleges (AAMC) recommended pulling medical students from clinical rotations. This turned medical education on its head but it also provided a unique opportunity for Indiana University senior medical students to participate in medical education curriculum design.
Methods: A 13-student student cohort was enrolled in the "Leadership in Medical Education During COVID-19" elective during the month of April. During this month, they used curriculum design approaches to create a core curriculum COVID-19 course under faculty guidance. Student engagement was measured in large synchronous sessions. Students' change in knowledge, skills, and abilities was measured via a pre-course and post-course survey.
Results: The 2-week course consisted of 16-modules that covered all six IUSM competencies and were mapped to 20 course learning objectives. Its first delivery was in May 2020 to 726 medical students in either their third or fourth-year of undergraduate medical training. Student engagement was measured via comments made during large synchronous sessions on zoom webinars. Pre-course survey rate was 98.5%. Post-survey results have not yet been finalized.
Discussion: Student-led curriculum design led to a course that was more student-friendly in the balance of synchronous to asynchronous content. Having students create content while faculty resources were overwhelmed also allowed for collation of a lot of material from many sources. This material can be adapted to graduate medical education in the future.

Unsuspecting Household Sounds With Risk for Hearing Loss

◆ **Kokoska, RE**, Kokoska, SE, Rohr-Kirchgraber, TM

Background: Environmental noise exposure literature provides little or no information on household appliances. Exposure to loud noises is known to result in hearing loss. Many household tasks such as vacuuming, cooking, care of pets, are frequently performed by women, either as employment (baristas, housekeepers, etc..) or home care. Hearing loss increases the risk for environmental harm, dementia, and poor quality of life. OSHA has standards regarding occupational noise exposure, but domestic exposure is unregulated and scarcely investigated.
Methods: Noise Levels A-weighted decibels (dBA) were measured with NIOSH sound level meter app and calibrated Apple Watch Model: watchOS 6.1.3. Both devices were held at the tester's ear level, at standard distance to appliance when in use, and at constant distance to the appliance or pet. Measurements were taken 3 times for 5 seconds duration, and the maximum dBA during each period was taken because of the lag to maximum motor speed and associated content grinding if applicable.
The tester wore ear plugs and / or ear protective covers when performing the measurements. dBA measurements were recorded indoors in quiet ambient environment (baseline was 30-33 dBA).
Results: None of the appliances tested offered manufacturer's noise warnings or measured levels. All emitted noise >/= 80 dBA. Normal use and exposure periods are normally >5 seconds.
Conclusions: Typical household appliances and pets can emit noise at levels >/= 80 dBA. Chronic exposure at and above these levels can cause temporary to permanent hearing loss.
Recommendations:
1) Advocate for Manufacturers' labels with dBA levels for appliances
2) Promote awareness of risk from household environmental noise exposure
3) Enhance strategies for managing appliances and pets that emit harmful noise levels.

Early Radiographic Osseointegration of a Modern 3D-Printed Highly Porous Patella Component Used in Cementless Total Knee Arthroplasty

◆ **Prado R**, Deckard ER, RM Meneghini

Introduction: Cementless fixation in total knee arthroplasty (TKA) is experiencing a resurgence. However, cementless patella components historically have been fraught with unacceptable failure and considered by many to be the "Achilles heel" of cementless TKA. Advances in technology have provided optimism that past failure mechanisms can be mitigated. This study purpose was to radiographically evaluate a modern 3D-printed cementless patellar component.
Methods: A retrospective review of 127 consecutive cementless TKAs from 2015 to 2018 utilizing one cementless 3D-printed highly-porous titanium patellar component was performed. Radiographs were evaluated with two blinded ratings for radiolucent lines and patellar tilt according to the Knee Society Radiographic Evaluation System at baseline 1-month and latest radiographic follow-up.
Results: Ninety-two cases obtained minimum one-year radiographic follow-up (mean 22.9 months). Mean age and BMI were 57.0 years and 36.8 SD kg/m2; respectively and 60% male. Mean preoperative and postoperative patellar tilt were 4.3 and 2.5 degrees, respectively. From 1-month to latest follow-up, radiolucent lines decreased in all zones (range, -0.2% to -21%). All radiolucent lines were <1mm in depth and 88% were isolated to the non-porous ends of pegs, indicating full ingrowth around the porous peg periphery and the porous ingrowth patella baseplate surface. With available numbers, age, BMI, gender, current tobacco use, and patellar tilt did not predict the presence of radiolucent lines ($p \geq 0.337$). No patellar components were revised and no radiographic osteolysis was observed.
Conclusion: Early radiographic results of this 3D-printed patella component with a highly-porous titanium ingrowth surface show promising osseointegration at minimum one-year. Radiolucent lines were generally small and located at the end of the porous pegs. Radiographic osseointegration was consistently evident around the highly-porous titanium pegs indicating some degree of differential ingrowth between the pegs' peripheral circumference and the ends. Further research is warranted for long-term follow-up of this cementless patellar component

Hif1a-miR-21 Signaling Exacerbates Beta Cell Dysfunction During Diabetogenic Stress

◆ **Ibrahim S**, Hernandez-Stephens C, Moore R, Mirmira R, Sims EK

A hallmark of diabetes is the loss of physical or functional Beta (β) cell mass. MicroRNAs (miRNAs), small RNAs that repress mRNA translation, serve as important regulators of β cell development and function. We previously showed that β cell microRNA 21 (miR-21) is increased by islet inflammatory stress and diabetes, that miR-21 induces β cell dysfunction by targeting mRNAs maintaining β cell identity, and that β cell miR-21 induction in vivo leads to hyperglycemia. However, upstream regulators of β cell miR-21 are poorly defined. We hypothesized that increases in the transcriptional regulator Hypoxia Inducible Factor 1 Subunit Alpha (Hif1a) during diabetogenic islet stress activate β cell miR-21 transcription, thereby contributing to loss of β cell identity occurring under these conditions. To test this, we examined Hif1a and miR-21 levels in β cell lines and mouse islets. Hif1a was increased in islets from mice after multiple low dose streptozotocin (STZ) or 4 wks of 60% high fat diet (HFD). Hif1a overexpression in INS1 cells increased miR-21 levels, insulin and glucagon co-expression, and aldehyde dehydrogenase 1a3 staining, all suggesting loss of β cell identity. By contrast, siRNA depletion of Hif1a abrogated cytokine-induced reductions in mRNAs regulating β cell identity. Chromatin immunoprecipitation studies verified increased HIF1a occupancy at the miR-21 promoter after IL1β treatment. To test if these HIF1a-mediated increases in β cell miR-21 exacerbate β cell dysfunction under diabetogenic conditions in vivo, transgenic mice harboring a β cell tamoxifen inducible miR-21 transgene (Tg(β-miR-21, Ins1(CreERT2)Thor) were treated with STZ or HFD. Compared to controls, STZ and HFD-induced hyperglycemia was exacerbated in Tg(β-miR-21) mice following tamoxifen administration. In conclusion, these findings implicate Hif1a-miR-21 signaling as a contributor to β cell dysfunction under conditions of inflammation and diabetes.

Novel Cranial Nerve VI Hypoplasia Causing Lateral Rectus Palsy with Pathogenic Variant in PPP1CB

◆ **White K**, Parikshak S, Christensen C, Curtin M

Introduction: We present a 2 year-old male with novel findings of cranial nerve (CN) VI hypoplasia with lateral rectus palsy in the presence of a pathogenic variant in protein phosphatase-1 catalytic subunit gene, or PPP1CB, (c.548 A>C,p.Glu183Ala). Changes to the PPP1CB gene have been reported via case series with Noonan syndrome-like disorder with loose anagen hair 2 (Noonan like-syndrome), a known RASopathy (appearing on some RASopathy panels). Changes to this gene have been previously described in 15 other patients with described clinical features including macrocephaly, ear findings, slow-growing hair, hypotonia, developmental delay, short stature, and feeding difficulties and imaging findings of white matter volume loss. Two patients in the series had the same variant as our patient, but the CN VI findings were not reported.
Case: Our patient initially presented with ophthalmological complications of alternating esotropia and nystagmus around 2-4 months of age, concerning for bilateral CN VI (lateral rectus) palsy. Pertinent imaging revealed bilateral CN II and VI hypoplasia, mild white matter volume loss, and thin corpus callosum. Developmentally, the patient has gross motor, fine motor, problem-solving, and speech delays. Other features included: hypotonia, short stature, delayed bone age, patent foramen ovale, unilateral preauricular pit, 2 café au lait spots, right sided cryptorchidism, and a right inguinal hernia. Genetic testing included karyotype analysis, chromosomal microarray (CMA), and Whole Exome Sequencing (WES). Karyotype analysis was normal. CMA produced a paternally inherited variant of uncertain clinical significance not likely causative of his phenotype. A WES trio followed and identified a pathogenic variant in the patient's PPP1CB gene; parents did not have this variant. The variant is a missense variant causing an amino acid change from Glutamine to Alanine (c.548 A>C,p.Glu183Ala).
Discussion: Of the 15 individuals with pathogenic variants in the PPP1CB gene previously described, including 2 with the same missense variant as our patient. The patient has many of the clinical features previously described, including relative macrocephaly, white matter volume loss on MRI, epicanthal folds, preauricular pits, developmental delay, hypotonia, short stature, delayed bone age, and cryptorchidism. Only one other individual was described as having a CN II hypoplasia like our patient in that case report. Our patient is currently the only individual with a diagnosis of bilateral CN VI hypoplasia with lateral rectus palsy. The findings from this case expand the PPP1CB phenotype and contribute to what is known about Noonan syndrome-like disorder with loose anagen hair 2 and RASopathies.

Enhancing Cytotoxic Chemotherapy Response Through Targeted BET Bromodomain Inhibition in Preclinical Pancreatic Cancer Models

◆ **Awasthi N**, Schwarz R, Schwarz M, Schwarz J, Singh S, McCauley R

Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis and the current standard of care regimen, nab-paclitaxel (NPT) plus gemcitabine (Gem), leads to a dismal 8.5 months median survival. Targeted inhibition of Bromodomain and Extra-Terminal (BET) protein is currently under investigation for several cancers. We hypothesized that BET protein pathway inhibition by iBet-762 will enhance cytotoxic chemotherapy response in PDAC. In vitro cell proliferation assays were performed using WST-1 reagent. Protein expressions were determined by Western Blot analysis. In vivo animal survival and tumor growth experiments were performed in NOD-SCID mice. Inhibition in cell proliferation in human PDAC cells at 1 μM concentration in NPT+Gem, iBET-762, and NPT+Gem+iBet762 was 64%, 27%, 76% in AsPC-1; 43%, 13%, 69% in Panc-1; and 42%, 51%, 75% in MIA PaCa cells. iBET-762 decreased oncogenic proteins c-Myc, b-catenin, Vimentin, and P-AKT while apoptosis-related proteins such as cleaved PARP-1 and cleaved caspase-3 and cell cycle inhibitors proteins P21 & P27 were increased. In a peritoneal dissemination model, median animal survival compared to control (21 days) was increased after therapy with NPT+Gem (33 days, a 57% increase), iBet-762 (30 days, a 43% increase) and NPT+Gem+iBET-762 (44 days, a 110% increase). These findings suggest that the effects of standard chemotherapy can be enhanced through specific inhibition of BET proteins activity, and supports the clinical application of iBET-762 in combination with standard chemotherapy in PDAC patients.

Limitations Impressed on Mobility Device Dependent Patients Due to Insurance Restrictions

◆ **Moore H**, Smith M, Gonzalez A, Rousseau E

Case: A 14-year-old male with history of localization-related epilepsy and spastic triparetic cerebral palsy, status post bilateral tibial rotation and foot reconstruction surgery has experienced a decline in his ambulatory function and endurance over the past several years. His main mode of mobility is a power wheelchair. He also requires a walker to assist ambulation at school for 20 minutes daily but cannot complete transfers independently. He is currently borrowing an ill-fitting transport chair and does not have a backup mobility device should any of his assistive devices malfunction. His private insurance and secondary Medicaid only cover one mobility device every five years. If his equipment failed, he would have no mode of independent mobility in the community which would greatly reduce his quality of life. This would limit him from attending school and medical appointments.
Conclusions: Pediatric patients would benefit from having access to multiple mobility devices and should not be restricted by insurance policies. Insurance coverage of only one device every five years is especially detrimental to pediatric patients because of their continued growth and development. Many of the guidelines established by insurance are geared toward the adult patient populations and are incompatible with the needs of pediatric patients. Insurance regulations, including the rules and requirements for coverage of mobility devices, should be reevaluated with greater consideration for the realistic needs of pediatric patients.
Significance: Understanding the impact of insurance on our future patients is crucial in providing the most appropriate and accessible care. Medical providers must educate themselves regarding medical insurance requirements and regulations to understand the limitations that their patients may face and to initiate change when possible. It is imperative for patients who rely on mobility devices to have access so that they can function at their highest potential at home and in the community.

Laparoscopic conversion of vertical banded gastroplasty to Roux-en-Y gastric bypass: outcomes of 44 patients.

◆ **Nader SM**, Bolhassani A

Background: Up to 50% of patients with vertical banded gastroplasty (VBG) experience failure or complications in the long-term and present for revisional bariatric surgery. This study aims to compare outcomes of VBG revision to primary gastric bypass (RYGB), in addition to reviewing our experience for indications and outcomes of VBG revisions.
Methods: Patients who underwent VBG revision surgery between 2009 and 2014 were identified. Perioperative outcomes and long-term weight loss, complications, reoperations and length of stay were analyzed and compared to those of matched primary RYGB patients. All patients enrolled in this study had failed VBG complications, weight loss of less than 50% in 2 years, stomal stenosis, stomal ulcers, intractable bleeding, reflux esophagitis, pouch dilation, GG fistula with weight regain.
Results: A total of 44 patients with a previous VBG who underwent revision after 17±7 years were identified. Mean age was 55 ± 9 years (female (n=39, 89%)). Thirty-nine patients converted to RYGB (89%), 1 to sleeve gastrectomy (2%), and 4 had VBG reversal (9%). Patients with VBG revisions were compared with 1589 patients after primary RYGB. VBG revisions were indicated because of weight gain (55%), dysphagia (20%), or both (25%). Of the 68% who were undergoing revision, 23% had strictures, 29% gastrogastric fistula, and 16% pouch dilation. Compared with primary RYGB patients, VBG revision patients stayed in the hospital longer, and experienced more complications. However, 2 years after revision to RYGB, BMI decreased significantly (36.7±6.2) compared to preoperation (49.8±11.9; $p<0.01$) except for patients who underwent VBG reversals gained weight (10 kg/m2 over 2 years). Dysphagia resolved in 100% and reflux in 95% of patients who underwent VBG conversion to RYGB.
Conclusion: Compared to primary RYGB complications after revision of VBG are substantial however they should not minimize its good outcomes. VBG revision to RYGB is effective in treatment of both weight gain and dysphagia.

Variable Presentations of Osteoporosis and the Importance of DEXA Screening

◆ **Swiezy S**, Junod C, Lewis K, Walker G

Case: 61-year-old Caucasian female, BMI 19.6. PMHx: total hysterectomy, smoker. FHx: osteoporosis. DEXA showed bone mineral density (BMD) L1-L4 vertebrae T-score = -1.6 and BMD femoral neck T-score = -3.6 (osteoporosis -2.5 [WHO]). Patient started on salmon calcitonin. Extensive dental caries necessitated prompt treatment and delayed bisphosphonate therapy (~1 year) due to risk of jaw osteonecrosis. Reclast (Zoledronate) then prescribed by infusion. Repeat DEXA 3 years after beginning Reclast: BMD L1-L4 vertebrae T-score = -1.6 and BMD femoral neck T-score = -2.4.

56 year old Caucasian female, BMI 34.2. PMHx: ER+ breast cancer treated with aromatase inhibitor, taking Ca and Vit. D. DEXA showed BMD L1-L4 vertebrae T-score = 0.9 and BMD femoral neck T-score = -0.15. Ca/Vit. D were continued, no further osteoporosis treatment was pursued. Clinical Significance: Osteoporosis affects 10 million Americans, with a disproportionate burden on women 65+ (24.8%, men 65+, 5.6%). It contributes to significant morbidity and mortality, with US women having a 1 in 2 lifetime risk of breaking a bone, often their hip, due to osteoporosis 2. And, 24% of hip fracture patients age 50+ die within the year following2. Sadly, 80% of Americans 65+ who have suffered fractures were never screened or treated for osteoporosis2, despite clear DEXA screening guidelines from the USPSTF, ACOG, and NOF3. While, osteoporosis often presents with no clinical symptoms, and risk factors are often not predictive of disease extent in individual patients, the availability of effective medical therapies implores physicians to be vigilant in their prescription of lifesaving DEXA diagnostic screening.
Conclusion: Osteoporosis represents a substantial health burden, especially for women. All women 65+ should receive DEXA scanning to assess bone density, while women with relevant risk factors should be screened earlier. Full implementation of current osteoporosis screening guidelines may drastically improve women's health.

Mollie Wheat Memorial Clinic: Missed Appointments Review and Improvements

◆ **Swiezy S**, Eckrote E, Ratcliffe B, Reyes E, Danek R

Introduction: Missed primary care appointments represent a potential cause for negative health outcomes in patients. As student clinicians, we have a responsibility to make sure patients with missed appointments are consistently and efficiently contacted for two purposes: 1) to reschedule appointments to facilitate access to needed care and 2) to evaluate and assess reasons for missed appointments so that, as providers, we can work to implement policies and procedures to overcome the barriers that cause our patients to experience delays in preventive assessment, treatment, and diagnosis.
Methods: Patients who 1) presented for a scheduled appointment, 2) did not present for a scheduled appointment, and 3) presented for a walk-in appointment were surveyed for relevant demographics. Patients in group 2) did not present for a scheduled appointment, were contacted via phone to understand reasons for missed appointment. Comparisons between the three groups of patients seen by MWMC will be made. Reason(s) for missing appointments will be evaluated and ranked from most to least common barriers to care. A literature review will then be undertaken to understand potential actions that MWMC can take to reduce the most common barriers to care and, thus, to decrease the percentage of missed appointments in our clinic population.
Future Directions: Through this prospective study, we hope to understand the basis for missed appointments in our population. Subsequent to the study, we plan to propose solutions aimed at decreasing the rate of missed appointments. We will continue to track rates of missed appointments after the implementation of our recommendations to evaluate their efficacy.

Temporal Bone Metastasis: A Systematic Review

◆ **Tucker BJ**, Jones AJ, Novinger LJ, Galer CE, Nelson RF.

Objectives: To describe a case and summarize all previously reported temporal bone metastases.
Methods: The PubMed, MEDLINE, Embase, and Web of Science databases were systematically reviewed according to the PRISMA guidelines to identify all reported cases of distant metastatic disease to the temporal bone. All articles with available English translation published until October 1, 2019 were included in our review. Descriptive statistics were performed on the extracted data.
Results: Out of 576 full-length articles included for review, a total of 119 met final inclusion and exclusion criteria for data extraction. Including our reported case of metastatic p16-negative tonsillar squamous cell carcinoma, a total of 276 individual cases of distant temporal bone metastasis were identified. There was a male predominance (55.4%) with median age of 60.0 years (range 2 – 90). The most common locations of primary malignancy included the breasts (19.9%), lungs (15.9%), and prostate (9.1%). Most tumors were carcinomas of epithelial origin (75.3%) and predominantly adenocarcinoma (50.5%). The commonest metastatic sites encountered within the temporal bone were the petrous (72.2%) and mastoid (49.5%) portions. Bilateral temporal bone metastases occurred in 37.9%. Patients were asymptomatic in 29.6% of cases. Symptomatic patients predominantly reported hearing loss (45.3%), facial palsy (32.8%), and otalgia (16.4%) for a median duration of one month. Management consisted primarily of chemotherapy and/or radiation (54.4%). Median recorded survival was 3.5 months.
Conclusions: Temporal bone metastasis is an uncommon phenomenon but should be considered in patients with subacute otologic symptoms or facial palsy and concurrent distant malignancy.

Oncology

"As the next generations of medical doctors the future of medicine and biomedical research rests on your shoulders. The successful practice of medicine requires continued rigorous scientific inquiry to find the best treatments for our patients. Your participation in research will make you a better doctor. That participation is broadly defined and can be anything from leading basic, translational or clinical research teams to being part of the team by providing patients for trials or simply using research to help guide your clinical decision-making. Your experience in research will prompt you to approach your patients as you would a research problem and to listen to them with a different ear. Research will provide you with the skills to solve their problems in this complex and ever-changing world. Be nimble and be aware of how quickly medicine can change. COVID-19 exposed extreme disparities in outcomes, and demands that we recognize, understand and address diversity in race, ethnicity, socioeconomic status, sexuality and more. Rigorous, sound research is needed now, move than ever. Medical doctors are needed for this research as they provide a unique and essential perspective to the research team. You are the ones charged to do this; embrace the challenge and embrace diversity to change the face of medicine for the betterment of us all."

Theresa A. Guise, MD
Jerry W. and Peggy S. Throgmartin Professor of Oncology
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