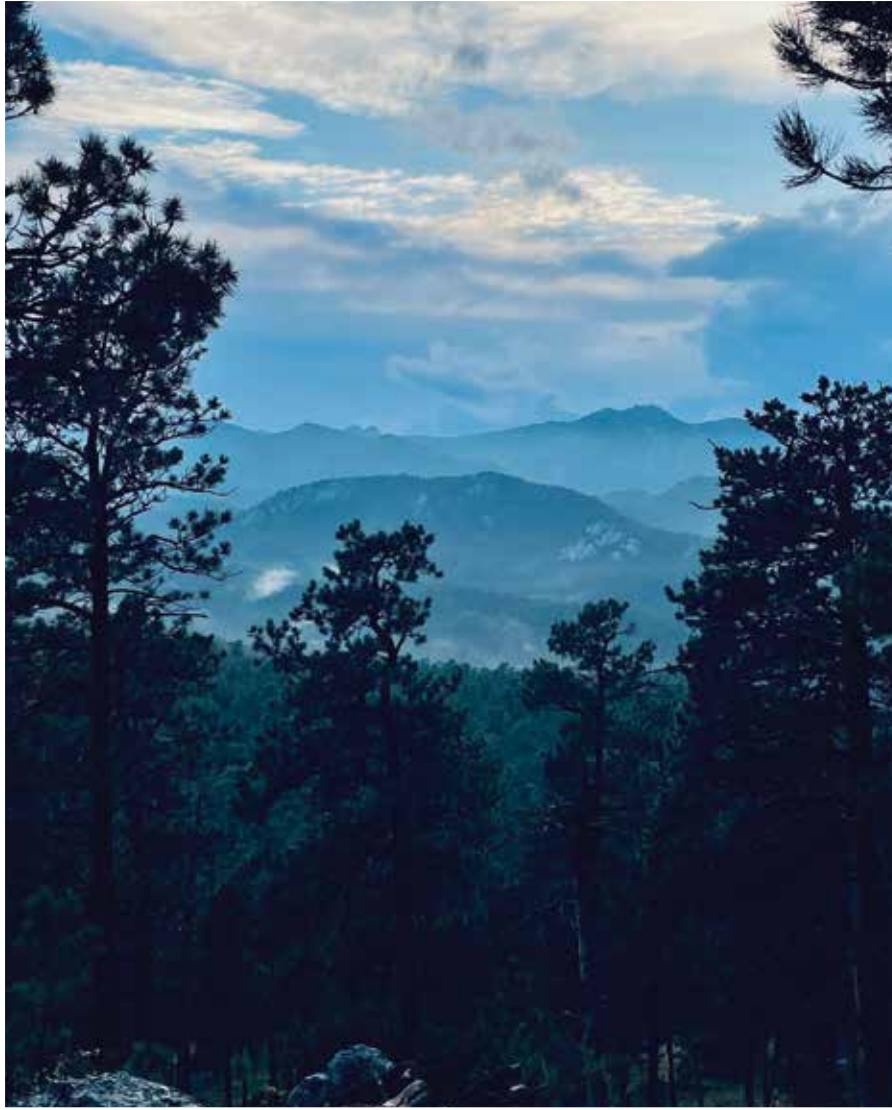


September 2024

Volume 77

Number 9



South Dakota
medicine

THE JOURNAL OF THE SOUTH DAKOTA STATE MEDICAL ASSOCIATION



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Prescription for Connection: Engaging Generation Z Medical Students in Today's Learning Environment

Alan Sazama, MD

About a year ago, I had a jarring experience. A new physician started in our group who happened to be one of the first medical students I worked with as a young attending. Now, I realize as a young millennial myself that I am not too far removed in age, but seeing the next generation start to join the ranks does bring up some important questions about relatability. Does my training match theirs? Is my knowledge base still current? Do we have the same philosophy for taking care of patients? While these questions certainly matter within the professional setting, they become even more pressing when considered within the realm of medical education. How do physicians who are 10, 20, or even 30 years post-residency relate to medical students now? There is not an all-encompassing prescription for relating to the newest generation of medical students, but I will attempt to log off my America Online account, turn off the anti-skip CD player, and provide 3 tips that I have found helpful when relating to this generation of learners.

Be a Person First, Physician Second

I graduated from the Sanford School of Medicine in 2014. Back then, we did not really meet with our senior leadership. We revered them, as if they were celebrities that we would be lucky to in the same room as. Today, accessibility to our medical school's leadership is incredible. Generation Z comes from an online culture with 24/7 availability of most resources that have existed for most, if not all of their educational journey. This translates to discussions with faculty and administration on a regular basis. What does that mean for us as physician faculty? Since reverence takes a back seat in many learners' minds, we need to also move away from an expectation of reverence. Students today are looking for people to relate to, a mentor who wants to spend time teaching them. I have an important job as a physician, but at the end of the day—as my wife will certainly confirm—I am just another imperfect person trying my best to help others. Let us not hide from that fact: let students see the real you, not the revered physician construct we've developed over years of practice.

Wellness is not a Four-Letter Word

Wellness is a word that brings up different feelings depending upon when you completed medical training. Older generations of physicians trained in an era before duty hour restrictions. For some with this experience, it can be hard not to equate the idea of wellness with laziness and a lack of resiliency. The generation of medical students coming up now has access to multitudes of resources talking about the crisis of physician burnout. The work we do in medicine carries a heavy responsibility. To prepare for this, medical training

requires a high level of responsibility and sacrifice. Our job, then, is to help students find a happy medium. It can be easy to hear a student lament about their lack of work/life balance and become frustrated. That balance certainly does not become any easier once you begin practice—I still struggle to achieve this! However, most of us can probably agree that we were better prepared for the rigors of the profession because our training was difficult, because it asked so much of us, because we sacrificed to get through it. However, we can also all probably agree that it would have been beneficial for us to consider personal wellness as the partner to rigor rather than its adversary. While we push our students to become great physicians, let us make sure we are also advocating for their own health and wellbeing, too.

Embrace Innovation

Gen Z tends to have a high preference towards continued innovation, and this carries into the academic setting. For instance, when I was a medical student, most of my learning happened via lectures with PowerPoint slides numbering into the hundreds. Today's students want something more, something active, something personal. As they become frustrated by the status quo of instruction, faculty feels the pressure of continuously finding new ways of delivering material. Whether it is active learning, asynchronous online modules, or even embracing newer technologies such as artificial intelligence or virtual reality, the days of recycling our old lectures and methods are gone. We should not take offense to newer generations having preferred instructional methods. Rather, we as faculty need to embrace these differences and innovate. I think we will find students will appreciate our efforts—and we may learn something new ourselves!

As I mentioned above, there is no catch-all prescription here. In fact, students reading this may even think I'm way off base. That is ok. I think the principles of being human, supporting student wellness, and embracing innovation are good goals for all physicians. However, I also believe that we can increase our buy-in from students by embracing these concepts regardless of how seasoned we are as faculty. The new generations of medical students have much to bring to the medical community. They are what keeps me working hard in medical education, and I am excited to see how they will continue to change healthcare for the better. Now, where did I put that VHS tape?

About the Author:

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THE SIGNIFICANCE OF AN EMERGENCY FUND

ANDY MULLAN, CFP®, Lead Advisor



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Recently, my family faced an unexpected financial challenge: Our home needed repairs that we hadn't factored into our annual budget. As we were talking about what to do, it suddenly dawned on us that this was why we had an emergency fund. Prior to this incident, our emergency fund had been out of sight and out of mind, because nothing happened that required it, which was a good thing. And while we hadn't anticipated tapping into those funds (that's why it's called an Emergency Fund!), the presence of that safety net provided immense relief.

Let's address the elephant in the room: Putting money aside for unforeseen circumstances isn't exciting. Yet, its importance cannot be overstated. Financial challenges consistently rank among the top stressors for individuals and families. Having a financial safety net can alleviate this stress and enable you to focus on finding solutions.

Many individuals often wonder, "How much should I keep in my emergency fund?" While the exact amount varies based on individual circumstances, a general rule of thumb is to aim for three to six months' worth of living expenses. This should cover essential costs such as housing, food, utilities, and insurance premiums during temporary

setbacks. If your emergency fund falls short today, now is the perfect time to begin building it up. Whether it's an unexpected medical expense, a major car repair, or an unforeseen job loss, these events can wreak havoc on a family's finances. This is precisely where your emergency fund steps in to provide a crucial safety net.

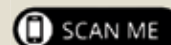
Another struggle people have is using their emergency fund when emergencies do happen. As I said above, we had more or less forgotten about our emergency fund. And when the incident happened, we didn't immediately think about using it. As we were talking, though, we realized that it was for things like this that our emergency fund existed. We didn't need to stress out about paying for the repairs. Now that the project is over, we will go about the task of steadily replenishing our emergency fund over the course of the next year.

Our recent experience drove home the importance of having an emergency fund. It's not merely about setting money aside; it's about cultivating peace of mind and stability when life throws unexpected challenges your way. While building and maintaining an emergency fund may not be the most thrilling financial goal, it undoubtedly ranks among the most essential.



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The Tube and the Telos

Wendell W. Hoffman MD, FACP, FIDSA

To the editor,

In Dr Henry Travers' *Reframing the Narrative* that appeared in the July issue of *South Dakota Medicine*,¹ he again is "...misunderstood..."¹, this while freeze-framing the pre-born human being as a "tube."¹ He also disconnects Embryology from its Epistemology – which is like disconnecting proof from its evidence. In Science, "Method" (knowing) *precedes* "Narrative" (telling). If not, Science is "Politics" (spinning).

Travers' science *was* compelling – including, "There is *no question* that our beginnings are human..."² – a *second party*, given that "Human embryos *are* self-organizing...in the absence of *any* maternal influence."² – *unique* given that, "...sperm and egg each contain chromosomes made up of genes characteristic of humans."² – and *continuous in development* given that, "Between the sperm's penetration of the egg, and the birth of an infant are *numerous steps* that each play a role in determining gestation's outcome..."² (italics mine)

Therefore, Travers' "...body of scientific evidence..."² framed the pre-born human being. But whether by irony or contradiction, his "Subjectivism"³ reframed that science into what appears sub-human – "...the vascular tube..."¹

Aristotle's "telos"⁴ is the adult human – before/after the "tube."¹ Per that great thinker, "...the telos of a member of a species is the complete and perfect state of that entity..."⁴ Dr. Travers is in a bind – for why would any of his, "...numerous steps..."² (including the "tube"¹) of Homo Sapiens, *be denied fulfilling its purpose?* The "tube"¹ may not yet be a four-chambered organ (gestational week 7) but it is the "heart" of its stage – speaking "lub-dub"²...and framing life.

With all due respect to a master thinker and formidable debater, this is semantic painting at its finest...*obscuring an entire forest with a single tree.*

Think again my friend.

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SDSMA's Collaboration With USD SSOM Runs Deep

Jen Tinguely, MD, MPH
President, South Dakota State Medical Association



Do you remember reciting the Affirmation of the Physician at your White Coat Ceremony? Being led through a series of statements that define the work and life of being a physician after having put on your school's white coat? As the SDSMA President, I was fortunate enough to be a part of this year's White Coat Ceremony for the Sanford School of Medicine Class of 2028 and was able to lead the students through the recitation of the Affirmation. It was an honor to be a part of something so defining in those students' lives and it is a testament to the deep level of involvement that the SDSMA has with our state's medical school.

At our SDSMA Annual Retreat this past July, Dr. Tim Ridgway, Dean of the Sanford School of Medicine, walked us through all the ways in which the medical association touches the medical school and reminded the Board of the vital role we, as SDSMA members, play in the medical school both now and historically. The very fact that Dr. Tim Ridgway, in his role as Dean, was in attendance is a wonderful example of that collaboration as the Dean of the Medical School is always an invited guest at the annual retreat of the SDSMA Board of Directors. The Dean is invited to participate in the entire retreat and their update on what is happening within the medical school is always a highlight of the retreat agenda.

The most obvious collaboration is the number of SDSMA members who are part of the medical school faculty and dedicate time and energy to teaching our students and residents. The Sanford School of Medicine is celebrating its 40th anniversary of being recognized as a four-year medical school this year. This designation was granted by the South Dakota State Legislature in 1974 under the purview of Dr. Karl Wegner. Dr. Ridgway reminded us that the medical association was integral to making that a reality as the school had only been a two-year program prior to that (starting in 1907). My guess is that, like all things in politics, much advocacy, information-sharing and relationship-building was done on the part of the medical association and its members.

Along the lines of politics and advocacy, members of the

SDSMA were key to creating an opportunity for all medical students to attend a Legislative Day at the Capitol in Pierre, SD. This event has been carried out for years, and for many medical students, it is their first entry into the world of legislation and advocacy. Be on the lookout this winter for the picture of all the medical students standing in their white coats in the rotunda smiling for a picture...oftentimes, the Governor will be in that picture, as well, which is a very special moment for the medical students!

Another wonderful example of the strong collaboration between the SDSMA and the medical school is the involvement of the Pierre Rural Family Medicine residents in the Doctor of the Day program at the Capitol. For those who are new, the Doctor of the Day program is a very successful program of the SDSMA in which a physician volunteers their time and spends the day at the Capitol, providing basic medical assistance to the legislators and staff as needed. Last year, each of the rural family medicine residents took a day and volunteered to be the Doctor of the Day. We hope to see the residency continue to do this year after year as it's a wonderful intersection between our learners and our SDSMA.

Other ways in which the SDSMA supports our medical students and residents is through scholarships that are granted through the SDSMA Foundation. Many of the districts have scholarships that are dedicated to students from those districts, and it is our hope that students who receive these dollars continue to serve in leadership roles both during medical school and residency and then continue their leadership through ongoing membership with the SDSMA. Another key example of collaboration between the SDSMA and the medical school is the fact that all medical students have their memberships in both the SDSMA and AMA paid for during the four years they are in medical school. This is a large financial investment and comes from generous donors within the SDSMA membership. A huge thank you to those members who sponsor a medical student for their SDSMA/AMA memberships!

Opportunities abound for medical students and residents to showcase their research and work through the poster session that has become a mainstay at the SDSMA Annual Leadership Conference. This is done alongside the Policy Council meeting and it's wonderful to see our Policy Councilors mingle through all the posters and learn something new. Also wonderful to see is how many medical students and residents submit articles to the *South Dakota Medicine* journal. It is evident that our students and residents are engaged in a plethora of research opportunities across the state. They are also incredibly talented writers and artists and we are excited to be highlighting some of their work in an upcoming supplement of the journal highlighting humanities in medicine!

Lastly, I want to highlight the amazing work that is being done within the South Dakota Physician Well-Being program. This is one of the programs that SDSMA members should be very proud of and we are happy to say that all medical students are given the opportunity to engage with the Physician Well-

Being program at least once during their years in medical school. It has been eye-opening to see how our students and residents are engaging with the program and it's not a stretch to say that the program has changed (or even saved) lives.

In closing, I would like to share a few lines from the Affirmation of the Physician that I was able to recite with the newly coated medical students in mid-July. *Now being admitted to the high calling of the physician, I solemnly pledge to consecrate my life to the care of the sick, the promotion of health and the service of humanity. In the spirit of those who have inspired and taught me, I will seek constantly to grow in knowledge, understanding and skills and will work with my colleagues to promote all that is worthy in the ancient and honorable profession of medicine.* To all of my colleagues across the state, thank you for the expert care you provide to your patients and thank you for the role that you play in teaching, guiding and supporting our soon-to-be colleagues in this beautiful profession we have dedicated our lives to.

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2024 Scholars' Research Symposium Abstracts

Paul A. Thompson, PhD, PSTAT®; Candace N. Zeigler, MD, FACP; Sherri D. Koch, MD, FAAFP; Benjamin Aaker, MD, FACEP; and Valeriy Kozmenko, MD, CHSE-A

The Sanford School of Medicine (SSOM) at the University of South Dakota (USD) continues to achieve recognition in medical education. SSOM offers a rigorous and challenging curriculum to help prepare students for a medical career. Students are expected to attain academic excellence, and maintain high standards of honesty, integrity, and perseverance.

The Scholarship Pathways Program (SPP) provides students with the opportunity to pursue research during their four years in medical school in a project that the student devises, under guidance from a mentor. Research during medical school continues to be an area of emphasis in SSOM. A good understanding of evidence-based medicine is required for physicians in today's medical environment. Research is considered a key component of the education of the medical student and is a subject of discussion during the interviews for residency.

SPP admitted its first students in 2007. This program gives approximately 20 students in each class the opportunity for hands-on, self-directed project experience, with the help of a mentor to provide guidance. Students design and propose a project in the areas of research, education, service, or social science. Students work closely with mentors and the SPP administrative staff, who provide vital and important support for SPP participants. The project is completed over the course of the students' four years of medical school, then presented as a poster, an abstract (which we publish here today), and as a manuscript. Participants are encouraged to present their work in one or more medical conferences, regionally, nationally, or internationally. SPP participants have had much success in the publication of the projects in peer-reviewed journals.

The annual Scholars' Research Symposium event is the culmination of the students' work over 4 years. This year was the sixth year it was held in conjunction with the Alpha Omega Alpha medical honorary society. In addition to the posters from the SPP Class of 2024, all medical students

performing research were invited to apply to present other research projects.

Four outstanding SPP students were invited to present their projects formally. Jennifer Lindgren Boleyn (mentor: Valeriy Kozmenko) examined the ability of medical students to become educators using a novel evaluation tool. Andrew Holmes (mentor: Jill Weimer) examined sex differences in CLN8-Batten disease, a neurodegenerative disorder, using a mouse model of the disease. Anna Myrmoe (mentor: Mark Beard) worked to establish an MD-MBA program at the USD medical school, under close direction of her mentor. Katherine Nielson (mentor: Valeriy Kozmenko) examined the preparation of medical students to handle cardiovascular emergencies who participated in Advanced Cardiac Life Support Instructors and assessed improvement in performance.

Assessing and Monitoring Competency of Medical Students as Simulation Educators Using Novel Rubric

Jennifer Lindgren Boleyn, MD | Mentor: Valeriy Kozmenko, MD

Introduction: Physicians are life-long learners and life-long educators. Through their entire careers, they educate patients, residents, medical students, and other health care professionals. There is currently no requirement for medical schools in the United States to provide courses in teaching or communication. Healthcare academia has recognized this need, which resulted in development of peer-assisted teaching and learning programs. USD SSOM has created a Medical Students as Simulation Educators (MSASE) program that teaches medical students the foundational concepts of adult education and how to effectively use them in simulation-based teaching. USD SSOM has demonstrated that learners' outcomes were similar whether they were taught by clinical faculty or by senior medical students. USD SSOM developed a novel Simulation Teaching Academic Competency Evaluation Rubric (STACER). STACER is a complex, multi-domain instrument that assesses multiple aspects of teaching. It allows for granular assessment and tracking of student-instructors' progress as educators.

Methods: MSASE enrolls 12-18 medical students per year. These students complete asynchronous modules that cover history of healthcare simulation, educational theories, simulation modalities, feedback and debriefing, assessment, and high-fidelity simulation (HFS). After completing the didactic portion, MSASE students participate in teaching junior medical students under the supervision of clinical faculty. During teaching, MSASE students are evaluated with the use of STACER. STACER consists of three written assessments: (1) learner evaluation of student-educators, (2) student-educator's self-assessment, and (3) clinical faculty evaluation of student-educators.

Results: There was a statistically significant correlation between the student learners' engagement during debriefing, as opposed to during the activity itself, and the perceived value of the activity ($p < 0.001$). There was a statistically significant negative correlation between the student learners' perceived judgment during the activity and their perceived value of the activity ($p = 0.0013$), with less judgement correlating to a higher perceived value. While learners and educators shared a positive perspective on the close relationship between pathophysiology and pharmacology, faculty expressed a more critical viewpoint. One notable discrepancy emerged regarding the three cohort's agreement with the statement, "theoretical concepts were linked to clinically relevant examples."

Conclusions: STACER is an effective instrument to measure medical students' teaching competencies over time. This data supports the position held by most simulation scholars, emphasizing the importance of engaging debriefing as an integral part of simulation-based learning. Fostering a nonjudgmental learning environment can contribute to a more valuable learning experience. Lastly, this project revealed High Fidelity Simulation as an opportunity for student-educators to both teach and learn.

Retrospective Cohort Study of Pediatric COVID-19 in a Rural Integrated Health System

Jamuna Buchanan, MD | Mentor: Santiago Lopez, MD

Introduction: The spread of the SARS-CoV-2 virus, which caused Coronavirus Disease 2019 (COVID-19), led to a global pandemic and public health crisis, which affected the physical health and mental well-being of Americans in every part of the country. Although the effect of the pandemic was ubiquitous, it has been more extensively studied in urban areas, which leads to an underscoring of the burden of COVID-19 in rural US. Health disparities adversely affect children in rural communities, each of which is unique and requires interventions based on regional needs. Characterization of COVID-19 disease in the pediatric population in rural areas is important for the development of protocols to address future surges of COVID-19 cases by the local health systems.

Methods: This study is a retrospective, cross-sectional chart review of 86 children hospitalized with the diagnosis of COVID-19 at three different hospitals that are part of an integrated rural health system in North and South Dakota. The population demographics of the surveyed states included Caucasian (84.2% SD; 86.6% ND), Native American (8.6% SD; 4.9% ND), Black (2.6% SD; 3.6% ND), and Asian (1.8% SD; 1.7% ND). All the charts identified from the EMR by filtering for patients hospitalized between October 2020 and May 2021, with an age less than 18 years, and with the ICD-10 code for COVID-19 infection were reviewed. Patients with Multi-system Inflammatory Syndrome in Children were excluded.

Results: More than half of the patients identified as Caucasian (58%), (24%) as Native American, (12%) as Black/African American, (5%) as Asian, and (1%) were unidentified. The median age was 12 years. Almost half of the patients, 42%, had a significant past medical history, defined as having one or more of the following diagnoses: asthma, diabetes mellitus, or immunodeficiency. The most common comorbidity was an elevated BMI>25 noted in 31 patients of which 11 (13%) were overweight and 20 (23%) were obese. 18 patients (22%) were admitted to the ICU with a median length of ICU-stay of 3.5 days. 34 patients (40%) required oxygen supplementation with a median length duration of 3-days. 8 patients (9%) required intubation. The median length of mechanical ventilation support was 3-days. There were no deaths.

Conclusions: It was interesting to note that in this study, pediatric patients with SARS-CoV-2 infection requiring hospitalization were disproportionately represented by minority groups (Native Americans, Blacks, and Asians) when compared to the proportion in the population. The predominance of Caucasian patients however was reflective of the general population of the surveyed states. Almost half the patients had one or more of the following diagnoses: asthma, diabetes mellitus, or immunodeficiency, risk factors previously identified for COVID-19. A common comorbidity among the patients studied was increased BMI, which has been noted as a risk factor for SARS-CoV-2 infection in the literature. This demonstrates that there are multiple common risk factors in rural and urban populations despite environmental differences.



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Effect of COVID-19 Pandemic on Routine Pediatric Vaccination Rates in 7 Upper Midwestern States

Benjamin P. Eastman, MD | Mentor: Paul A. Thompson, PhD

Introduction: The COVID-19 pandemic stressed healthcare systems by increasing patient loads and creating shortages of both staffing and medical supplies. As a result, the process of administering routine pediatric vaccinations was affected. Multiple studies have reported ongoing decreases in vaccination opportunities. Completed vaccinations on the vaccination schedule for the pediatric population is a highly effective public health intervention and therefore should be maintained at high rates. Decreases in routine pediatric vaccinations could lead to the spread of multiple infectious diseases. The aim of this study is to assess the impact the COVID-19 pandemic had on routine pediatric vaccination rates in South Dakota and surrounding states.

Methods: ChildVaxView, a publicly available and de-identified dataset, was utilized in this research. The initial focus of this study was the vaccination rates for the state of South Dakota. To give context for vaccination rates for this state, responses of participants from South Dakota as well as those from the surrounding states of Iowa, North Dakota, Nebraska, Minnesota, Montana, and Wyoming from 2012-2022 were utilized for this project. The data was divided into 2 cohorts: “pre-pandemic vaccination” and “intra-pandemic vaccination”. The rates of 5 different vaccinations from these 7 states were analyzed. The basic analysis method was an independent samples test of proportions which compared the “pre-pandemic” and “intra-pandemic” vaccination rates. P-values ≤ 0.05 were considered statistically significant.

Results: Responses compared the vaccination rates of the “pre-pandemic” period to the “intra-pandemic” period for all 7-states examined. OR values and 95% CI values are shown, where values < 1 indicate higher “intra-pandemic” rates. In terms of 24-month PCV rates, Iowa (OR=0.76, 95%CI:0.60-0.97), Montana (OR=0.75, 95%CI:0.61-0.93), Nebraska (OR=0.77, 95%CI:0.61-0.99), and North Dakota (OR=0.77, 95%CI:0.61-0.96) had higher “intra-pandemic” rates; Wyoming, South Dakota, and Minnesota showed no difference. For the 24-month polio vaccine, Montana had significantly higher “intra-pandemic” rates (OR=0.73, 95%CI:0.54-0.98); the remaining states showed no difference. For the 24-month DTaP vaccine, North Dakota (OR=0.84, 95%CI:0.72-0.98), MT (OR=0.84, 95%CI:0.72-0.97), and Wyoming (OR=0.84, 95%CI:0.73-0.97) had significantly higher “intra-pandemic” vaccination rates, with no difference for the other states. The 6 surrounding states did not differ from South Dakota in polio vaccination rates “pre-pandemic” ($p=0.54$) nor “intra-pandemic” ($p=0.36$); there was additionally no difference between those states and South Dakota in the “pre-” vs “intra-pandemic” comparison ($p=0.27$). Similar results were seen for other vaccines.

Conclusions: In this study, rates of a substantial proportion of pediatric vaccinations increased in the states of South Dakota, Iowa, Nebraska, North Dakota, Minnesota, Montana, and Wyoming since the onset of the COVID-19 pandemic. Several reasons for this surprising outcome were considered including amendments made to the Public Readiness and Emergency Preparedness (PREP) Act, reimbursement for clinics providing vaccinations under the Vaccination for Children (VFC) program, and increasing public awareness of the safety and efficacy of routine pediatric vaccinations.

Analysis of First 50 Liver Transplants in a Rural Midwest Medical Center

Kyler Hardie, MD | Mentor: Hector Saucedo-Crespo, MD, FACS

Introduction: Chronic liver disease, a progressive deterioration of liver function, has become a significant health problem in the United States. According to the National Vital Statistics Report 2017 from the Center for Disease Control and Prevention, approximately 4.5 million adults have been diagnosed with chronic liver disease and cirrhosis (end-stage liver disease), which is 1.8% of the adult population. Liver transplant (LT) is the only definitive treatment with a long-term survival benefit for patients with end-stage liver disease. Over 9,000 LTs are performed in the United States each year. Avera McKennan Hospital and University Center is home to the only LT center in the state of South Dakota. The first LT was performed in 2016 and since then, 50 LTs have been performed to date. In this study, transplant recipient and donor characteristics were reviewed and compared to national data. Also, the study included an assessment of the overall experience with LT at this center.

Methods: This study was IRB approved through Avera McKennan Hospital. A retrospective review of all LTs between November 2016 and July 2022 was performed. Donor information and recipient details were reviewed from a prospectively maintained transplant database. This regional data was then compared to national data using the Scientific Registry of Transplant Recipients (SRTR). Recipient data included age, gender, race/ethnicity, body mass index (BMI), etiology of liver disease, model for end-stage liver disease (MELD) score at transplant, and length of post-transplant hospital stay (LOS). Donor information included age, gender, BMI, cause of death, and cold ischemia time (CIT).

Results: During the study period, 50 LTs were performed. Of these, multi-organ transplants were performed in 5 recipients, all of whom received combined liver and kidney transplants. The most common indication for LT was end-stage liver disease due to alcoholic cirrhosis, which represented the primary diagnosis in 54% of the recipients, vs 35.2% nationally. Hepatocellular carcinoma was present in 20% of the patients. Recipient characteristics included 30 men and 20 women with a median age of 52 years and a median BMI of 28.7 kg/m² respectively. The most common race/ethnicity was white followed by Native American at 62% and 36%, respectively. The median MELD score at transplant was 33.5 and the median length of post-transplant LOS was 9-days. This center has a cumulative 98% death-censored graft survival rate and 85.7% patient survival rate at one year after transplant. With regards to medical urgency, 42% of the patients received transplants with MELD ≥ 35 and 34% of the patients with MELD 30-34 compared to the national averages of 20.9% and 18.3%, respectively, in 2020. The median donor age was 29-years and median BMI was 26.1 kg/m². The main cause of donor death was head trauma at 52%, followed by anoxia, and cerebrovascular stroke at 30% and 18%, respectively. Median CIT was 10.77 hours.

Conclusions: LT recipients in South Dakota had higher MELD scores compared to the national average. Native Americans, who represent an underserved population and are under-represented within national transplant database, accounted for more than a third of the total LT recipients. End-stage liver disease, due to alcoholic cirrhosis, was the most common primary pathology necessitating LT exceeding the national rate by 18.8%. Part of the comprehensive liver transplant care was the provision for interventions focused on addressing alcohol relapse and medical adherence through systematic integration of behavioral therapies and addiction treatments.

Metacognitive Analysis of Simulation-Based Education Identifies a Gap in Healthcare Education

Brianne K. Haskell Hanisch, MD | Mentor: Valeriy Kozmenko, MD

Introduction: Simulation has become an integral part of healthcare education. Studies demonstrate rapid knowledge and skill acquisition with the use of simulation and rapid knowledge degradation if it is not further reinforced. Effect of simulation on metacognitive processes, or the ability to understand one's own knowledge, is not well-investigated yet. The University of South Dakota Sanford School of Medicine in the U.S. and Royal College of Surgeons in Ireland – Bahrain campus, collaborated on combining the best simulation-based and team-based learning (TBL) practices to investigate team dynamics and knowledge exchange among team members in high-fidelity simulation (HFS) for 3rd year medical students. The purpose of the study was to assess metacognitive processes and their impact by simulation.

Methods: The activity consisted of four clinical scenarios (atrial fibrillation, anaphylaxis, meningitis complicated with septic shock and ARDS, and burns). A total of 68 students were tested before the activity for their concrete knowledge and its level of assurance. Immediately after the activity and prior to debriefing, students were assessed for their conceptual knowledge relevant for the simulation scenario and its level of assurance. Knowledge test answers had values of “+1” and “-1” for correct and incorrect answers respectively, while the assurance level was assessed on a scale from 1 to 4. Calibration index (CI) was calculated as a product of knowledge-based answer value and level of assurance, thus its value ranged from “-4” to “+4.”

Results: Data analysis revealed a weak correlation between individual-readiness assurance test (I-RAT) and in-simulation decisions (Spearman correlation, 0.336, $p < 0.001$). Performance in I-RAT showed non-significant correlation with either the decision making in the simulation or post-simulation test. Irrespective of accuracy, students maintained the same level of certainty across all the assessments (I-RAT, in-simulation, and post-simulation) with Spearman correlation Rho: I-RAT vs in-simulation (case 1) = 0.354, $p < 0.005$, I-RAT vs in-simulation (case 2) = 0.419 $p < 0.001$, and in-simulation (case 1) vs in-simulation (case 2) = 0.505, $p < 0.001$.

Conclusions: The obtained results demonstrated low correlation between knowledge correctness and level of certainty. Additionally, learners demonstrated misinformed confidence. This was true for both extremes: some students were overconfident in their wrong answers while others struggled to be assured in their correct answers. This indicated that current simulation educational curricula do not enhance skills in self-assessment. Furthermore, multiple studies have shown medical students lack this skill, highlighting the prevalence of both imposter syndrome and cognitive bias contributing to overconfidence. These are concerning findings considering healthcare requires its providers to be involved in lifelong learning. Efficient, reliable learning with a high level of accuracy is unlikely to occur without a correct knowledge of self-appraisal. Formal healthcare curricula should address this need.

Oral Health Education Enhancement For South Dakota Medical Learners

Layne Hohn, MD | Mentor: Michelle Schimelpfenig, DO

Introduction: Medical education focuses on the biochemical origins, pathophysiologic pathways, diagnosis and treatment of human illnesses. While this educational training attempts to be all-encompassing, oral health and the associated pathologies are not commonly emphasized in medical training. Disparities in oral health have detrimental effects on systemic disease and impacts patient well-being. This project aimed to evaluate the integration of an oral health education pilot program into the medical school curriculum by assessing students' and residents' baseline understanding and perspectives of oral health, followed by a lecture on oral health basics. The goal was to enhance physicians' knowledge so they can help future patients recognize the impact good oral health care has on their overall health.

Methods: 27 Center for Family Medicine (CFM) residents, 15 USD pediatric residents, and 64 USD SSOM Pillar 2 (MS3) medical students received a lecture on oral health basics. Medical learners received a 10-question pre-lecture quiz to assess their baseline knowledge, followed by the same 10-question post-lecture quiz to assess knowledge gained. Students who attended in person also practiced the application of fluoride resin on oral cavity models and on one another. Lectures were given in various formats, with both the CFM and pediatric residents receiving the presentation through a live Zoom meeting. The Pillar 2 medical students were able attend the lecture, either in person or through Zoom, with 10 students attending the in-person lecture.

Results: Of the 106 learners, 88 (83%) completed pre- and post-lecture questionnaires. Quiz results demonstrated that the session helped learners gain knowledge in oral health basics, pathology, and treatment, with almost a 20% increase in average quiz scores across all participants. Further statistical analysis, with paired t-tests, demonstrated that the increase in examination scores were all statistically significant with $p < 0.05$ in all groups.

Conclusions: The oral health education pilot program, using lecture presentation format over Zoom, was an effective method to increase both resident and student knowledge of oral health basics, pathology, and treatment. Considering the statistical increase in student performance and comfort level with performing essential examinations, this project also demonstrated that students and residents were engaged in the topic and emphasized the importance of oral health education. Based on the positive response to this pilot project, it is suggested that faculty consider integrating this into the medical school curriculum.

Sex-Split Analysis of Pathology and Motor-Behavioral Outcomes in a Mouse Model Of CLN8-Batten Disease

Andrew Holmes, MD | Mentor: Jill Weimer, PhD

Introduction: CLN8-Batten disease is a rare neurodegenerative disorder characterized phenotypically by progressive deterioration of motor and cognitive abilities, visual symptoms, epileptic seizures, and premature death. Mutations in *CLN8* result in characteristic Batten disease symptoms and brain-wide pathology including accumulation of lysosomal storage material, gliosis, and neurodegeneration. Recent investigations of other subtypes of Batten disease (CLN1, CLN3, CLN6) have emphasized the influence of biological sex on disease and treatment outcomes; however, little is known about sex differences in the CLN8 subtype.

Methods: To determine the impact of sex on CLN8 disease burden and progression, a *Cln8^{md}* mouse model was utilized to measure the impact and progression of histopathological and motor-behavioral outcomes between sexes. Immunohistochemistry staining utilized markers for intracellular storage materials, astrocytes, and microglial cells; sections were obtained of the thalamus and the somatosensory cortex of *Cln8^{md}* mice.

Results: Several notable sex differences were observed in the presentation of brain pathology, including *Cln8^{md}* female mice consistently presenting with greater GFAP⁺ astrogliosis and CD68⁺ microgliosis in the somatosensory cortex and ventral posteromedial/ventral posterolateral nuclei of the thalamus when compared to *Cln8^{md}* male mice. Female *Cln8^{md}* mice experienced a diminished lifespan by 0.5 months compared to their male counterparts ($p < 0.05$). Furthermore, sex differences in motor-behavioral assessments identified *Cln8^{md}* female mice experience poorer motor performance in the Morris Water Maze assessment, reverse Morris Water Maze, and increased tremors.

Conclusions: Female *Cln8^{md}* mice perished earlier, performed worse on motor-behavioral assessments, and demonstrated marked microglial and astrocyte reactivity compared to their male counterparts. Taken together, the results provide further evidence of biological sex as a modifier of Batten disease progression and outcome, thus warranting consideration when conducting investigations and monitoring therapeutic impact.

ARPID-I: Initial Findings in Medical Students' Professional Identity Development

Madison McLaury, MD | Mentor: Valeriy Kozmenko, MD, CHSE-A

Introduction: Professional identity is one of the frequently used and least clearly defined terms in healthcare education. Its simplest definition includes feeling, thinking, and acting like a representative of a given professional group. Many other aspects of professional identity exist. Professional identity development (PID) adds another layer of complexity to the topic for educators attempting to assess the process and dynamically measure its individual components. The project's aim was to re-define the term professional identity and create a battery of instruments to assess its development in medical students.

Methods: The first module, Assessment Rubric of Professional Identity Development (ARPID) was developed, piloted, reviewed, and deployed. ARPID is a 20-item multi-domain survey that assesses the following medical student characteristics: knowledge, skills, attitudes, feelings, readiness to act like a professional, confidence in decision-making, ability to sort relevant and irrelevant issues, ability to shift from fact-based to concept-based and meta-cognitive reasoning, ability to address ethical issues, and operate in the areas of clinical uncertainty. Answers to each question covered the range from novice to experienced professional. The survey was distributed to an entire body of medical students at a mid-western medical school in the U.S. 74 student responses were collected (26% response rate). Statistical analysis of the collected data included mean and standard deviation of confidence levels in each medical school class. Additionally, Spearman's rho analysis was performed on two sequential questions to better assess correlation of student's self-assessment and actual knowledge.

Results: Survey questions analyzing mean confidence, knowledge, and competence levels exhibited a positive relationship between these factors and years in medical school. Additionally, several aspects of data exhibited a Dunning-Kruger like trend involving knowledge and mean confidence level as medical students progressed through training. Spearman's rho analysis assessing correlation between confidence and competence level in students displayed a positive correlation in the first- and fourth-year student cohorts, and no correlation in the second- and third-year cohorts. The first-year cohort displayed a rho value of 0.510 with a p-value of 0.009. The second-year cohort displayed a rho of 0.000 with a p-value of 1.000, the third-year cohort displayed a rho of 0.002 with a p-value of 0.995, and the fourth-year cohort displayed a rho value of 0.497 with a p-value of 0.042.

Conclusions: ARPID is a component in the battery of instruments used to measure and monitor medical students' PID. Given the importance of determining and following medical students' PID to optimize medical curricula and support students, this tool will enhance the way educators approach healthcare education and training.

Immunosuppressive Opioids are Associated with Longer Hospital Length of Stay in SARS-CoV-2 Patients

Luke Merrill, MD | Mentor: Benjamin Aaker, MD

Introduction: Since late 2019, SARS-CoV-2 has infected over 767 million people worldwide with over one million deaths in the United States alone. One risk factor identified for possible worse outcomes from the virus is medication-induced immune suppression. Some opioids have been associated with immunomodulatory effects. One immunomodulatory effect that has been linked to the use of these medications is reduced lymphocyte proliferation and macrophage dysfunction. Immune dysfunction has been associated with increased length of stay (LOS) in SARS-CoV-2 hospitalized patients. In the early years of the pandemic, hospitals quickly became overwhelmed by the number of patients needing hospitalization for treatment of the virus. Identifying risk factors and decreasing patient length of stay can ease the burden on staff and equipment needs. It was hypothesized that previous or current use of an immunosuppressive opioid is associated with longer hospital LOS for patients with SARS-CoV-2.

Methods: A retrospective chart review with 732 patients included in the final analysis was performed. Patient charts were collected from a regional Midwestern health system for hospitalized SARS-CoV-2 patients between July 1, 2020 through December 31, 2020. LOS stay was categorized as long (≥ 5 days) or short (<5 days). Patient demographics/comorbid conditions were gathered and statistical analysis was performed using Microsoft Excel.

Results: Patients who have previously used morphine or fentanyl at any point in the prior year are associated with longer LOS ($p < 0.02$). Starting morphine or fentanyl in-hospital was associated with longer LOS compared to those who have previously used ($p < 0.001$ morphine, $p < 0.001$ fentanyl). There was no significant difference between starting fentanyl or morphine in the hospital ($p = 0.55$).

Conclusions: The use of immunosuppressive opioids are associated with longer LOS in patients hospitalized for SARS-CoV-2. Starting an opioid in-hospital is associated with longer LOS than pre-hospital opioid use. No difference in hospital length of stay was found between patients treated with fentanyl or morphine. While it is possible that sicker patients may require more opioids, healthcare providers should consider avoiding the use of opioids with immunomodulatory effects and consider alternative drugs in patients hospitalized with SARS-CoV-2.



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Development of an MD-MBA Program at University of South Dakota

Anna Myrmoe, MD, MBA | Mentor: Mark Beard, MD, MHA

Introduction: Over the last 20 years nationwide, the number of MD-MBA programs have seen an increase from 6 to 65 with an estimated annual enrollment of 500 students. Many of the healthcare challenges providers are witnessing are business challenges, varying from designing quality improvement initiatives to managing rising costs. Studies have shown those who obtained an MD-MBA degree were better prepared to face these challenges than their traditional counterparts. The aim of this study is to demonstrate a regional need and market demand for a joint degree program between the Sanford School of Medicine and the Beacom School of Business at the University of South Dakota.

Methods: To generate a needs assessment for an MD-MBA degree, an IRB approved online survey was constructed and sent by email to physicians across the state of South Dakota. Recipients included members of the South Dakota State Medical Association, Sanford School of Medicine Alumni, and currently enrolled Sanford School of Medicine students. All submissions were kept confidential, and data was collected and stored in an Excel document.

Results: The survey generated responses from 108 participants, 58 of which were current medical students and 54 were physician alumni or practicing physicians. Of the total respondents, 58% indicated they would apply or would have applied to an MD-MBA program if available. 84% of respondents agreed with the need for continued education in medicine and business to overcome the multifaceted challenges faced in healthcare. Survey questions requiring additional explanation of answer choices qualitatively demonstrated 92% of respondents strongly support a dual-degree and its benefits to the medical profession.

Conclusions: Following submission of the study results in a comprehensive proposal for an MD-MBA program, the South Dakota Board of Regents approved and implemented the program, effective since Spring 2022. The MD-MBA program will allow for completion of training prior to beginning a medical career. Medical education at the university now provides healthcare industry support through healthcare provider acquisition of skills needed for meaningful and effective administrative capabilities.

ACLS Instructor Course to Enhance Medical Students' Resuscitation Competency and Confidence

Katherine Nielson, MD | Mentor: Valeriy Kozmenko, MD

Introduction: Physicians are expected to be competent in the management of cardiovascular emergencies. Despite the demand, there is a lack of research regarding how to better provide training for medical students to address cardiovascular emergencies. The authors of this project hypothesize that medical students participating in the Advanced Cardiac Life Support Instructors (ACLS-I) program will improve their emergency management and clinical teaching competencies and confidence.

Methods: At the beginning of Pillar 2 (MS2) and after completion of ACLS training and certification, 16 medical students were accepted into the ACLS-I course. During Pillar 2 (MS2- MS3) participants completed the ACLS Instructor training course, obtained ACLS Instructor certification status, and taught at least 2 ACLS classes under supervision of the experienced ACLS instructors. At the end of Pillar 2 (MS3), 5 student-instructors and 58 non-instructors took a multiple-choice question (MCQ) quiz enhanced with the level of assurance rubric. Obtained data were analyzed to investigate ACLS instructors' competency in ACLS/non-ACLS knowledge compared to their peers. Students' performances were also assessed for correlation between knowledge accuracy and confidence in selected answers on the quiz. Additionally, the project investigated if course participants were more confident to participate in ACLS codes as providers and teach ACLS to healthcare students or providers using the 5-point Likert scale.

Results: There was significant evidence ($p < 0.05$) to suggest that ACLS-I students had a greater or equal mean raw score, were more competent in ACLS-I factual questions, and felt more comfortable teaching medical professionals and healthcare students how to manage cardiopulmonary emergencies and ACLS codes. There was not sufficient evidence ($p > 0.05$) to suggest that ACLS-I students were more competent in ACLS-I conceptual questions, more confident in their answers (correct and incorrect), and more confident in performing as a provider or team-leader in ACLS codes and cardiopulmonary emergencies.

Conclusions: Completing an ACLS instructor course and participating as an ACLS instructor throughout medical school increases a medical student's factual ACLS knowledge and confidence in teaching ACLS codes compared to their peers. It does not increase accuracy and confidence of conceptual knowledge of cardiovascular emergencies.

Analysis of Collegiate Athlete Body Composition Using MuscleSound® Technology

Matthew N. Pohlmann, MD | Mentor: Thayne Munce, PhD

Introduction: Body composition is studied in athletes as a means of measuring physical fitness and progression of training. Athletes can utilize body composition in multiple ways to guide training toward athlete specific goals. Several different methods exist with varying levels of cost, invasiveness, reading complexity, and availability. Ultrasound is a method which, while being affordable and portable, is limited by the training needed to properly read scans. The proposed benefit of MuscleSound® is to alleviate the challenge of interpreting scans by providing a program to estimate body composition in ultrasound images. This study compared the use of MuscleSound® with skinfold testing, an accepted method of body composition measurement. The hypothesis of this study was that MuscleSound® software would correlate with skinfold testing and serve as an alternative body composition method.

Methods: This study was IRB approved through Sanford Research. 35 participants were recruited from a local collegiate men's basketball team over the span of 2018-2023 at varying start points. Each athlete was weighed and measured for body composition metrics using both skinfold testing and ultrasound. Skinfold testing was performed at multiple sites of adipose collection while ultrasound scans were obtained of the rectus femoris. Skinfold testing was assessed through fat mass, skinfold thickness, body fat %, lean mass, and lean mass index while MuscleSound® was assessed through intramuscular adipose tissue (IMAT) % and muscle thickness (MT). Variables were divided into muscle-related and adipose-related before being compared between the two methods. For muscle-related variables, correlation analysis was performed between MT and lean mass, lean mass index, and body weight. Correlation analysis was also performed between IMAT % and fat mass, skinfold thickness, body fat %, and body weight.

Results: The MuscleSound® measures were found to have varying levels of correlation to adipose-related variables and muscle-related variables. Adipose correlations included fat mass ($r = 0.79$, $p < 0.01$), body fat % ($r = 0.76$, $p < 0.01$), skinfold thickness ($r = 0.71$, $p < 0.01$), and body weight ($r = 0.55$, $p < 0.01$). Muscle-related variables had lower correlation values with MuscleSound®-derived MT, which had correlation values to lean mass ($r = 0.27$, $p > 0.05$), lean mass index ($r = 0.01$, $p > 0.05$), and body weight ($r = 0.25$, $p > 0.05$).

Conclusions: MuscleSound® presents a potential solution for ultrasound use in studying body composition. Correlation between the results from this tool and current standard values vary. Of the variables studied, IMAT% correlated best with adipose-related skinfold measurements while MT lacked correlation with muscle-related skinfold measurements. This misalignment of results suggests a potential lack of reliability with either MT obtained through MuscleSound® or the muscle-related variables of skinfold testing. In either group, body weight was not well correlated with MuscleSound® measurements. The affordability and portability of ultrasound makes it a useful method in studying body composition. MuscleSound® presents a unique opportunity to increase accessibility, however, should be used with a focus on adipose tissue when studying body composition.

Kindling Wellness: Creating a Student-Run Podcast Series on Medical Student Wellness

Kristi Pond, MD | Mentor: Michelle Schimelpfenig, DO

Introduction: Research has consistently shown that the prevalence of burnout symptoms (such as emotional and physical exhaustion, cynicism, or lack of interest in schoolwork, the sense of incompetence, or the feeling that you cannot be effective) in medical students is greater than the prevalence in the general population. Students with preexisting anxiety, depression, mood disorder or other psychological distress are more vulnerable to burnout. It is estimated that at least half of U.S. medical students experience or are affected by burnout during their education. With the high rates of burnout symptoms in medical students, it is becoming increasingly important to implement strategies to build student resilience to burnout. Overall, one of the first steps to decrease rates of burnout and improve medical student wellbeing is for students and faculty to develop an awareness and understanding of burnout, by exploring issues that may contribute to it. The *Kindling Wellness* podcast was created to serve as a wellness resource for medical students and health professionals.

Project description: The initial 5-episode series of the podcast *Kindling Wellness* was built on the metaphor of a fire as one's wellness and the necessary components needed to keep a fire burning (heat, oxygen, and fuel). The Podcast was developed in 3 phases. Phase 1: Content Development included planning topics for discussion, choosing guests to interview, and deciding what platform on which to publish content. Phase 2: Podcast Interviews involved researching discussion topics, writing interview questions, interviewing guest speakers, and editing the content. Phase 3: Deployment and Awareness included publishing the Podcast on application platform – Spotify for Podcasters. The podcast was advertised using flyers posted in the medical school building, emails distributed to current medical students, and promotional posts via social media pages dedicated to the podcast. The podcast utilization was evaluated using analytics captured from the podcast application platform.

Outcomes: Podcast episodes were released over a 6-month span from November 2022 to June 2023. The 1st podcast was a discussion with Michelle Schimelpfenig, DO about an overview of the podcast series and of medical student wellness. The 2nd podcast discussed mental health and counseling with Rebecca Glover, LPC-MH. The 3rd podcast was entitled "Creating margin and practicing gratitude" with Craig Uthe, MD. The 4th podcast was "Finding your Fire" with Gary Timmerman, MD and Jenny Guido, MD, and the 5th podcast was entitled "Fueling your wellness and leadership" featuring Tim Ridgway, MD. Podcast analytics were recorded simultaneously as listeners played the podcast episodes. There were 98 all-time plays; the first episode was the most listened to at 60 plays. The age of listeners ranged from 18-59 years old with most listeners in the 23-27 age range (35%).

Conclusions: The *Kindling Wellness* student-run podcast was created as a wellness resource for medical students and health professionals to develop awareness and understanding of burnout. The 5-episode podcast was deployed on Spotify for Podcasters and accessed by 98 listeners. It is interesting to note that based on the age range of the listeners, people other than medical students accessed the site. This podcast series serves as a resource, in a novel medium, available at University of South Dakota Sanford School of Medicine for medical students and the public. Future podcasts could be added to this platform.

Rapid Cycle Deliberate Practice (RCDP) to Master Airway Intubation

Kirsten R. Kim Sawtelle, MD | Mentor: Valeriy Kozmenko, MD

Introduction: Simulation has become an integral part of health care education curricula that is used to teach a variety of topics, from emergency situations to physical diagnoses. Without further reinforcement, the skills learned through the simulation are subject to deterioration over time. Rapid Cycle Deliberate Practice (RCDP) is a teaching method that was developed to resist this deterioration and achieve mastery of skills. In RCDP, learners cycle through a series of high-intensity and fast-paced scenarios until performance mastery was achieved. The individualized feedback is optimized with a 2:1 learner: instructor ratio. The goal of RCDP is to ensure 100% competency and time-efficiency of learners' performances. This study examined two sub-types of RCDP-style teaching to determine retention after 6-months.

Methods: A two-day airway management course was conducted using RCDP to teach endotracheal intubation to second-year medical students using Medical Students as Simulations Educators (MSASE) as instructors. On Day 1, learners participated in 40-minute training sessions using a 2:1 ratio of learners to educators to practice intravenous induction into anesthesia and endotracheal intubation. Half the groups used an immediate-feedback (IF) RCDP approach while the other half used a delayed-feedback (DF) RCDP approach. Day 2 was completed 1 week later using similar methods. Learners participated in a 1-day simulation course in 6 months to assess retention (Day 3).

Results: On Day 1, the IF group achieved mastery in fewer trials compared to the DF group ($p = 0.004$). The DF group required an average of 1.14 (CI = 0.845 – 1.433) trials until mastery, while the IF group required 0.516 (CI = 0.226 – 0.806) trials. The IF and DF groups demonstrated 98% knowledge and skills proficiency on Day 3, which is a significant increase from Day 1 and Day 2 scores of 92% and 88%, respectively. There was no significant difference in retention between the IF and DF groups.

Conclusions: RCDP is an effective teaching method to achieve mastery with performing endotracheal intubation to second-year medical students. There was no significant difference between immediate-feedback and delayed-feedback when retention of this clinical skill was reassessed at 6 months.

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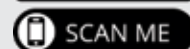
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Characteristics of Play Associated with Head Impact Severity During Tackling in Youth Football

Meaghan Sievers, MD | Mentor: Thayne Munce, PhD

Introduction: In the last decade, concussions and subconcussive brain trauma in football and other high impact sports have become of increasing concern. Tackling, in youth football, accounts for a high proportion of head impacts and injuries, including concussions. Thus, minimizing head impact severity during tackling may help in reducing concussion risk and subconcussive brain trauma. However, it is unknown how discrete aspects of play in youth football relate to head impact severity during tackling.

Methods: 25 youth tackle football players (12.9 ± 0.6 yr) wore helmets outfitted with the Head Impact Telemetry (HIT) System during two football seasons (64 practices and 18 games). Measures of head impact severity, including linear acceleration (LA) and rotational acceleration (RA), were collected at each session, along with videography. Videos and HIT System data were cross analyzed using a validated rubric to code each registered head impact based on several pre-identified characteristics of play. Sample distributions of play characteristics were compared using the nonparametric Mann-Whitney U test. Level of significance for all tests was $\alpha = 0.05$.

Results: There were 1025 head impacts identified for players making a tackle or being tackled. LA of head impacts was significantly greater ($p = 0.017$) for players making a tackle ($n = 614$; 21.70 [16.40 - 30.13] g) than players being tackled ($n = 411$; 20.50 [15.90 - 30.10] g). In comparing head impacts on tackles, LA was significantly greater ($p = 0.010$) for special teams ($n = 39$; 29.10 [21.40 - 39.70] g) over defense ($n = 348$; 22.50 [16.90 - 31.55] g), and RA was significantly greater ($p = 0.003$) for special teams ($n = 39$; 2241 [1223 - 3175] $\text{rad} \cdot \text{sec}^{-1}$) over defense ($n = 348$; 1618 [1004 - 2293] $\text{rad} \cdot \text{sec}^{-1}$). While being tackled, player-to-ground head impacts LA values ($n = 102$; 25.85 [18.65 - 35.13] g) were significantly greater ($p < 0.001$) than player-to-player head impacts ($n = 308$; 19.75 [14.95 - 26.68] g), and player-to-ground head impacts RA values ($n = 102$; 1687 [1108 - 2690] $\text{rad} \cdot \text{sec}^{-1}$) were significantly greater ($p < 0.001$) than player-to-player head impacts ($n = 308$; 1313 [906 - 1832] $\text{rad} \cdot \text{sec}^{-1}$).

Conclusions: There are certain characteristics of play in youth football that were associated with higher magnitude head impacts during tackling, including being the tackler, special teams plays and head contact to the ground while being tackled. These characteristics of play may serve as targets for mitigation efforts aimed at reducing head impact severity in youth football.

Education on the Understanding of Noise-Induced Hearing Loss in Vulnerable Undergraduate Population

Henry Wei, MD | Mentor: Andrew Ridder, MD

Introduction: With the introduction of increasingly powerful audio equipment and increase of personal mobile audio devices in the 21st century, the prevalence of noise-induced hearing loss (NIHL) in young adults is expected to increase. This increase, estimated to impact 30 million adults in the next four decades, is due in part to recreational exposure. While many young adults have a general understanding of NIHL, a detailed education on various topics of NIHL could further promote adherence to the use of preventive measures. This project therefore involved gauging understanding of NIHL and providing in depth education on various topics of NIHL geared to an undergraduate population at 3 universities located in South Dakota.

Methods: The project was approved by the Institutional Review Board (IRB) of the University of South Dakota. A 45-minute PowerPoint presentation was developed and presented about NIHL. The following 5-topic areas were discussed: pathophysiology of hearing loss, healthcare impacts, Occupational Safety and Health Administration (OSHA) guidelines on noise exposure, adherence to OSHA guidelines in recreational spaces, and preventive measures, to include decibel meters and earplugs. A pre-presentation survey was given to score students' baseline knowledge in each of the topic areas covered, followed by a post-presentation survey to score knowledge gained. A one-tailed paired t-test was performed to evaluate the changes from pre- to post surveys. In addition to the education, decibel meter mobile applications were introduced, and 120 high-fidelity earplugs were donated at the sites of presentation.

Results: PowerPoint presentations and pre- post-surveys were given during the recital hour, a required course, to 120 students enrolled in music degree programs at 3 universities in South Dakota. Comparison of all the pre- to post-survey responder scores showed a statistically significant change in the students' confidence in their knowledge for all 5-topic areas discussed. There was also statistically significant change in knowledge confidence in all 5-topic areas between responder groups who were already using preventive measures compared to those who were not using preventive measures at the time of testing. For example, the knowledge confidence to wear preventive measures notably increased nearly threefold, 1.68 to 4.26 amongst those who were not using preventive measures.

Conclusions: This project demonstrated that young adults with a current knowledge of NIHL still gained additional insight through this presentation. While there was a significant change in knowledge confidence in each category in the total responders, the project also demonstrated that amongst current users of preventive measures, there was statistically significant change in knowledge confidence as well. Students also indicated, through the surveys, that they are more likely to use preventive measures in loud recreational spaces after this educational experience. Many, but not all students, took advantage of the high-fidelity earplug donations.

Eczema Herpeticum: A Fatal Rash That Mimics Many

Amanda Ricke, MD; Kristi Pond, MD; and Peter Paul Lim, MD

Abstract

Eczema herpeticum (EH) is a potentially life-threatening condition, especially in the pediatric population, that occurs among patients with atopic dermatitis (AD). AD is a chronic inflammatory skin disorder with a complex pathophysiology that predisposes patients to EH. Herpes simplex virus (HSV) 1 is implicated in 90 % of EH cases and often initially presents with gingivostomatitis. HSV 1 can also lead to more systemic disease such as keratoconjunctivitis, meningitis, encephalitis, and hepatitis. Rapid diagnosis of EH is vital, and prompt treatment is essential to preclude these complications. We describe a 5-month-old male with poorly controlled atopic dermatitis who presented with generalized polymorphic rash diagnosed with EH and superimposed MSSA cellulitis. This clinical scenario, while not uncommon, is often missed and underlies the importance of a strong clinical suspicion for EH among patients with AD presenting with complicated rash. EH is an infectious complication that is easily misdiagnosed causing treatment delays that lead to dire consequences. This report also includes an abridged review of literature on EH.

Introduction

Atopic dermatitis is a common skin disorder, especially amongst children. Eighty-five percent of patients diagnosed with AD have symptoms that manifest before age 5.^{1,2} AD typically presents as scaly/dry patches on an erythematous base.³ EH is a viral complication related to AD. The disease is caused by herpes simplex virus, primarily HSV 1.⁴ It presents as a monomorphic rash on an erythematous base.¹ Diagnosis of EH is typically clinical with supporting evidence through HSV PCR of skin lesion swabs.⁴

There are many pathophysiologic aspects of AD that lead to increased risk of infection from both viral and bacterial pathogens. Structural disruptions including mutations in filaggrin structural proteins, adherens junction breakdown, and decreased tight junction proteins are important avenues for HSV entry into cells.^{1,4} Immunological breakdown including varying levels of cytokines, disrupted natural killer cells, and disordered regulatory T cells also play an important role.^{4,5} It is also evident that skin microbiome in patients with AD differs from the general population and can predispose to infectious complications.^{1,4,6}

Treatment for EH is initiated as soon as clinical suspicion is determined. Acyclovir is the treatment of choice for EH and dose depends on severity of disease.^{1,4,7} Bacterial superinfection is also common and should be considered when initiating treatment, especially if rash is polymorphic. Antibiotic coverage against MSSA and MRSA is important,

although any bacteria forming the skin flora can be an agent of superinfection.^{1,6,5}

EH can be a harbinger of more systemic complications affecting other organ systems.⁶ These include meningoencephalitis, viremia, and keratoconjunctivitis.⁶ It is often difficult to differentiate it from other infectious skin disorders based on physical exam findings making the diagnosis challenging.¹ However, with its propensity to lead to further complications, high index of clinical suspicion is imperative for prompt diagnosis and treatment.

Case Summary

A 5-month-old male with poorly controlled eczema presented with one-day history of fever, generalized polymorphic rash, runny nose, and cough. Primary physician prescribed topical over the counter therapy with no improvement. He was up-to-date on vaccines through 2 months of age but had not yet received 4-month vaccines. Mom denied known sick contacts. On exam, he was found to be lethargic with bulging anterior fontanelle when coughing. There was a concern for motor delay due to head lag and inability to support himself when prone. The exam also showed a generalized, complex rash over scalp, bilateral cheeks, right ear, and neck consisting of monomorphic lesions with honey colored crusting on an erythematous base. His trunk and bilateral upper extremities showed erythematous patches with generalized papules (Figure 1). Initial labs including complete blood count, C-reactive protein, lactic acid, and

Figure 1. Complex rash with monomorphic eruptions on erythematous base (characteristic of EH) with some honey crusting implicating an impetiginous process from bacterial superinfection.



comprehensive metabolic panel were unremarkable (Table 1). His respiratory viral panel was negative.

Impetigo was the initial impression on admission because of the honey-colored crusting. Patient was empirically started on broad spectrum antibiotics with poor initial response. Further elucidation of history revealed primary maternal cold sores about two weeks prior to rash progression. HSV work up including PCR of facial lesion and plasma was initiated and acyclovir was empirically added to his regimen. Due to persistent lethargy and concern for hypotonia, MRI of the brain was also performed which showed a 2 mm mass concerning for right frontal subdural hematoma versus developing empyema. CSF studies including culture were reassuring and full meningitis panel was negative. Thus initial imaging impression was reconsidered. Blood and wound

PCR came back positive for HSV-1. CSF HSV PCR was negative. MRI result eventually implicated to be a baseline incidental finding rather than a new acute process. It was deemed unnecessary to repeat MRI with this information. On hospital day 5, the patient's clinical course was complicated by re-worsening of the rash with erythroderma noted on neck, trunk, and extremities. Suspicion for MSSA scalded skin syndrome was high prompting addition of clindamycin to his regimen for toxin modulation. This resulted in favorable clinical response. He was discharged on hospital day 8 to complete 14 days of acyclovir and 10 days of cephalexin. A few days following completion of therapy, however, the patient's rash recurred, now characterized by formation of new vesicular lesions concerning for continued herpes infection with superimposed bacterial infection. The patient was restarted on oral acyclovir and antibiotic treatment. He completed 14 more days of oral acyclovir and 7 days of clindamycin with full recovery noted at 1 month follow up. Mom was educated on AD optimal care, HSV latency, and increased risk for EH in the future.

Discussion and Abridged Review of Literature

Atopic Dermatitis Epidemiology and Presentation

AD is the most common inflammatory skin condition in the world. It affects nearly 20% of children in most countries, and up to 5% of adults.^{5,8} Most cases present in early childhood, with 80-90% of cases presenting before age 5.⁹ It equally affects males and females. There is some variation with race, and in America, Black children have a 3% increased prevalence of AD.¹⁰ There has been a significant rise in prevalence of AD, especially in low-moderate income countries. Environmental factors such as pollution and exposure to allergens also play a large role in the disease.^{2,11} Some of the greatest risk factors for AD include family history, urban setting, and dry climate.⁹ The prevalence of this disease worldwide and the systemic nature of the disease often leads to decreased quality of life in patients with chronic disease.¹²

AD presents in a variety of ways depending on course of disease, age, race, and severity of lesions.⁹ Typically, the rash is described as a scaly, dry patch on an erythematous base.² Patches are often found on flexor surfaces but can be found throughout the body. Pruritis is an extremely common symptom which can present with skin excoriations.³ In more severe disease, papulovesicular lesions may lead to weeping wounds and crusting.² Chronic lesions may lead to lichenification.¹⁰ Diagnosis is clinical and based on history and presentation of disease.³

Table 1. Patient lab results and normal value ranges.

Lab test	Patient value	Normal range
WBC	12.1 K/uL	4.0- 19.5 K/uL)
Neutrophils	62.2 %	31.2-38.8 %
Lymphocytes	22.5 %	50.0-61.0 %
Hgb	12.5 g/dL	9.4-12.0 g/dL
Platelet count	253 K/uL	150-350 K/uL
BUN	6 mg/dL	4-17 mg/dL
Cr	0.3 mg/dL	0.2-0.4 mg/dL
POC lactic acid	1.6 mmol/L	0.5-2.0 mmol/L
CRP	<0.2 mg/dL	<0.5 mg/dL

Eczema Herpeticum Epidemiology and Presentation

EH is a disseminated skin infection commonly caused by herpes simplex virus. HSV is an enveloped double stranded DNA virus.¹³ This virus replicates in epithelial cells, especially keratinocytes. There are two main types of HSV. HSV-1 is associated with gingivostomatitis, meningoencephalitis, and EH, while HSV-2 is more commonly associated with genital herpes.¹³ It is estimated that about 3.7 billion people of the global population under age 50 is colonized with HSV-1.^{13,14} HSV-1 is the underlying cause of EH in 90% of cases.^{4,13} Eczema herpeticum most often occurs among patients with atopic dermatitis due to the pathophysiological factors innate to AD, predisposing to HSV infection.⁴

EH affects 7-10% of patients with AD.⁴ This is especially true for patients with a low socioeconomic status.⁴ EH is most associated with herpes simplex virus-1.^{1,4} This virus is transmitted through contact with herpetic lesions, infected skin, or mucosal secretions infected with the virus.^{13,14} While transmission can occur with both asymptomatic and symptomatic individuals, it is much more common with symptomatic individuals due to increased viral load. Prevention of transmission is through avoiding contact with people who have active symptoms.¹³

EH presents as widespread, non-grouped vesicles on an erythematous base that crust and erode around 1-2 weeks.^{1,4} This often leaves behind ulcerations and punched out lesions. Lesions are commonly found on face/neck and trunk, but this varies by case.¹⁵

Diagnosis

Appropriate approach to diagnosis and treatment is vital due

to EH's physical exam similarities to other skin conditions and propensity to lead to life threatening disease if missed.^{1,4} Diagnosis is typically clinical although available diagnostic tools such as PCR are readily available. Another vital part of diagnosis is inquiring about exposure to HSV in history taking. Positive exposure increases suspicion for EH. There are no specific diagnostic criteria making definitive clinical diagnosis difficult.⁴ EH can also present similarly to other skin diseases which further complicates diagnosis.⁵ One example of similar disease is eczema coxsackium, which is a skin infection most often caused by coxsackievirus A6 or enterovirus 71 (Figure 2).^{2,5,16} It leads to a rash consisting of vesicles and erosive eruptions.⁶ One other similar condition is eczema vaccinatum which is caused by the vaccinia virus in smallpox vaccines (Figure 3).^{4,6,17} While exceedingly rare due to the discontinuation of the smallpox vaccine in the US, eczema vaccinatum is a life-threatening disease.⁶ EH can also be confused for bacterial impetigo and severe eczema eruptions.⁶

Due to clinical similarity to other skin disorders, the diagnosis of EH should be supported by laboratory testing such as skin PCR of lesion samples showing positive results for HSV.⁴ This test is highly sensitive and provides rapid results.^{4,14} Other modes of confirmational support include viral wound culture, serological testing, tzank test, and immunostaining, but these are more rarely used.⁴ This is in large due to the time-consuming nature of some of these tests as well as decreased sensitivity and specificity compared to PCR.^{4,14} For instance, tzank testing can be done somewhat rapidly, but it is not specific to HSV. Viral culture has a high sensitivity (>90%), but can take days to complete.¹⁴

Figure 2. Eczema coxsackium in 19-month-old child.



From: Horsten HH, Fisker N, Bygum A. Eczema Coxsackium Caused by Coxsackievirus A6. *Pediatr Dermatol*. 2016 May;33(3):e230-1. Epub 2016 Apr 18. Copyright © 2016 Wiley Periodicals, Inc. All rights reserved.

Figure 3. Eczema vaccinatum in 2-year-old child.



Photo/John Marcinak

From: Centers for Disease Control and Prevention. (2007, May 18). Household transmission of vaccinia virus from contact with a military smallpox vaccinee -- Illinois and Indiana, 2007. Centers for Disease Control and Prevention. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5619a4.htm>

Treatment

Whether diagnosis is confirmed with PCR yet or not, clinical suspicion for EH based on history should prompt immediate empiric treatment. Before the start of antiviral treatment in EH, the disease had a historical mortality rate ranging from 10-75%.⁷ Current recommendations state that acyclovir is considered the gold standard treatment.⁴ Route of administration and length of treatment varies based on severity of disease. Mild or recurrent cases can be treated outpatient with oral acyclovir or valacyclovir for 7-21 days.^{4,7} More severe cases like that presented in this case, require inpatient systemic acyclovir.^{1,4,7} For severe disease, the NIH recommends IV acyclovir every 8 hours until lesions crust and clinical improvement is evident. At this point, it is safe to transition to oral acyclovir.⁷ If clinical suspicion is high and treatment is being initiated in visibly sick individuals, IV acyclovir should be heavily considered as oral acyclovir has a low bioavailability of 10-20%.¹⁸ In patients that are resistant to acyclovir, foscarnet and cidofovir can be considered.¹

One complication of EH is superimposed bacterial infection, most commonly from *S. aureus*.⁶ In general, patients hospitalized with infection related to AD have a 20% rate of bacterial infection.⁶ In a study evaluating rates of superinfection in EH patients, 30.3% of hospitalized pediatric patients with EH had *S. aureus* infection.⁷ Due to the risk of bacterial infection, it is common to treat EH patients with topical antimicrobials.⁷ In patients with signs of severe bacterial disease or systemic symptoms, antibiotic coverage for *S. aureus* is vital.⁶ This includes vancomycin as well as an anti-staphylococcal beta lactam. If toxin-mediated superinfection is suspected, clindamycin is a notable option if used alone or as an addition to a beta-lactam for toxin modulation if resistance rates are low in the area.⁶ For suspected MSSA bacteremia, IV cefazolin is an adequate first line option but culture guidance is ideal.⁶ In our case, the initial concern was widespread impetigo, so the patient was started on oral cephalexin and topical mupirocin. However, after concern for meningitis arose, the patient was switched to IV ceftriaxone and vancomycin. Vancomycin was eventually removed after MRSA cultures came back negative. Ceftriaxone was switched back to oral cephalexin after no growth was seen on CSF culture for 2 days. When the patient displayed worsening lesions, MSSA superinfection was suspected, so ceftriaxone was restarted along with clindamycin for alpha toxin control. Eventually antibiotic coverage was deescalated based on culture result, and the patient was discharged on only oral acyclovir and topical mupirocin.

Associated Complications

Immediate treatment with acyclovir or other antivirals is vital in EH due to the life-threatening sequela that can occur if treatment is delayed.^{1,4,6} If HSV becomes systemic, it can lead to disseminated infection and often with end-organ involvement such as hepatitis and meningoencephalitis or a local invasive infection such as keratoconjunctivitis.⁶ If the virus becomes disseminated, it can lead to organ dysfunction and potentially death.⁷ These complications are especially prevalent in immunocompromised individuals.⁷ Bacterial superinfection associated with EH can lead to systemic disease including bacteremia, osteomyelitis, septic arthritis, and staphylococcal scalded skin syndrome.⁶ This is why not only early diagnosis and treatment of EH is imperative, but also continued observation for superimposed disease. Knowing that patients with moderate-severe AD are at higher risk for EH can help when evaluating for this disease.¹⁹

Predisposing risks of Atopic Dermatitis

Atopic dermatitis is the most common inflammatory skin condition in both children and adults.³ There are several factors in the pathophysiology of atopic dermatitis that lead to an increased risk of infections including but not limited to EH. These include breakdown of the skin barrier, cellular adhesive changes, cytokine variability, immune defects, and skin dysbiosis (Figure 4).^{1,3,4} Each of these will be briefly discussed.

Skin abnormalities in patients with AD predispose them to EH. Different studies have shown that mutations in filaggrin, a structural protein in the stratum corneum, shows an increased risk for EH in AD populations.^{1,3,4} These mutations allow easier entry of HSV into keratinocytes and decreases these cells' ability to acidify environments and halt viral replication.⁴ Adherens junctions play an important intracellular adhesive role in cells. In cases of AD with disrupted adherens junctions, proteins that propagate HSV entry into cells are exposed, leading to increased risk for EH.^{1,3} Tight junctions also typically protect from viral entry by blocking necessary receptors, however, in some AD patients, a reduction of proteins necessary for this function showed an increased risk for EH.^{1,4}

There are immune functions that typically protect from viral pathogens. Antimicrobial peptides typically activate the innate immune system to kill pathogens.⁴ However, in atopic dermatitis patients with EH, protective peptides such as LL-37 and human β defensin have lower expression and lead to decreased ability to halt entry and replication of HSV within



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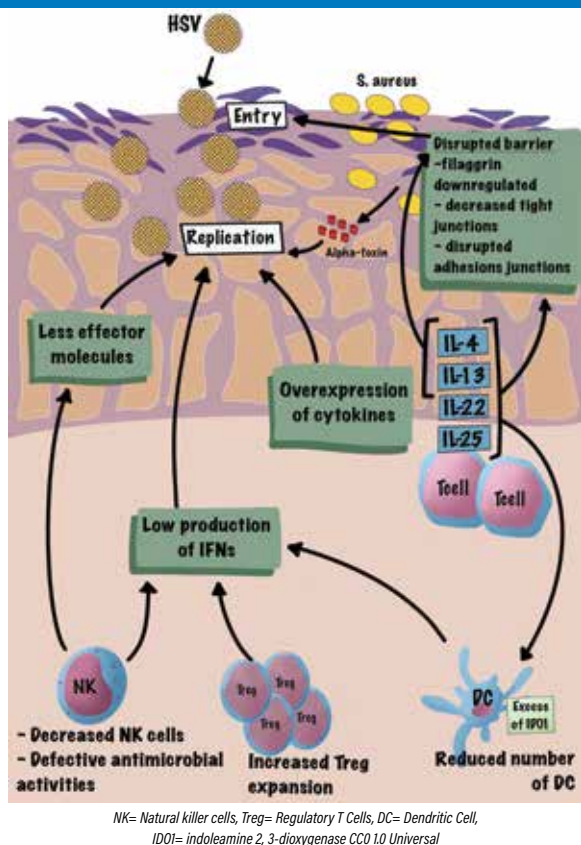
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Figure 4. Physiologic breakdown in atopic dermatitis leading to increased susceptibility to eczema herpeticum.



cells.^{1,4} Natural killer cells also have an antiviral function that is reduced in these patients. Dendritic cells (DCs) play a vital role in healthy antiviral response by activating different T cell responses. In patients with eczema herpeticum, certain DCs are found in lower levels.^{1,4,6} DCs contribute to the production of indoleamine 2,3-dioxygenase (IDO1). IDO1 catabolizes tryptophan and aids in cellular antiviral response. In a typical antiviral response, low levels of IDO1 inhibit HSV replication. In EH, elevated IDO1 excessively catabolizes tryptophan which decreases T cell response. It also leads to lower IFN γ further contributing to decreased antiviral response.^{1,3,4} Regulatory T cells which work to suppress the immune system have been found in higher concentrations in ADEH+ which furthers cell's inability to respond to entrance of HSV1.^{1,5}

Cytokines are another important risk factor in AD/EH patients. IL-4, IL-13, IL-31, and IL-22 are all found in increased levels in this population. IL-4 and IL-13 specifically function to downregulate filaggrin which can contribute to the breakdown of the skin barrier.^{1,5} IFN γ has an important

role in controlling viral pathogens. In AD patients, a decreased level showed an increased risk for EH.^{5,6}

Skin microbiome is also an important aspect impacting AD patients. The skin is an essential barrier to infectious organisms. In healthy people, this protection is partially driven by a diverse microbiome.²⁰ These microorganisms play a role in regulating host immunity to protect against pathogens and decrease inflammatory response.⁶ In AD patients, there is microbiome dysbiosis. These patients have a less diverse microbiome.^{1,4,6,20} Typical commensal bacteria are found in lower levels while Staphylococcal organisms have elevated rates. *S. aureus* specifically, makes up 90% of skin bacteria on lesions in AD patients having an acute flare.^{1,19} This bacterium increases risk of HSV infection due to α toxin, a virulence factor of *S. aureus*.^{1,4} Studies have found that increased levels of α toxin in AD patients increases rate of HSV infection by promoting HSV entry into cells.¹

All these physiologic breakdowns lead to increased risk of EH in patients suffering from atopic dermatitis. This is why it is vital to maintain an increased level of suspicion for this disease in patients with AD.

Conclusion

Eczema herpeticum is a potentially life-threatening disease, especially in young children and immunocompromised patients with atopic dermatitis. Patients with atopic dermatitis are at increased risk of developing EH due to factors impacting skin barrier, immune function, cellular adhesion, and skin microbiome. A strong index of clinical suspicion is important for prompt diagnosis and treatment which are vital for timely intervention and prevention of complications.

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A Rare Combination of Bleeding Disorders in South Dakota: A Case Report

Dallas Petroff, OMS IV; and David Ring, MD

Abstract

Hemophilia A is a clotting disorder due to factor VIII deficiency, leading to prolonged bleeding. Acquired hemophilia A results from the immune system attacking factor VIII, typically occurring later in life. Factor V Leiden is a genetic mutation causing abnormal blood clot formation, primarily in veins. This mutation is inheritable and increases the risk of clotting. A combination of these conditions is extremely rare. Correct management of a patient with any bleeding disorder is imperative for a surgical case to prevent catastrophe. We present a surgical case involving both hemophilia A and Factor V Leiden.

Introduction

Hemophilia A is a hereditary bleeding disorder characterized by a deficiency or dysfunction of clotting factor VIII, a crucial protein involved in blood coagulation.¹ It is primarily passed from carrier mothers to their male offspring through X-linked recessive inheritance, whereas females can carry one normal X chromosome and one with the hemophilia gene, often remaining asymptomatic. Usually, if a female carries a hemophilia allele on one X chromosome, her other X chromosome carries a normal allele, providing some protection against hemophilia by producing a normal clotting factor. Such females, referred to as heterozygous or carriers, may display bleeding symptoms, typically less severe than those seen in affected males. However, in rare cases, a heterozygous female may experience bleeding symptoms as serious as those in males with hemophilia. Moreover, a female can have hemophilia if she inherits hemophilia alleles from both parents or if she inherits one hemophilia allele and her other X chromosome is absent or malfunctioning.²

The hallmark symptoms of hemophilia A include excessive and prolonged bleeding following minor injuries, surgeries, or spontaneous events, easy bruising, and common bleeding episodes involving joints and muscles.^{3, 4} Internal bleeding, such as into the joints, can result in chronic joint damage if not properly managed. Severity varies and is categorized as mild, moderate, or severe based on factor VIII levels. Severe cases, with less than 1% normal factor VIII, experience frequent and prolonged bleeding, while mild cases (5-40% factor VIII) may bleed primarily in response to major trauma or surgery.^{1,4,5,6}

In contrast, acquired hemophilia A presents similarly to the genetic variant but usually appears later in life with little history of childhood bleeding episodes.⁷ It is characterized by an autoimmune attack against factor VIII.

Factor V Leiden, another genetic condition, inherited via autosomal dominant pathways, increases the risk of abnormal blood clot formation primarily in veins. It results from a point mutation in a gene responsible for producing clotting factor V, making it less responsive to natural anticoagulants in the body.⁸ Factor V's normal function is to promote the conversion of fibrinogen to fibrin in the blood clotting process. In Factor V Leiden, the mutated factor V is less susceptible to inactivation by a protein called activated protein C (APC), which regulates blood clotting, leading to an *increased* tendency to form blood clots.

Individuals with Factor V Leiden have a heightened risk of developing blood clots, particularly deep vein thrombosis (DVT) and pulmonary embolism (PE).⁹ DVT occurs when clots form in the deep veins of the legs, while PE occurs when these clots dislodge and travel to the lungs, potentially causing life-threatening blockages. Notably, many individuals with Factor V Leiden may not exhibit symptoms until they experience a blood clot. DVT symptoms can include leg pain, swelling, warmth, and redness, while PE symptoms can manifest as chest pain, shortness of breath, and hemoptysis.

Both conditions have significant implications for individuals' health, requiring careful management and awareness of potential complications. This report details the presentation, treatment, and outcome of a patient that was diagnosed with

both hemophilia A and Factor V Leiden in South Dakota.

Case Presentation

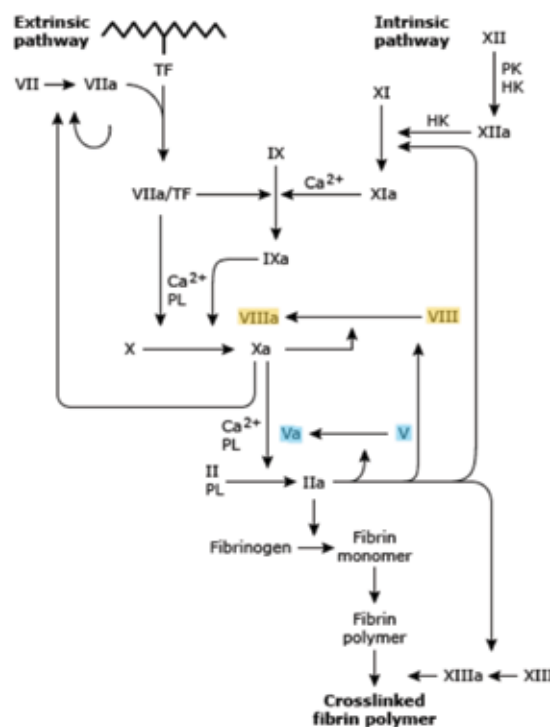
A 24-year-old adopted male, presented to the emergency department for sudden right sided chest pain. After physical exam and chest X-ray, spontaneous pneumothorax was diagnosed. Swift diagnosis led to the successful placement of a chest tube, mitigating complications associated with his pneumothorax. The root cause was attributed to bleb disease, and plans were made for a Video-Assisted Thoracoscopic Surgery (VATS) right wedge resection to address the underlying issue.

During the preoperative evaluation for the VATS wedge resection, a significant twist emerged. He reported that he had been previously diagnosed with acquired hemophilia A and had factor V Leiden. The patient was adopted, but further questioning revealed a history of recurrent nosebleeds, occasional instances of blood in his stool, no history of bleeding in paternal grandfather, mom's sister with similar bleeding history, and a history of post-operative hematomas following surgical interventions for a benign chest mass removal and testicular torsion at the ages of 20 and 21, respectively. This history helped lead towards a congenital hemophilia A diagnosis. These new factors necessitated the postponement of the planned VATS procedure for an in-depth assessment of his bleeding risk.

The hematology team was consulted to help diagnose, treat, and balance the coagulopathies with surgery. Several laboratory tests were ordered: INR was 1.0, Prothrombin Time (PT) was 13 seconds (normal: 11-15 seconds), Partial Thromboplastin Time (PTT) was 57 (normal: 25-40 seconds), mix PTT baseline was 37 (normal: 24-36), Von Willebrand antigen was 70 (normal: 50-200), Factor VIII levels were 46 (normal: 50-150), vWF Ristocetin cofactor was 52 (normal: 50-150), and lupus anticoagulant was negative.

Considering these findings, the Hematology team devised a comprehensive treatment plan. The goal was to optimize the coagulation profile in preparation for surgery. An infusion of recombinant factor VIII infusion (rFVIII) was chosen. The infusion regimen included treatments to bring his FVIII levels to 100 preoperatively and 80-100 postoperatively. 1500 units of the recombinant FVIII were given 30-60 minutes preoperatively with an additional 750 units rFVIII given 12 hours after the first infusion. Factor VIII levels were drawn 30 minutes after the first infusion and before the second infusion to verify dosing. On days 2 and 3, the patient received 750 units of rFVIII twice a day, and on days 4 and

Figure 1. Depiction of the Coagulation Cascade. Highlighted yellow represents Hemophilia A's part of the coagulation cascade, while highlighted blue represents Factor V Leiden.¹⁰



5, the patient received 750 units of rFVIII each day. DVT prophylaxis was managed with Enoxaparin, a low molecular weight heparin, to reduce clotting risk associated with the factor V Leiden mutation as well.

With his FVIII levels maintained, the VATS right wedge resection was executed with meticulous care, minimizing blood loss, and ensuring patient safety. The postoperative course was remarkably uneventful, leading to the patient's discharge from the hospital three days after surgery.

Ten days later, during the follow-up visit, the patient exhibited excellent overall health with no reported adverse events. His journey continues with ongoing monitoring and management by the Hematology team to ensure his long-term well-being and any necessary adjustments to his treatment regimen.

This case underscores the intricacies of managing coagulation disorders in surgical contexts and serves as a reminder of the importance of a thorough evaluation and tailored treatment plan for each patient.

Discussion

Acquired hemophilia is a rare bleeding disorder characterized

by the development of autoantibodies (inhibitors) against clotting factor VIII. It has an overall prevalence of 1.5 per million per year.^{7, 11} This condition typically arises in individuals who have no prior history of bleeding disorders.⁹ It can affect people of any age but is more frequently observed in older adults, often in association with underlying medical conditions, autoimmune diseases, or medication use.

On the other hand, congenital hemophilia is an inherited bleeding disorder caused by a deficiency or dysfunction of clotting factor VIII. The prevalence of genetic hemophilia A varies among populations but is generally estimated to occur in approximately 1 in 5,000 to 1 in 10,000 male births.¹² Notably, hemophilia A primarily affects males due to the FVIII gene being located on the X chromosome. Females can carry the gene but are typically unaffected unless they inherit two X chromosomes with a mutated FVIII gene.

Factor V Leiden is a genetic mutation that increases the risk of developing abnormal blood clots, a condition known as venous thromboembolism. The prevalence of the Factor V Leiden mutation varies among different populations and ethnic groups. In individuals of European descent, particularly those of Northern European origin, the prevalence of Factor V Leiden is relatively higher, estimated to be around 5% to 7% in some populations.^{8, 13} However, it is less common in other racial and ethnic groups.

The co-occurrence of genetic hemophilia A and Factor V Leiden is statistically exceedingly rare, where it can be as low as 1 in 10000000 people and presents challenges in management because these conditions affect opposing aspects of blood coagulation. Individuals inheriting both conditions would experience prolonged bleeding tendencies due to hemophilia A and an increased risk of clot formation, particularly in veins, due to Factor V Leiden. However, some studies report a potential protective property from being co-diagnosed.¹⁴

Hemophilia is identified by an extended activated partial thromboplastin time (aPTT). Nonetheless, individuals with milder factor deficiencies, such as those with factor activity exceeding 15 percent, may exhibit a normal aPTT, particularly in hemophilia B (resulting from factor IX deficiency). In some cases of type A hemophilia, stress can temporarily *elevate* factor VIII levels, leading to a 'pseudo' normal aPTT level, potentially causing inaccurate factor level assessments. This can lead physicians to incorrectly categorize the severity of the disease, if diagnosed at all.¹⁵ In such cases, factor activity testing should be repeated under

low-stress conditions if possible.

In hemophilia patients, the aPTT should normalize during mixing studies, except when an inhibitor is present. This primarily applies to those who have received factor infusions or have autoantibodies like a lupus anticoagulant or an acquired factor inhibitor. If mixing studies fail to correct a prolonged aPTT, it suggests a different diagnosis, such as an acquired factor inhibitor.¹⁶

Platelet count and prothrombin time typically remain within normal ranges in individuals with hemophilia. Thrombocytopenia or prolonged PT may indicate the possibility of an alternative diagnosis, either instead of or in conjunction with hemophilia. The plasma von Willebrand factor antigen (VWF:Ag) remains within normal levels in individuals with hemophilia. A reduction in VWF:Ag levels suggests the potential presence of von Willebrand disease (VWD), either alongside or instead of hemophilia.

To determine Factor V Leiden, one has the option to select either a functional assay or genetic testing. In this case, since the patient had a reported history of the condition, we conducted a genetic test.

Collecting a comprehensive medical history from a patient is consistently crucial. Nevertheless, this task can become difficult when dealing with adopted individuals who lack ties to their biological family. In addition, the sporadic occurrence of hemophilia A, affecting up to 55% of cases, can add complexity to the process of gathering a concise medical history.¹⁷ Hence, clinical suspicion should trigger a more thorough inquiry following unexplained or suspicious bleeding episodes.

Individuals afflicted with hemophilia A may experience a range of bleeding manifestations, including spontaneous episodes and those triggered by injuries. These manifestations encompass intracranial hemorrhaging, joint and muscle bleeds that can lead to significant disability, as well as instances of epistaxis and gastrointestinal bleeding.^{3, 4} Individuals with factor V Leiden may encounter deep vein thrombosis, which can progress to venous thromboembolism (VTE), including portal vein thrombosis, cerebral vein thrombosis, or even an isolated pulmonary embolism.^{9, 18, 19} There is some debate surrounding studies that propose a potential connection between factor V Leiden (FVL) and arterial thromboembolism, such as stroke or myocardial infarction.^{20, 21, 22}

People with FVL should be treated with low-molecular-

weight heparin, such as fondaparinux prophylactically for surgery. Especially when attempting to correct Factor VIII levels to prevent potential thromboembolism.

Hemophilia A requires factor replacement therapy. The dosage is determined by multiplying the patient's weight in kilograms by the desired increase in factor VIII level (expressed as a whole number, such as 100), and further multiplied by a correction factor that accounts for the volume of distribution (0.5 for factor VIII). It is advisable to administer an initial dose of factor to raise the peak factor level to a range of 80 to 100 percent of normal FVIII levels. Subsequent doses should be timed to align with the expected (or confirmed) factor activity level of around 50 percent to prevent the patient's circulating factor level from dropping below 50 percent.^{4, 5} An alternative approach involves delivering a factor dose to increase the level to 80 to 100 percent, followed by continuous infusion to maintain a steady hemostatic level.²³

Conclusion

This case illustrates the unique and challenging clinical scenario of a young male with hemophilia A and Factor V Leiden undergoing a right lung wedge resection. The successful outcome was achieved through close collaboration between surgical and hematological teams, timely diagnosis, and a comprehensive treatment plan tailored to the patient's coagulation profile. This case underscores the importance of considering rare bleeding disorders in surgical candidates and highlights the critical role of interdisciplinary care in achieving favorable outcomes in such cases.

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SGLT-2 Inhibitors: A Narrative Review

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Abstract

SGLT2 inhibitors have emerged as a remarkable class of drugs, revolutionizing the management of various medical conditions beyond their initial purpose of controlling diabetes. With their proven benefits in cardiovascular health, kidney disease, hypertension, and even potential applications in cancer treatment, SGLT2 inhibitors have broadened their scope. While concerns about adverse effects and contraindications exist, these medications hold great promise for a diverse range of patients. Moreover, as generic alternatives become more accessible and affordable, the potential benefits of SGLT2 inhibitors are poised to reach a wider audience, making them a significant player in modern healthcare.

Introduction

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are frequently referred to as a new class of glucose-lowering drugs. They work by inhibiting the SGLT2 protein located in the proximal convoluted tubule of the nephron.¹ Under normal circumstances, approximately 180 grams of glucose is filtered by the renal glomerulus, with virtually all of it subsequently reabsorbed in the proximal convoluted tubule.² This reabsorption (approximately 90%) occurs at the level of the SGLT2 protein at the S1 segment of the nephron. Another SGLT protein, SGLT1, is located at the S3 segment (downstream to S1) and is responsible for reabsorbing the remaining 10% of the glucose load. The combined action of these two proteins results in a urine glucose of less than 25 mg/dL.³

The inhibition of SGLT2-dependent glucose and sodium reabsorption increases distal tubular sodium load. The resultant inhibition of the renin-angiotensin-aldosterone system and reduction of afterload and preload is cardioprotective and generally results in more favorable hemodynamics.⁴

SGLT2 inhibitors (SGLT2-i) were first approved for treating type 2 diabetes mellitus by the U.S. Food and Drug Administration (FDA) in 2013. Both SGLT proteins are not limited to the nephron and are found throughout the body. Notably, the SGLT1 protein is also responsible for intestinal glucose absorption. Combined SGLT1/SGLT2 inhibitors have recently been approved for treating heart failure by the FDA.

Although there is much excitement about these medications,

with them often being considered a new class of drugs, the natural compound (Phlorizin) from which the modern SGLT2-gliflozins are derived, was first discovered by French chemist Henri Braconnot in 1835. The mechanism by which this compound lowered blood glucose levels was unknown, but it was known that parenteral Phlorizin was reported to decrease plasma glucose levels in animal models of diabetes. Phlorizin is degraded by intestinal lactase-phlorizin hydrolase, and the glucosuric effect of a single enteral dose wanes over several hours, necessitating multiple large oral doses to sustain maximal glucosuria. This made it very impractical for pharmaceutical use. Diabetes research expanded in the 20th century, and phlorizin's effects on glucose metabolism were explored in further animal studies, but its clinical use was still limited.

Development of the modern SGLT2-i class of medication began in the early 2000s after researchers Ernest M. Wright and Lukas C. Koster published a seminal paper in 1987 describing the identification and characterization of SGLT2 protein.⁵ After clinical trials confirmed the safety and efficacy of SGLT2-i in managing diabetes, the FDA approved the first SGLT2-i, canagliflozin, in 2013. Since then, they have been approved for broader use, including in patients with heart and kidney disease, due to their cardiovascular and renal benefits.

Recently, the FDA has tentatively approved multiple generic formulations of dapagliflozin and empagliflozin.⁶ These will be available in February 2025.

Accepted Guidelines for Use

SGLT2-i are currently approved for glycemic control in type 2

diabetes mellitus, reduction of major adverse cardiovascular events in patients with type 2 DM, decreasing cardiovascular hospitalization risk for patients with heart failure with reduced ejection fraction (HFrEF), improvement of cardiovascular outcomes in patients with heart failure with preserved ejection fraction (HFpEF), and reduction of eGFR decline in patients with chronic kidney disease at risk of disease progression. Off-label use includes use for obesity management along with GLP-1 agonists and non-alcoholic fatty liver disease.^{7,8}

Cardiovascular Disease

Heart failure is classified based on whether the ejection fraction is reduced ($\leq 40\%$), mildly reduced (41 to 49%), or preserved ($\geq 50\%$).⁹

Heart Failure — Reduced Ejection Fraction (HFrEF)

Multiple trials for HF with reduced EF have shown mortality benefits with the use of SGLT-2 inhibitors.

The Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure, DAPA-HF found that among individuals with HFrEF with or without T2DM, the addition of the SGLT-2 inhibitor dapagliflozin decreased rates of cardiovascular mortality and hospitalization (HR 0.74; 95% CI 0.65-0.85; $P < 0.001$).¹⁰ It was a multicenter, double-blind, parallel-group, randomized, controlled trial with a sample size of 4,744 patients published in the NEJM in 2019.

The Cardiovascular and renal outcomes with empagliflozin in heart failure EMPOROR-Reduced trial found that in patients with HFrEF on guideline-directed medical therapy, irrespective of whether T2DM is present or not, the addition of empagliflozin reduces cardiovascular mortality and hospitalization for heart failure exacerbation at 16 months (HR 0.75; 95% CI 0.65-0.86; $P < 0.001$).¹¹ It was a multinational, multicenter, double-blind, parallel-group, randomized, controlled trial with a sample size of 3,730 published in NEJM in 2020.

The Randomized Trial of Empagliflozin in Nondiabetic Patients With Heart Failure and Reduced Ejection Fraction (EMPA-TROPISM) found that the effect of empagliflozin administration to nondiabetic HFrEF patients significantly improves LV volumes, LV mass, LV systolic function, functional capacity, and quality of life when compared with placebo, independent of glycemic status.¹² This was a double-blind, placebo-controlled trial with 84 nondiabetic HFrEF patients. It was published in the Journal of the American College of Cardiology in 2021.

Heart Failure—Preserved Ejection Fraction (HFpEF)

The first trial to indicate the benefit of SGLT2-i therapy in HFpEF was “The Effect of Sotagliflozin on Cardiovascular Events in Patients With Type 2 Diabetes Post Worsening Heart Failure”, the SOLOIST-WHF trial.¹³ This was the first trial to indicate that SGLT-2 inhibitors may benefit from reducing hospitalizations and urgent visits for HFpEF (HR 0.64, 95% CI 0.65-0.86; $P < 0.001$). However, it could not show that the use of Sotagliflozin resulted in a statistically significant reduction in death from a cardiovascular cause (HR 0.84, 95% CI 0.58-1.22; $P = 0.36$). SOLOIST-WHF was a phase 3, double-blind, randomized, placebo-controlled trial with Sotagliflozin (A combined SGLT2-i and SGLT1-i) that was stopped early due to loss of funding due to COVID-19. The trial was underpowered and was unable to identify significance. It was published in the NEJM in 2021.

The Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction (EMPEROR-Preserved) trial in August 2021 found reduced cardiovascular death and heart failure hospitalizations in patients with EF $> 40\%$ with and without diabetes (HR 0.79; 95% CI 0.69-0.90; $p < 0.001$; NNT=30). EMPEROR-Preserved was a double-blind trial with 5988 patients with class II–IV heart failure with EF $> 40\%$ randomized to receive empagliflozin or a placebo in addition to usual therapy.¹⁴ It was published in the NEJM in 2021.

The Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction (DELIVER) trial showed regardless of diabetes status, among patients with HFmrEF (41-49%) or HFpEF, the addition of dapagliflozin reduces HF hospitalizations (HR 0.77; 95% CI 0.67-0.89), urgent HF visits (HR 0.76; 95% CI 0.55-1.07), and cardiovascular disease mortality (HR 0.88; 95% CI 0.74-1.05).¹⁵ This, too, was a multicenter, double-blind, randomized controlled trial with a sample size of 6263 and published in the NEJM in 2022.

Hypertension

Retrospective data analyses from recent clinical trials have noted SGLT2-i to have a long-term impact on both systolic and diastolic blood pressure.¹⁶ The mechanism of this effect is still unclear; however, it is probably related to the natriuretic effect, renin-angiotensin-aldosterone system modification, and/or the reduction of sympathetic tone.

Chronic Kidney Disease

The Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy, also known as the CREDENCE trial,

was a groundbreaking clinical study in diabetes and kidney disease management.¹⁷ In this double-blind, randomized trial, patients with type 2 diabetes and albuminuric chronic kidney disease were selected to receive either canagliflozin or placebo daily. Primary outcome encompassed a composite outcome, which included progression of end-stage kidney disease (defined as dialysis, transplantation, or sustained estimated GFR <15ml/min/1.73m²), a two-fold increase in serum creatinine levels, or death from renal or cardiovascular causes. The study had to be stopped early due to the overwhelming benefit of the canagliflozin group. Patients on canagliflozin had a 30% lower outcome compared to the placebo group (HR 0.70, CI 0.59-0.82, $p=0.00001$) of end stage renal disease progression, doubling of baseline serum creatinine, renal mortality, or cardiovascular mortality.

The Dapagliflozin in patients with chronic kidney disease, DAPA-CKD, explored the use of Dapagliflozin in patients with CKD with and without type 2 DM.¹⁸ 4304 participants, irrespective of diabetes, with an eGFR of 25-75 and urinary albumin to creatinine ratio of 200-5000, received either dapagliflozin or placebo. The composite endpoint included a decline of $\geq 50\%$ in eGFR, new ESRD, renal mortality, or cardiovascular mortality.¹⁷ Dapagliflozin reduced the risk of the composite endpoint (HR 0.61, 95% CI 0.51-0.72; NNT=19). Importantly, this benefit was similar regardless of T2DM status. Like the CREDENCE trial, this trial had to be stopped early, after a median time of 2.4 years.

Diabetes Mellitus

The Canagliflozin and cardiovascular and renal events in type 2 diabetes, 'CANVAS' study published in the NEJM 2017 found that in addition to a lowered risk of cardiovascular events, rate of renal decline, and the likelihood of heart failure hospitalization, SGLT2-i use was associated with a change in glycated hemoglobin of -0.58% (CI -0.6% to -0.56% ; $P < 0.001$).¹⁹ Similarly, the EMPA-REG trial, which studied the effects of cardiovascular outcomes and mortality in diabetic patients, showed a difference in HbA1c of -0.54% (95% CI, -0.58 to -0.49) in the 10-mg group and -0.60% (95% CI, -0.64 to -0.55) in the 25-mg group.

The VERTIS trial showed an A1c improvement of -0.7% (95% CI, -0.73 to -0.67) in the patients on the 5-mg dose of ertugliflozin and -0.72% (95% CI, -0.75 to -0.69) in patients who received the 15-mg dose of ertugliflozin.²⁰

Recent studies have found that the pericytes in the human retina also express SGLT2 proteins. Targeting this receptor using SGLT2-i may allow for a decrease in diabetic retinopathy

incidence and progression. Recent research in mice has found that empagliflozin reduces both albumin and vascular endothelial growth factor (VEGF) retinal vascular leak.²¹ These molecules play a crucial role in diabetic retinopathy proliferation, and further human studies are necessary to elucidate outcomes.

Emerging Uses

While the primary effects of SGLT 2 inhibitors have been mentioned above, there have been secondary desired outcomes of these drugs. The CANVAS trial noted a mean difference in body weight of -1.6 kgs (95% CI -1.70 to -1.51 , $p < 0.001$).¹⁹ Meta-analyses conducted to investigate the effects of SGLT-2 inhibitors on weight in overweight and obese populations without diabetes noted the impact of various SGLT2-i on weight and body mass index was statistically significant.²¹

The use of SGLT2-i in managing polycystic ovarian syndrome is an emerging area of research. In a trial, empagliflozin was compared against metformin for 12 weeks in patients with PCOS. While there was significant improvement in anthropometric parameters and body composition in overweight and obese women with PCOS, no changes were seen in hormonal or metabolic parameters.²²

Research being conducted on the use of SGLT2-i in individuals with non-alcoholic steatohepatitis remains hazy. No concrete outcomes are reportable as of yet. However, recent metaanalysis demonstrated the efficacy of canagliflozin and dapagliflozin in enhancing liver function parameters, with a notable improvement observed in gamma-glutamyl transpeptidase levels.²³

SGLT2-i are also recognized to have some anti-inflammatory properties as they significantly reduce the risk of pneumonia and septic shock in patients with diabetes mellitus type 2, as noted by a meta-analysis that pooled data from 26 trials and 59,264 patients.²⁴

Interestingly, SGLT2-i are being researched for their anti-cancer effects. The mechanism is not yet understood. Neoplastic cells are known to be highly aggressive and replicate via the uptake of glucose. Researchers are trying to use SGLT2-i to prevent glucose uptake in these cells, consequently preventing their growth.²⁵ Empagliflozin and doxorubicin synergistically inhibit the survival of triple negative breast cancer cells in vitro via disrupting the mTor pathway. It may also provide cardioprotective effects in diabetic patients taking doxorubicin.²⁶ This is an exciting

and active area of research.

Cautions and Adverse effects

Contraindications to SGLT2-i use include hyperglycemia in the setting of type 1 diabetes, type 2 diabetes with an eGFR <45 mL/min/1.73 m² (ertugliflozin), or <30 mL/min/1.73 m² (empagliflozin, canagliflozin, dapagliflozin) or a known prior episode of diabetic ketoacidosis (DKA).

Known adverse effects of SGLT2-i use include an approximately three-fold increase in the risk of genitourinary infections across all age groups. The risk was highest in patients above 60 years of age.²⁷ Several case reports of Fournier's gangrene (necrotizing infections of the perineal and genital soft tissue) are associated with SGLT2-i use. Patients should be counseled regarding the signs and symptoms of genitourinary infections (dysuria, etc.) and notify their provider at symptom onset. Patients with a history of recurrent, severe, or difficult-to-treat infections should discontinue SGLT2-i therapy and avoid future use. Listing SGLT2-i as an allergy in the patient's online medical record might be helpful in these situations.

In the CANVAS study, canagliflozin was associated with a 2-fold increased lower extremity major and minor amputation risk compared to placebo (HR 1.97; 95% CI 1.41–2.75). EMPA-REG and DECLARE trials failed to show any increased amputation risk. Recent retrospective studies also failed to demonstrate an increased risk of bilateral knee amputation with canagliflozin.¹⁸ The mechanism by which SGLT2-i increases amputation risk remains a matter of speculation. Some degree of reduced tissue perfusion may be due to medication-induced volume depletion and hemoconcentration. In 2020, the FDA removed the black box warning regarding the increased risk of lower extremity amputations related to canagliflozin use.²⁹ Caution should be used in patients with risk factors for foot ulceration, and patients should be encouraged to perform daily foot examinations as should be done by their provider during routine wellness visits.

SGLT2-i have been associated with increased fracture risk in some studies but not in others.³⁰ It is unclear whether fracture risk results from changes in skeletal physiology or SGLT2-i-mediated blood pressure reductions. They should be used cautiously in those at risk for falls and fractures. The risks of falls with SGLT2-i are similar to those of dipeptidyl peptidase-4 inhibitors and diuretic use in the elderly.

Euglycemic DKA has been associated with patients taking SGLT2-i; recent studies have found the highest associated

with female sex, concurrent metformin use, recent surgery, and infection. Patients should be counseled to monitor for symptoms of DKA (e.g., myalgia, nausea, volume depletion, fatigue). Providers should consider holding medications in times of increased DKA risk. SGLT2-i should not be started in patients with ketosis-prone type 2 diabetes, those with significant alcohol use disorder, ketogenic diets, or a prior history of DKA.

SGLT2-i can induce volume depletion. There have been some reports of an AKI with SGLT2-i initiation. They should be used with caution with other medications that predispose to AKI. When starting in patients with normal eGFR, it is recommended to monitor creatine every three months, and if stable, then annually if there is no other indication. If eGFR is between 30 and 60 mL/min/1.73 m², it is recommended to measure serum creatinine every three months or as clinically indicated. A short-term eGFR reduction of up to 30 percent can be seen after starting SGLT2-i, presumably due to a reduction in glomerular pressure. eGFR reductions greater than 30% should prompt an assessment of volume status and a consideration to temporarily the medication and then consider rechallenging the patient once appropriate.

There have been some disproportionately high reports of bladder cancer with SGLT2-i. Dapagliflozin showed the strongest association.³¹ Follow-up analyses have not shown any causal relationship. The time to tumorigenesis was short, approximately six months of dapagliflozin use. Regardless, dapagliflozin is not advised in patients with hematuria or a history of bladder cancer.

Other reported adverse effects of SGLT2-i use include a slight increase in LDL-C and HDL levels, Hyperkalemia (especially with canagliflozin and concurrent ACEi³²), and hypersensitivity reactions. SGLT2-i shows drug interactions using lithium, digoxin, and UGT enzyme inducers. They may also lead to false positive urine glucose tests.

Costs

The out-of-pocket cost of SGLT-2 inhibitors ranges from 400 to 600 dollars for a one-month supply.³³ According to the FDA, with one generic producer, the cost of a generic drug is 39% lower on average than that of a brand-name drug. With two generic producers, the cost of the generic drugs is an average of 54% lower than that of the brand-name drug. With six or more generic producers, the cost of the generic drugs is an average of 95% lower than the cost of the brand-name drug. With the cheaper formulations of SGLT2-i like Bexagliflozin and the upcoming expiry on the patent for

dapagliflozin, the cost of one month of SGLT2-i therapy will be within budget for most uninsured patients.

Conclusion

In conclusion, SGLT2 inhibitors have emerged as a significant class of medications with broad therapeutic implications beyond their original use in glycemic control. Since the discovery of Phlorizin in 1835, the modern SGLT2-i has undergone significant interactions. They demonstrated efficacy in managing type 2 diabetes mellitus, cardiovascular disease, heart failure, hypertension, chronic kidney disease, and obesity. Their positive impact on various clinical outcomes, including cardiovascular mortality, hospitalization

rates, and renal function, has been substantiated through rigorous clinical trials. Their use is being expanded as research explores the anti-inflammatory properties and potential anti-cancer effects. Prescribers should be cognizant and comfortable identifying patients with contraindications for SGLT2-i use and be quick in recognizing the adverse effects of these medications. The imminent availability of cheaper generic formulations represents an exciting time in the management of many chronic diseases.

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Corrigendum: Raoultella planticola Urinary Tract Infection Presenting as Hyperbilirubinemia in a 3-Day-Old Infant. David Jensen, MD; Anthony Drazick, MS IV; Rochelle Boote, MD, FAAP; Peter Paul Lim, MD, FAAP

South Dakota Medicine – 2024;77(6):274-9. PMID 39013101. An acknowledgement was not stated in the case report. It is as follows: Acknowledgement to Cory Gunderson for providing the high-quality plated images shown in this case report.

REDUCING SYPHILIS RATES

doh.sd.gov/std/

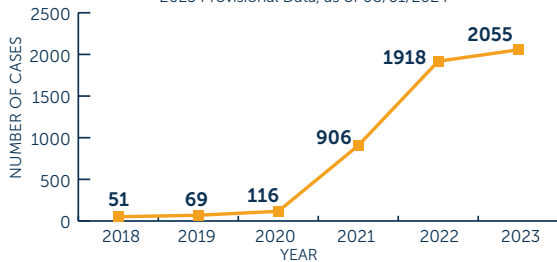


SD REPORTED CASES

2,055

ADULT SYPHILIS CASES
(ALL STAGES) IN 2023

Reported Adult Syphilis Cases 2018-2023 - South Dakota
2023 Provisional Data, as of 08/01/2024



TESTING & TREATING



Syphilis Diagnosis

Serologic testing helps detect patients infected with syphilis in routine clinical practice. Point of Care testing is valuable with clients that may not return for results as it provides rapid results using whole blood from a fingerstick.



Syphilis Treatment

Syphilis can be successfully treated per the CDC 2021 Treatment Guidelines with Bicillin L-A or recommended alternative treatment.



2021 Treatment Guidelines, with app available!

CDC's *Sexually Transmitted Infections Treatment Guidelines, 2021* provides current evidence-based prevention, diagnostic, and treatment recommendations intended to be a source for clinical guidance. Scan the QR code in the lower right corner for information.

COURSE OF SYPHILIS WITHOUT TREATMENT



Infected/Exposed
No symptoms
(1-90 days)



Primary Syphilis
Chancres at site of infection (commonly in the genital area - disappears after some weeks)*



Secondary Syphilis
Localized rash (predominantly located on palms and soles; after 1-6 months; lasts for 3 months)*



Latent Syphilis
Serological proof of infection but no/minor signs and symptoms*



Tertiary Syphilis
Benign gummas, cardiovascular, or neurosyphilis*

*Ocular/Optic/Neurological syphilis can happen at any stage.

RISK FACTORS



Pregnant Women



Multiple Sex Partners



History of STI



Unstable Housing



IDU & Substance Abuse



Incarceration



SD Syphilis Healthcare Guidance



Find information and resources like important health updates and STI training opportunities

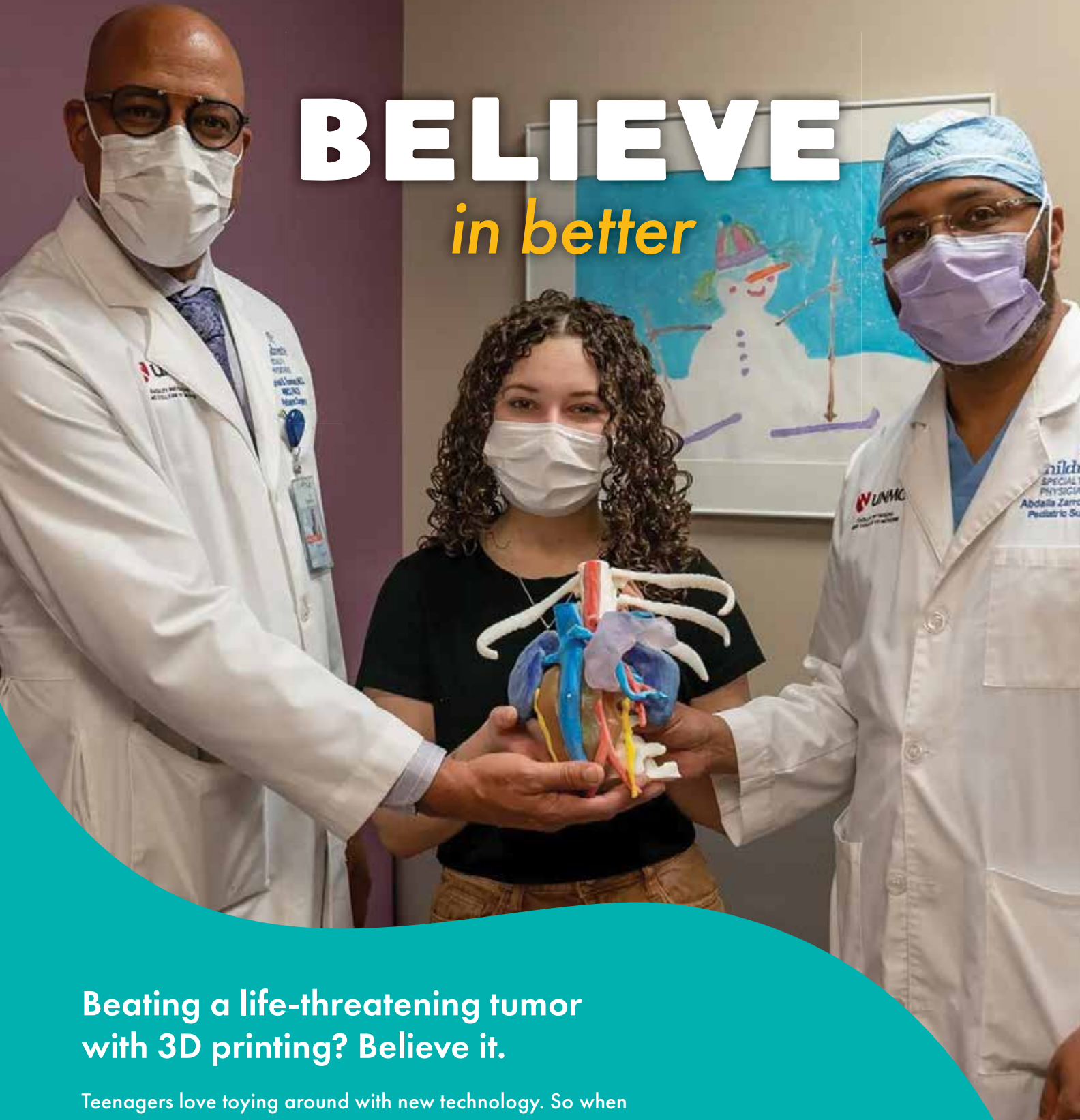


CDC's Sexually Transmitted Infections Treatment Guidelines, 2021

This publication was supported by Centers for Disease Control and Prevention (CDC) grant number, 6 NH25PS005161-03-04 as a part of an award totaling \$1,000,000.00 with \$0.00 state funding. The views expressed in this written material or publication do not necessarily reflect the official policies of the Centers for Disease Control and Prevention (CDC), Department of Health and Human Services.

BELIEVE

in better



Beating a life-threatening tumor with 3D printing? Believe it.

Teenagers love toying around with new technology. So when 18-year-old Karys was diagnosed with a dangerous tumor, she was filled with hope when she saw devices like virtual reality headsets and 3D printers being used as vital tools in planning her operation. Her successful procedure is further proof that innovative surgical techniques paired with an unwavering commitment to kids and families is a combination that can't be beat.

ChildrensNebraska.org/Surgery



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Member News

Visit www.sdsma.org for the latest news and information.

The Issue Is...

SDSMA Meets With Senator Thune

SDSMA members and staff met with Senator John Thune on August 21 to talk about key issues impacting patients and physicians. We thanked him for his leadership on Medicare reform and telemedicine and discussed concerns about administrative burdens including prior authorization which harms patient care. Pictured with Senator Thune are SDSMA Director of Advocacy & Policy Justin Ohleen; AMA Alternate Delegate Robert Summerer, DO; SDSMA President Jen Tinguely, MD, MPH; AMA Delegate Mary Carpenter, MD; and SDSMA CEO Barbara Smith.



South Dakota Physician Well-Being Program Launches New Website and Video

The South Dakota Physician Well-Being Program has launched a new website, www.sdpwbp.org. Now, it's even easier to stay connected with the program.

Helping physicians quickly find resources and contact information, the new site also features a video, supporter recognition and testimonials. The South Dakota State Medical Association led the creation of the new site specifically to focus on making it easier to learn about the program and locate valuable information for participating.

South Dakota physicians are invited to explore the new site. With a commitment to offering confidential, supportive services and empowering physicians to move beyond burnout and lead more satisfying lives, the SDPWBP's new website is a way to help physicians reach resources for the support they need to address normal life difficulties and the challenges of



a medical career, reclaiming satisfaction in career and personal life.

The new website was funded through supporter contributions from Avera, COPIC, Monument Health, Sanford Health, SDSMA and Wellmark Blue Cross Blue Shield of South Dakota.

More About the South Dakota Physician Well-Being Program

The South Dakota Physician Well-Being Program is a confidential resource for all South Dakota-licensed physicians. **Call 605-275-4711 to reach an expert.**

- No insurance billing
- No medical record or reporting

In-person and remote consultation is available. Through confidential one-on-one sessions, individuals can receive well-being resources and help with:

- Mental health
- Preventing burnout
- Career fatigue
- Grief and loss
- Professional and personal life changes
- Financial stressors
- Stress and anxiety
- Depression
- Substance abuse
- Behavioral concerns
- Work/family balance
- Personal and family stressors
- Suicide prevention

Enroll in the Upcoming Cohort of the SDSMA Health Leadership Institute

Given the enormous changes now taking place in health and healthcare across the nation, there has never been a greater need for physician leadership.

The SDSMA Health Leadership Institute helps physicians balance life and work, sharpen their skills in practice management, and train for future leadership positions.

What is the Health Leadership Institute (HLI)? The HLI aims to prepare physicians to lead the transformation of health care by furthering their knowledge, skills and insights. Learn ways to bring the clinical perspective to decisions that are essential to the delivery of quality, efficient and cost-effective health care.

The HLI offers current and future leaders the opportunity to gain an in-depth knowledge of the role leadership plays in medicine, and prepares participants for roles within their practice location/health system, and greater professional development and leadership skills training.

The program consists of six monthly sessions held Friday evenings and Saturday mornings from October through March. Sessions 1 and 6 will be held in Sioux Falls. Sessions 2-5 will be virtual.



CME: Approximately 50 Category 1 CME credits

- Session 1 – Self Awareness - October 18-19, 2024
- Session 2 – Interpersonal Communications - November 15-16, 2024
- Session 3 – Teamwork and Collaboration - December 13-14, 2024
- Session 4 – Systems Awareness - January 24-25, 2025
- Session 5 – Wellness Centered Leadership - February 21-22, 2025
- Session 6 – Influencing Organization Change & Culture - March 21-22, 2025

How do I apply? Those interested in participating may contact Justin Ohleen at 605-336-1965 or johleen@sdsma.org.

Lifestyle Medicine and Food as Medicine Essentials

Physicians can register free of charge for "Lifestyle Medicine and Food as Medicine Essentials," a 5.5-hr accredited online CME/CE course that introduces physicians to the therapeutic use of lifestyle medicine. Find the link to register at www.portal.lifestylemedicine.org/ACLM and click "Free CME."

Lifestyle modification is often listed as the first-line approach in chronic care guidelines. Lifestyle medicine addresses the root cause of most chronic

disease and is shown to improve patient outcomes, reduce the major drivers of healthcare costs in the US, and even reignite your passion for healing. The webinar is provided by the American College of Lifestyle Medicine, which is offering 200,000 complimentary registrations for physicians and other healthcare professionals across the U.S. in support of the White House Conference on Hunger, Nutrition and Health.

Indigenous and Integrative Health Summit

Registration is open for the South Dakota Department of Health's Indigenous and Integrative Health Summit. This event will take place on September 24 in Oacoma, and is intended to create a bridge between western

medicine, traditional healing practices, and integrative health approaches. Registration information and overviews of keynote speakers can be found at <https://doh.sd.gov/topics/american-indian-health/>.



South Dakota Physician Well-Being Program

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NO medical record or reporting.



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for physicians and medical students coping with:

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Board News is a monthly feature sponsored by the South Dakota Board of Medical and Osteopathic Examiners. For more information, contact the Board at SDBMOE@state.sd.us or write to SDBMOE, 101 N. Main Avenue, Suite 301, Sioux Falls, SD 57104.



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