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# South Dakota medicine

THE JOURNAL OF THE SOUTH DAKOTA STATE MEDICAL ASSOCIATION

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Photo by Theresa Campbell, MD

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# Crossing Bridges Before You Come to Them: Anticipating the Uneven Path Toward Clinical Kindness

Ann Cook, PhD; and Jerome W. Freeman, MD, FACP

The adage "don't cross the bridge until you come to it" has long been part of American folklore. Henry Wadsworth Longfellow refers to the term in his long narrative poem "Golden Legend" (1851). But societal truisms aside, there are times when anticipating negative consequences or behaviors is helpful. One may feel less blindsided, less disoriented. Our faculty believe this to be the case when teaching medical students about the importance of kindness in clinical medicine, while also preparing them for the reality that they will encounter examples of unkind behavior.

Institutional policies as well as the behavior of individuals may play an adverse role. Arguably, the unkindness medical students experience may undermine their well-being, playing a significant role in the frustration and "burn out" these future clinicians may experience. Alerting students to potential stressors and negativity they will likely encounter may, in effect, help students learn to "cross those bridges" in an anticipatory manner that supports their future careers and satisfaction in practice.

Our faculty emphasizes to students that kind behavior is an important part of attaining wisdom. Unlike some topics such as professionalism and resiliency which students may critique, wisdom is almost universally regarded as a crucial skill in medicine. A discussion of kindness as an element of wisdom begins with lectures during Pillar 1 and is part of the online *Becoming: Clinical Ethics, Patient Care, Well-Being* course that all students take during Pillar 2. This linkage between kindness and wisdom is also a major theme in the various elective ethics courses that are available for Pillar 3 students. Throughout training, students are also taught that kindness embodies a level of engagement, a willingness to move beyond personal, sometimes passive feelings of compassion and empathy to action. At SSOM, faculty members carefully emphasize that kindness is action—*what* we do and *how* we do it.

A prior essay in *South Dakota Medicine* postulated that students view kindness as four distinct domains: (1) the kindness displayed by attending physicians to students and patients; (2) the kindness offered by patients who agree to let students participate in their care; (3) the kindness that students offer to the patients they encounter; (4) the kindness students extend to each other.[1] In the online dialogue between students in their Pillar 2 *Becoming* course, students regularly comment on the importance of each of these domains. They consistently note instances when kindness is lacking. They also allude to the moral distress they experience when kindness is compromised and institutional factors inhibit a corrective response. Students' comments underscore the extent to which they yearn for kindness. When they recognize instances of unkindness, students seek guidance for effective remediation. This awareness suggests that students who learn to embrace the reality and practicality of kindness have learned to value its utility.

But there is an important caveat. While kindness can be modeled and taught as an attribute that students should adopt, it is less clear how kindness can be enforced as an organizational value. Some researchers have suggested that an erosion of values like kindness and empathy occurs during the medical education process. A study by Haidet found that the attitudes of medical students change as they progressed from their first year to their fourth year.[2] This erosion of kindness may continue as physicians enter practice. Healthcare clinics and institutions depend on a wide variety of clinicians and support staff who inevitably have varying degrees of appreciation, understanding and acceptance of kindness. The impacts linked to experiences of unkindness can be considerable. Research continues to suggest that it takes at least three positive interactions to outweigh a negative interaction. Some studies demonstrate that even more positive interactions are required (five to one and even seven to one ratios) to offset a negative experience and achieve and maintain a healthy and productive response.[3,4]

Our faculty believes that acknowledging and discussing times when kindness is lacking is not unduly pessimistic or cynical, but is a recognition that negative behaviors do occur in the diverse realm of healthcare. Even when an institution might champion the ideal of kindness, individual employee

motivations to act kindly may vary. If an institution was to embark on a global plan to ensure universally kind behavior, the project would almost certainly prove to be fiscally and socially impractical. Especially given the tight budget margins most healthcare institutions are experiencing, the allocation of extensive resources to enforce kind behavior as a norm seems unlikely.

This somewhat gloomy prediction is not meant to discourage a concentrated focus on kind behavior. Rather, this observation is meant to emphasize that kindness must be learned and adopted on an individual level, not by administrative decree. The practice of kindness requires personal vigilance. Importantly while healthcare institutions may not succeed in achieving a universal adherence to kindness, academic institutions should feel particularly empowered to structure student experiences that highlight and reinforce kind behavior as a key component of good patient care.

USD Sanford School of Medicine has made kindness the central focus of its current strategic plan. As SSOM works to optimally prepare students for a future in medicine, setting realistic expectations is essential. Most of our medical students will receive residency training and subsequently practice in some type of healthcare institution. These students will likely need to navigate difficult and sometimes adversarial terrain within their clinical practice settings. They should understand that even when institutions present barriers to kindness, individuals still can and should be kind. Orienting students toward a focus on wisdom and an understanding of potential pitfalls in institutional medicine may enable them to successfully "cross bridges before they come to them". Tools students acquire may help them confidently provide effective patient care and maintain personal well-being, even in challenging situations. Students who understand and adopt kindness as their motivating orientation will be well-positioned to critique and improve the healthcare institutions they ultimately join. They will be better physicians.

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# American Medical Association Annual Meeting: Advocacy Progress on Numerous Public Health Priorities

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

If given the choice, would you want to see how a hot dog is made? Perhaps some of you would, but I would bet the majority of us are happy to avoid that particular experience and would rather simply enjoy the taste of a grilled hot dog on a warm summer night. This was a reference used at the recent Annual Meeting of the American Medical Association (AMA) House of Delegates that I was fortunate enough to take part in in early June in Chicago, home of deep dish pizza and the infamous Chicago dog. I attended the meeting with our outstanding state delegation that included Mary Carpenter, MD (delegate), Rob Allison, MD (delegate), and Robert Summerer, DO (alternate delegate). Barb Smith also represented the SDSMA in her role as CEO. The meeting highlighted the work that happens "behind the scenes" and is a wonderful example of dedicated professionals working tirelessly over five days to craft, mold and vote on the policies and positions that AMA holds and carries out.

The work actually began weeks before the actual meeting when I received a 270-page document containing multiple resolutions and policies that were related to public health efforts as that was the committee I was assigned to. Each participant of our Chicago delegation was assigned to a different committee, and we met with other delegates, alternate delegates and medical association staff from other Midwest states that make up the North Central Medical Conference (NCMC) to talk though all the different resolutions, policies and decided what our position would be on those policies when the House of Delegates met in Chicago. This truly was the start of the "sausage making" process and it was fascinating to watch and be a part of.

The House of Delegates is the legislative and policy-making body of the AMA. State medical associations (or, in our case with the small size of our state, banding together with other small Midwest states to make up the NCMC) and national medical specialty societies are represented in the House of Delegates along with AMA sections, national societies such as the American Medical Women's Association, professional interest medical associations and the federal services, including the Public Health Service. The House of Delegates is a mighty group of professionals who get through an inordinate amount of work during their time together and the result is what we see the AMA fighting for in Washington and across the U.S.

Key priorities for the AMA include fixing the prior authorization issue, reforming the Medicare payment system, fighting scope creep, making technology work for physicians (including both artificial intelligence implementation and EHR adoption and usability), and reducing physician burnout. These are not new issues and many of them have been top priorities of the AMA for many years. Here in South Dakota, we are certainly no stranger to the scope creep issue having successfully fought back legislation aimed at giving physician assistants independent practitioner status. We have certainly benefited from the support of the AMA on this particular issue and we will continue to rely on their support as scope creep will almost certainly be something we see again this coming legislative season. Read more about the highlights of the meeting in the Member News section of this issue.

One question I often hear from prospective members regarding membership in the AMA or SDSMA is why it matters or is it worth the money. My answer is how can I afford not to support them? Decisions are being made in regard to how I am told to practice, and these decisions are often made by people who have no knowledge of medical practice whatsoever. As a single provider and constituent, I do not have the time or energy to call or write on every piece of legislation that might impact my practice. But I find comfort in the fact that our SDSMA lobbyists work so hard for us in Pierre. I also know that the AMA is a formidable player at the national level as they craft legislation and guide governing bodies in the direction that will positively impact physicians and our patients. As members of the AMA and SDSMA, we are given the opportunity to be a part of that process which may be a bit chaotic and overwhelming at times. So, while not everyone will want to see how that hot dog is made, you do want to be the one putting in the order. And in Chicago, the hot dog reigns supreme.

# PASSING ON THE SPIRIT OF GENEROSITY IN A TAX SMART WAY

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CALEB BROWN, CFP®, Lead Advisor

As financial advisors we are privileged to help our clients think through and facilitate giving strategies to the organizations and people they care about. My observation is that most people have no problem giving to loved ones (family and friends) during life and at death. I believe giving to charities (501c3 organizations) is a little more challenging for people. It's understandable. You might feel like the money is going to overhead expenses or you have less control over what they might do with the money. You might not be confident in your own financial situation, or you are still working on other goals before you start giving money away to charities.

If you are giving to charities now or plan to in the future, you may possess the "Spirit of Generosity." This is a belief that giving some money to charitable organizations is of more value than spending it on yourself. There is no shortage of great organizations that can benefit from your generosity. However, what I want to focus on is this Spirit of Generosity. How do you pass that "Spirit of Generosity" on to your children and/or grandchildren? I've worked with many clients who have helped their children understand the financial basics of saving, investing, and living within their means but only a few who have passed the Spirit of Generosity on to the next generation. Of the clients who do give to charities I can't think of one that wouldn't want their children or grandchildren to continue the Spirit of Generosity. But it's not that easy. Or is it?

In "A Christmas Carol" Ebenezer Scrooge receives the gift of being a fly on the wall during different settings of his life; past, present, future. As an experiment, go to the future when you have passed away and are watching your family gather at Christmas. Imagine them sitting around the room discussing charities that have impacted them or people they know the previous year. They talk about the way Mom and Dad modeled the Spirit of Generosity by giving to specific organizations. In the next scene, your family is at the computer giving money to those organizations. That's the moment of knowing your "Spirit of Generosity" transferred to the next generation. If that sounds appealing, let's consider how you can make that happen.

Many people have IRA or pre-tax 401(k) accounts. Until the SECURE Act of 2019, passing those accounts to your family at death was straightforward and tax friendly. Since that bill was enacted into law, those accounts have become far less tax friendly to inherit. Most non-spouses that inherit IRAs or pre-tax 401(k)s, your kids, for instance, will have 10 years to fully distribute the account and pay the taxes that go along with the distribution. The government taxes these distributions at ordinary income tax rates. Most people tend to inherit funds in their 50s and 60s, which coincides with their prime earning years. So, being forced to distribute money from an Inherited IRA means even higher taxes! Contrary to all of the above, giving IRA dollars to a qualified 501c3 is a tax-free transaction. That means that no one pays taxes, ever! You don't pay taxes as the dollars go in. You don't pay as the values grow. And no one will pay taxes when the money comes out. That is an incredible deal.

We often pair gifts from an IRA with a Donor Advised Fund. What's a Donor Advised Fund (DAF)? Simply put, it's a separate account for your giving. It is a qualified 501c3 charitable organization, and you can direct what charities ultimately benefit. You can name your DAF as a beneficiary of your IRA or pre-tax 401k accounts. At death, the money would flow through to your DAF tax-free, and this would create a pool for your heirs to have the "ghost of Christmas future" experience. This doesn't have to be a big amount either. Shaving 5%-10% of those accounts to your giving account will not likely impact your heirs much, and it will save them tax because they must distribute the accounts within ten years. You can even open a Donor Advised Fund and simply label it as a testamentary fund, which means it will be funded after you pass away.

I encourage you to have a conversation with your Foster Group Financial Advisor to see how much your heirs might inherit in IRA and pre-tax 401(k) funds. Then, consider testing out what it would look like if a portion of those accounts go to a DAF. Also, if you were to make a provision like this, we encourage you to talk with your family about how this decision is connected to continuing the Spirit of Generosity.

SCAN ME

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# Substance Use Disorder in Adults with ADHD in South Dakota

Connor McMahon, MD; William Schweinle PhD; and Vivek Anand, MD

**Abstract**

*Objective*: Attention-deficit hyperactivity disorder (ADHD) increases the risk for comorbid psychiatric and substance use disorders. This study examined the prevalence of ADHD in residential addiction treatment and the prevalence of monosubstance, comorbid substance, and polysubstance use disorders (PUD) as a function of ADHD status.

*Method*: All adults admitted to residential substance use disorder treatment center in South Dakota during November 2021 to June 2022 were included (N= 55). The participants underwent a clinical interview and objective assessment to determine ADHD status. The participants were also administered ADHD questionnaire developed by investigators to assess ADHD history and treatment. SAS statistical software using an $\alpha$level of 0.05 was used for all analyses.

*Results*: Almost half, 25 of the total 55 participants, had ADHD (45%). A quarter (n=14) of participants were diagnosed with ADHD during childhood. A fifth (n=11) of participants were diagnosed with ADHD during this study. Thirty participants (54%) were not found to have ADHD. A majority of ADHD patients (n=21; 84%) were diagnosed with PUD. Participants with ADHD had a higher prevalence of PUD (p=0.054) compared to participants without ADHD. Approximately a quarter of patients with alcohol use disorder and three-quarters of patients with methamphetamine use disorder had ADHD.

*Conclusions*: ADHD and substance use disorders have notable comorbidity. This study demonstrates a high prevalence of ADHD in populations with substance use disorder. The presence of ADHD may be a risk factor for PUD.

## Background

Attention-deficit hyperactivity disorder (ADHD) is a highly prevalent psychiatric disorder affecting approximately 9.8% of children between the ages of 3-17 years in the U.S.[1] The adult form of ADHD additionally occurs in up to 5% of the general adult population.[2,3] Because of the notable prevalence of ADHD, it is vital that any comorbidities associated with this disorder are carefully examined, screened, and appropriate interventions including prevention and treatment be instituted to prevent associated morbidity and mortality. The most frequent comorbid psychopathologies include mood and anxiety disorders, substance use disorders (SUD), and personality disorders. Substance use disorders are possibly the most common comorbid condition with ADHD, with the use of tobacco, cannabis, alcohol, and cocaine being notable within this population.[4] Substance use is approximately twice as common in individuals with ADHD compared to the general population.[5] Studies indicate that 15-20% of adolescents and young adults with ADHD have a concurrent SUD. Comorbid ADHD and substance use can be present in up to one of every four patients with substance-related disorders.[3,6]

The association between ADHD and SUD seems to be bidirectional, and partly relates to behavioral characteristics such as novelty-seeking or impulsivity and attempts to self-medicate ADHD symptoms. In addition to behavioral correlates, it is speculated that decreased executive/inhibitory functioning with ADHD and differential functioning in the limbic and reward systems may contribute to the increased risk of substance abuse disorder.[7] Other theoretical explanations include a possible genetic pathway between the two disorders and the possibility of self-medication via substances of abuse.[8]

Comorbid ADHD and SUD have been shown to increase the risk of mood and anxiety disorders. In addition to their respective comorbidities, studies indicate that ADHD increases risk of substance use, precipitates earlier onset of

experimentation with substances, progression to substance use disorders, suicide attempts, and lead to adverse psychiatric outcomes leading to hospitalizations, while also lowering odds of treatment adherence and abstinence from substance use.[9] Furthermore, frequently associated social determinants of mental health along with SUD related impairment in daily living, as well as interpersonal and emotional distress among ADHD patients increase substance use related cravings.[6,10] Owing to the adverse occupational, recreational, social, interpersonal, psychological, and physical outcomes related to comorbid ADHD and SUD, it is important to have regional epidemiological data to inform appropriate preventative efforts, screening and treatment interventions.

### Objective

This study aims to provide regional data to compare prevalence of SUD in relation to ADHD status to further inform the complex and bidirectional association between SUD and ADHD. Additionally, better understanding of relationship between SUD and ADHD will help healthcare providers to better engage this subset of substance using population in an impactful way with timely screenings, risk assessments and appropriate therapeutic interventions. Additionally, determining whether certain types of substance use have a notable prevalence among patients with comorbid ADHD is clinically valuable data that can help guide treatment for patients with substance use. The aims of this study are as follows:

1. Investigate the prevalence of ADHD among adults admitted to residential treatment of substance use disorder.
2. Compare substance use history among patients with ADHD and patients without ADHD
3. Compare substance use history among patients with different ADHD statuses – no ADHD, ADHD diagnosed and treated during childhood, and ADHD diagnosed during adulthood.

### Methods

All adult patients admitted to inpatient SUD treatment setting during the months of November 2021 to June 2022 at a Midwest regional residential treatment center were included. The study was approved by the institutional review board. The participation in the study was voluntary. The decision to not participate did not affect treatment or any other outcomes related to their admission to residential addiction treatment. Appropriate consents were taken from the participants by the attending provider. All patients were clinically evaluated by a board-certified addiction medicine specialist and collateral information was obtained from family members (with consent) and residential staff during the course of patient's stay. As a part of ADHD evaluation, all patients were given a written Wender Utah ADHD rating scale and an ADHD history questionnaire approximately 14 days following the time of admission to residential addiction treatment. Completing these forms required approximately 10 minutes of time, however participants were given as much time as required to complete these forms; and incomplete forms were excluded from the final results. Data were transferred electronically to Microsoft Excel for data management, and all data collection was re-checked for accuracy during the scoring and recording stages of data collection. The Wender Utah ADHD rating scale is used to retrospectively screen for ADHD in adult patients based on the recall of childhood behaviors.[11] All patients were administered Wender-Utah ADHD rating scale per the instructions provided by the attending physician. A cutoff score of 46 was used to determine a positive score in the presence of ADHD. This score has an associated sensitivity of 86% in determining the presence of ADHD as well as a specificity 99% in determining participants without ADHD.[11] Altogether, the clinical interview was diagnostic of ADHD and was supported by the Wender Utah assessment.

A 14 item ADHD history questionnaire was developed and administered by the authors of this study (Table 1) along with the clinical interview to elucidate childhood ADHD and treatment status. This questionnaire was piloted by this study and serves the purpose of collecting historical data. The data from this questionnaire was not used for diagnostics. Substance use history was self-reported by participants during patient intake interview and objective assessments. SUD were then categorized into a specific mono-substance use disorder, comorbid substance (two substances) use disorder, or polysubstance (3 or more substances) use disorder. Statistical analysis was completed using SAS statistical software. Statistical significance was set with an alpha level of 0.05. Differences in the prevalence of SUD as a function of ADHD status were explored and compared.

**Table 1. Demographic data for the study group.**

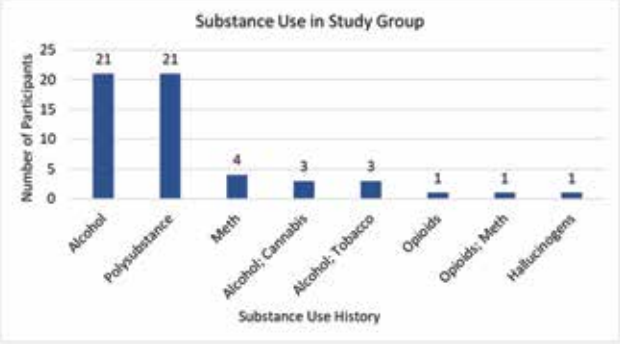
| Demographic data | | | | |
|---|---|---|---|---|
| Gender | | | Age (years) | |
| Gender | Total | % | Lowest | 20 |
| Male | 34 | 62% | Highest | 63 |
| Female | 19 | 35% | Mean | 41.1 |
| No gender reported | 2 | 4% | Median | 41 |

## Results

In total, 55 patients participated in this cross-sectional study. The demographics of this study was 61.8% male (n=34) and 34.5% female (n=19), with 3.6% of participants not identifying a gender (n=2). The mean participant age was 41.1 years, and the median age was 41 years. Demographic data is shown in Table 1.

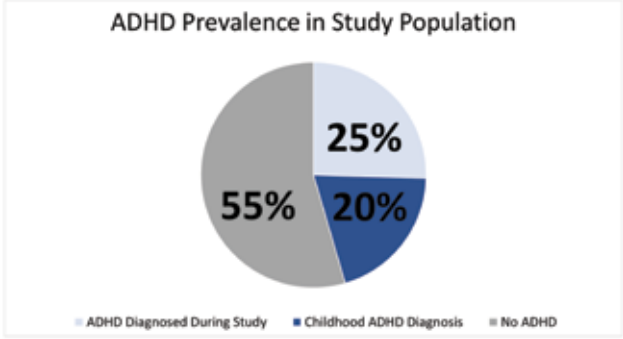
The most common substance use disorder diagnoses among participants were alcohol use disorder (n=21) and polysubstance use disorders (n=21). Among the participants with polysubstance use disorder, over half of polysubstance users consisted of cannabis, alcohol, methamphetamine, or cocaine. Fewer participants reported non-alcohol monosubstance use disorder or comorbid substance use disorders (Figure 1). Four patients were diagnosed with methamphetamine use disorder only. Most patients with comorbid SUD included alcohol use disorder as one of the two disorders. One participant each reported history indicated of opioid and hallucinogen use disorder.

**Figure 1. Number of participants reporting substance use history in this study group. The number of participants reporting a history of each type of substance use is shown as bars with the number above the bar denoting the exact number of participants responding with that type of substance.**



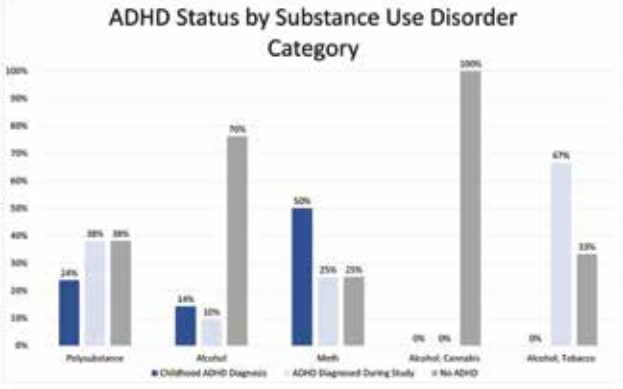

The overall prevalence of ADHD was 45% (or 25 out of the 55 participants) as determined by positive Wender Utah ADHD scores, childhood history, clinical interview and presentation during their residential treatment. Of these 25 participants with ADHD, 11 (44%) were diagnosed with ADHD during childhood. Within this group, 8 participants had a positive Wender Utah score when reassessed as part of this study. The remaining 3 participants with a childhood ADHD diagnosis had a negative Wender Utah score suggesting remission from ADHD symptoms over time. Fourteen participants were diagnosed with ADHD during the study using clinical interview, objective scales and collateral information obtained from family and residential staff (Figure 2).

**Figure 2. The ADHD status of participants categorized by age at diagnosis. Participants without ADHD were the majority, with 55% (n=30). Forty-five percent of participants had ADHD, with 20% being diagnosed in childhood (n=8) and 25% (n=14) being diagnosed during the course of our study.**




Methamphetamine use disorder (75% vs. 25%) followed by comorbid alcohol and tobacco use disorder (67% vs. 33%), and polysubstance use disorder (62% vs. 38%) were much higher among patients with ADHD compared to patients without ADHD diagnosis. A large majority of polysubstance use disorder patients (62%) had ADHD. Participants with ADHD (either during childhood or adulthood) had a nearly significant higher prevalence of polysubstance use disorder compared to participants without ADHD (p = 0.05). Among the polysubstance use disorder group, 24% were diagnosed with ADHD during childhood, and 38% were diagnosed with ADHD during this study (Figure 3).

**Figure 3. Clustered bar graph of ADHD prevalence by substance use group. Comorbid opioid/methamphetamine use (n=1) and opioid (n=1) and hallucinogen (n=1) mono-substance use disorder not shown due to small sample size.**




*Methamphetamine is abbreviated as "Meth."*

In contrast to polysubstance use disorder, alcohol use disorder alone incurred a lower comorbidity within ADHD group, but comorbid alcohol and tobacco use disorder were highly prevalent. Alcohol use disorder alone was more prevalent among patients without ADHD (n = 21; p = 0.01). Two of the

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three (67%) participants with comorbid alcohol and tobacco use were diagnosed with ADHD as adults during the study, with the remaining participant in this category not having ADHD, though none of these relationships showed statistical significance due to small sample sizes.

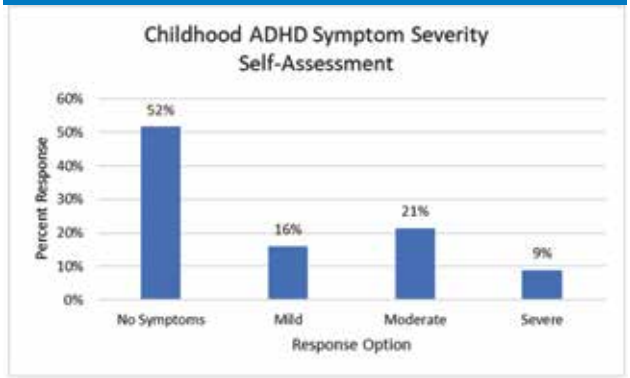
Among participants, methamphetamine users had the highest rate of ADHD. Three participants (75%) in the methamphetamine use group had ADHD, though this correlation is not significantly different (n=4; p = 0.21) presumably due to low sample size. The other monosubstance use disorder groups of opioid and hallucinogens each had one participant, neither of whom had ADHD. This study contained one participant with comorbid opioid and methamphetamine use disorder who was diagnosed with ADHD during our study.

The responses for ADHD questionnaire from all participants are displayed in Table 2. Per self-report, all participants who were diagnosed with ADHD during childhood received medication management for ADHD. Thirteen participants (24%) reported a current diagnosis of ADHD. Of the participants who reported childhood ADHD symptoms, the most reported functional impairment as "moderate" (Figure 4). Additionally, 27% of participants reported a family history of ADHD.

**Table 2. ADHD history questionnaire. Participants were asked to circle the response that best describes their history. The left column shows the ADHD history questionnaire question, and the responses are displayed in the middle and right columns. The amount of participants selecting the option is shown as a percentage (%) next to the respective option. IEP refers to an individualized educational plan as outlined by the Individuals with Disabilities Education Act which outlines specific goals and regular educational updates for an individual student.12 A 504 plan refers to section 504 of the U.S. Rehabilitation Act of 1973, which creates certain allowances for students with disabilities which impact their ability to learn or complete classroom activities.[13]**

| ADHD HISTORY QUESTIONNAIRE | Please circle your answer | | | |
|---|---|---|---|---|
| As a child, did you have Attention-deficit hyperactivity disorder (ADHD)? | YES (20%) | | NO (80%) | |
| Were you prescribed medications for ADHD? | YES (20%) | | NO (80%) | |
| If you have received medications for ADHD, did you consistently use your medications? | YES (16%) | | NO (84%) | |
| Do you have a current diagnosis of ADHD? | YES (24%) | | NO (76%) | |
| Do you have a family history of ADHD? | YES (27%) | | NO (73%) | |
| Have you used medications without prescription to treat your ADHD symptoms? | YES (16%) | | NO (84%) | |
| Did you ever abuse or misuse prescription stimulants like Adderall? | YES (27%) | | NO (73%) | |
| Did you struggle in school due to ADHD symptoms? | YES (36%) | | NO (64%) | |
| Did you need educational interventions (IEP or 504 plan) to help with learning? | YES (15%) | | NO (85%) | |
| Did you ever fail in school? | YES (36%) | | NO (64%) | |
| Did you drop out of school? | YES (16%) | | NO (84%) | |
| Did you pursue college? | YES (73%) | | NO (27%) | |
| Were you able to obtain a degree (associate, bachelor's, master's, or doctoral degrees)? | YES (21%) | | NO (79%) | |
| How severe were your ADHD symptoms? | No symptoms (52%) | Mild (17%) | Moderate (22%) | Severe (9%) |

**Figure 4. Bar graph demonstrating the percent response to the question: "How severe were your ADHD symptoms during childhood?" as presented in the ADHD history questionnaire. Participants were asked to circle the response that best described their ADHD symptoms during childhood. The selection provided on the questionnaire included "no symptoms" (n=28), "mild." (n=9), "moderate" (n=12), or "severe" (n=5). Response rates are shown as a percentage of the entire participant responses.**




Of the participants with a childhood diagnosis of ADHD (n=11), nine (82%) participants reported that they consistently used their ADHD medications during childhood. Participants in our study also reported a notable prevalence of prescription misuse, with 16% of participants using medications to treat the symptoms of ADHD without a prescription. A larger portion of patients (n= 27%) reported having misused or abused prescription stimulants.

The educational implications of ADHD symptoms were also assessed during this study. A larger proportion of respondents reported struggling in school due to ADHD symptoms than were diagnosed in childhood. Overall, 20 participants (36%) reported that ADHD symptoms impacted their schoolwork. Despite this, fewer patients (15%) received educational interventions such as an IEP or 504 Plan to accommodate ADHD. Overall, 20 participants (36%) reported failing in school, with 9 participants (16%) having dropped out of school. The majority of this study group had pursued college (n=40), though slightly more than half were able to obtain a college degree (n=21).

## Discussion

There has been a wide reported range of ADHD prevalence among SUD cohorts. The National comorbidity study reported an ADHD prevalence of 10.8% among adults with

SUD.[3] In adult SUD patients, the prevalence of ADHD is estimated at around 20%.[14,1516] A meta-analysis including 29 studies found the prevalence of ADHD to be around 23% among SUD patients.[6] The ADHD prevalence in our sample was much higher than the National comorbidity study, however, the results of this study are consistent with literature examining ADHD problems among SUD patients in therapeutic community or residential treatment programs. With a prevalence of 45%, the prevalence of ADHD in our study is similar to other studies of community addiction treatment centers which have determined a relative prevalence of ADHD ranging as high as 44-51%.[17,18] These data support screening for SUD in patients with ADHD and vice versa. Having attention deficit hyperactivity disorder increases odds of having a SUD and several studies have found that adults with ADHD are more likely than their peers without ADHD to develop a SUD. Additionally, the prevalence of ADHD in SUD patients is much higher than ADHD prevalence in the general community. In the general population, ADHD occurs in about 6% of children and adolescents and about 2.5% of adults.[19,20] Understanding the relationship between these two disorders may prove valuable in preventing associated morbidity and mortality.

While there is a notable correlation between these disorders, the relationship is also influenced by factors other than aforementioned psychiatric diagnoses. Other psychiatric variables, such as genetic predisposition, genetic polymorphisms, childhood temperament, environmental stressors, exposure to trauma and adverse childhood experiences, have also been predictive factors in the development of SUD.[18,21] Additionally, prenatal and environmental exposures to drug use are correlated with both SUD and ADHD.[22,23] ADHD and SUD belong to the more heritable psychiatric conditions and both twin and genome-wide association studies have indicated a strong shared heritability of ADHD and SUD suggesting that the frequent co-occurrence of these conditions has a shared biological background, with ADHD and SUD having a degree of heritability as high as 70-80% and 30-80%, respectively.[24,25,26] With these considerations, effective clinical practice requires screening for a multiplicity of potential concurrent biological factors and careful consideration of psychosocial context. It is vital, therefore, that further research be dedicated to examining the effects of early diagnosis and treatment of ADHD in reducing the prevalence of SUD.

The lower prevalence of alcohol use disorder among ADHD patients in our study was notable and contrary to the available literature. In our sample, 24% of alcohol use disorder patients had ADHD while the majority (76%) did not have a diagnosis of childhood ADHD and did not meet criteria for ADHD during subjective and objective evaluations. The current literature indicates that impulsive decisions and a maladaptive reward system among ADHD patients puts them at a higher risk of developing alcohol use disorder. It is estimated that up to 43% of patients with ADHD develop alcohol use disorder.[27] Among adults with AUD, ADHD occurs in about 20%, but is vastly under-recognized and under-treated.[27] The prevalence of alcohol use disorder among ADHD patients in our sample was similar to these estimates. While standalone alcohol use disorder was shown to have a smaller proportion of patients with ADHD compared to other mono- or polysubstance use disorder, it should be noted that the prevalence of ADHD in this group still exceeds the prevalence of ADHD in the general population.

The higher rates of polysubstance use disorder in patients with ADHD in our study is remarkable. The majority of the polysubstance users in this study had used stimulants such as methamphetamine, prescription stimulants, or cocaine. While this study cannot discern the contributing factors in the development of polysubstance use disorder or the substances used therein, the risk of self-medicating ADHD symptoms with these substances is a key aspect to consider in the context of developing SUD.[27] Biological mechanisms underlying stimulant use disorder among ADHD patients, in particular, should continue to be of research interest. Additionally, the prevalence of polysubstance use among patients who were treated for childhood ADHD was noteworthy. Both prescription stimulants and methamphetamine were commonly used by the polysubstance users in our study sample. Current prescription amphetamine derivatives used to treat ADHD symptoms exhibit a similar mechanism of action to methamphetamine by increasing dopamine release at the axon terminal.[28,29] The increasing rates of stimulant use disorder, particularly methamphetamine, is a rapidly growing public health issue in the midwestern U.S. particularly South Dakota leading to substantial morbidity and mortality.[30,31] Because of these significant public health implications, further research should be structured to examine the relationship between ADHD and methamphetamine use.

The prevention of adverse outcomes due to substance use is a high priority in decreasing life-years lost to substance use.[31] Of the participants in this study with ADHD, slightly less than half (44%) of those participants had been diagnosed

during childhood. While each of these participants reported having taken medications, medication adherence in both adults and children with ADHD is variable, with discontinuation ranging from 13.2% to 64%.[32] Further studies should consider treatment compliance and duration of adequate treatment in patients with comorbid ADHD and SUD.

Current research consistently demonstrates that treating ADHD reduces the risk of SUD as well as its associated morbidity and mortality. Despite the potential benefits, providers may be hesitant to prescribe stimulant-type medications to patients with a history or risk of substance abuse.[33] While these medications do pose the potential for misuse, ADHD pharmacotherapy does not increase the risk of SUD. [9,34] Previous research demonstrates that the use of stimulant medication or atomoxetine in adolescents and adults with ADHD reduces substance use related adverse events by 31-35%.[35] Further studies have demonstrated that ADHD pharmacotherapy significantly decreased the rate of SUD in both adults and children.[36,37] It is important, therefore, that early detection of ADHD could reasonably be partnered with substance use screening and preventative measures.

A key limitation with our study group is over representation of Caucasian and middle-to-upper socioeconomic status. The participants were able to access residential treatment for addiction, which can prove costly and difficult to find. As an additional socioeconomic consideration, the majority of participants had pursued some college. Further studies should include other social economic statuses, varied educational attainment, public health insurance beneficiaries and other diverse populations who have marked disparity in access to care. Another limitation of this study was the self-reporting of substance use history, which introduces recall bias. Lastly, it should be noted that substance use may vary between geographical regions, so the generalizability of this study outside of midwestern U.S. should be carefully considered.

## Conclusion

ADHD and SUD have notable comorbidity. This study, among other similar studies, demonstrates a high prevalence of ADHD in populations with SUD. The presence of ADHD may influence what substances patients use. The disparity in patients diagnosed and treated for ADHD during childhood and those having ADHD demonstrates a deficit in effective childhood ADHD screening. As such, effective screening for ADHD may be a useful tool in reducing the risk of developing SUD in a population underdiagnosed with ADHD. On the other hand, adequate education and screening of substance use could be a useful strategy in preventing development of SUD in patients with ADHD.

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# Early Sepsis Response System Does Not Correlate with Pediatric Early Warning Score in Sepsis Recognition

Jody Huber, MD, FAAP; Shelley Feng, MD; Amber Veldman, MD; Ashley Sandeen, DO, FAAP; David Sturdevant, MS; and Gokhan Olgun, MD

**Abstract**

Sepsis is a leading cause of pediatric morbidity and mortality worldwide with early recognition and management improving patient outcomes. Early recognition warning systems, utilizing the electronic medical record (EMR), are recommended for children's hospitals. Validated pediatric early warning score (PEWS) recognize hospitalized children at risk for worsening and need for higher level of care. The goal of this study was to develop a novel pediatric sepsis early response warning system and compare this tool with the existing generic PEWS system in recognizing sepsis. A novel early sepsis warning system was integrated into the EMR of a tertiary pediatric children's hospital. In patients meeting criteria a best practice alert (BPA) triggers and children with a sepsis BPA trigger were evaluated from December, 2018 through May, 2020. BPA data was analyzed and identified children meeting sepsis criteria. Subjects identified as having sepsis were then correlated with PEWS scores at the time of the BPA. The BPA triggered in 736 pediatric subjects, with 181 in the emergency department, 275 in the pediatric inpatient floor and 280 in the pediatric intensive care unit. Pediatric sepsis criteria identified 524 of 736 (71%) as having sepsis. PEWS scores identified only 66 (13%) of the 524 subjects who had sepsis. Implementation of a sepsis trigger tool into EMR is feasible. Best practice alerts identify subjects with early sepsis and can be implemented to electronic medical record.

## Introduction

Pediatric sepsis is a leading cause of mortality and morbidity worldwide. Pediatric severe sepsis has a global prevalence of 8.2% and mortality ranging 4-25%.[1-3] Bundled care models focusing on early recognition and management of sepsis are commonly deployed, showing improved sepsis-related morbidity and mortality.[4,5] The Surviving Sepsis Campaign recommended implementation of systematic screening for timely recognition of septic shock or other sepsis-related organ dysfunction but does not make a recommendation regarding a particular sepsis screening tool.[6] There are different successfully implemented tools utilizing manual data or electronic medical record (EMR) for patients hospitalized or in emergency department (ED). [5,7,8]

Pediatric early warning score (PEWS) systems are validated tools commonly utilized in children's hospitals to recognize children at risk for decompensation and need for a higher level of care. Children's hospitals commonly use a PEWS system to trigger a rapid response team for further patient evaluation and need for a higher level of care.[9] There is concern for having multiple recognition tools and whether these tools could be combined or use PEWS rather than implementing a new sepsis screening tool.

The aim of this study was to implement a pediatric sepsis early warning system at our institution, executed as a sepsis best practice alert (BPA) in the EMR, and correlate accuracy via expert chart review, utilizing current pediatric sepsis guidelines.[10] The secondary goal was to compare the sepsis BPA to an existing, validated PEWS system, already implemented at our institution.[11]

## Methods

This was a cohort study with a retrospective chart review of children in whom a sepsis trigger tool, labeled as a BPA, triggered in the EMR. This project received IRB approval and consent for the study was waived by the IRB.

In 2018, our children's hospital created pediatric sepsis early warning tool. This tool, embedded as a BPA in the hospital EMR, includes nine criteria pertaining to the physical exam and health history (Table 1). These criteria are similar to recommendations from the American College of Critical Care Medicine in 2017.[12] The BPA fires when three or more

**Table 1. Sepsis BPA components. BPA fires if 3 or more of the 9 components are true within the last 6 hours (temperature is required to be 1 of the criteria).**

| | |
|---|---|
| Temperature | <36°C or>38°C |
| Heart rate | Age specific abnormal values per PALS guidelines |
| Respiratory rate | Age specific abnormal values per PALS guidelines |
| Systolic blood pressure | Age specific abnormal values per PALS guidelines |
| Peripheral pulses | Absent<br>Bounding<br>Diminished<br>Thready<br>Weak |
| Capillary refill | Absent<br>Greater than 3 seconds<br>Greater than 2 seconds (pediatric) |
| Skin assessment condition and temperature | Ashen<br>Dusky<br>Flushed<br>Gray<br>Mottled<br>Ruddy<br>Clammy<br>Cool |
| Level of consciousness/mental status | Agitated<br>Confused<br>Drowsy<br>Irritable<br>Inappropriate<br>Lethargic<br>Restless |
| Problem list | Malignancy<br>Asplenia<br>Bone marrow transplant<br>Presence of central line<br>Solid organ transplant<br>Severe cerebral palsy<br>Immunodeficiency, immunocompromised status or immunosuppression |

of the recognition criteria are met over a six-hour period. Temperature abnormality was required as a criterion due to its outsized role in pediatric SIRS and sepsis criteria. The alert will fire again after a 12-hour refractory period if criteria continue to be met.

All medical records of children in whom the sepsis BPA fired were reviewed from December 2018 through April 2020. Inclusion criteria included children aged 0 to 18 years of age in whom the sepsis trigger tool fired in the EMR. These subjects were located as patients in the ED, pediatric inpatient floor and pediatric intensive care unit (PICU). The BPA fired when a medical professional (nursing, physician, therapies, etc.) entered the EMR. There is a required response to the BPA with the following options: physician alerted, patient already being treated, no new or progressive symptoms of infection, defer to the primary team and surgery or trauma in the last 24 hours. When the option 'physician notified' was chosen, the physician was expected to evaluate the patient within 15 minutes. The physician determined the possibility of sepsis after examining the patient. If sepsis was a concern, an order set was utilized to order laboratory work, antibiotics, and a fluid bolus. A pediatric sepsis response team was also notified which included pediatric nursing staff with IV placement skills to provide prompt IV placement. If the patient was not determined to have sepsis, no further evaluation took place.

Data collected from these charts included age, gender, ethnicity, location of BPA firing (emergency department, inpatient floor, PICU), diagnosis of sepsis. Indications for BPA firing were also collected including temperature, heart rate, respiratory rate, systolic blood pressure, peripheral pulse strength, capillary refill time, skin color, level of consciousness

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**Table 2. SIRS and sepsis criteria.**

| | |
|---|---|
| Systemic inflammatory response syndrome(SIRS)* | ●Core temperature of >38.5°C or<36°C.<br>●Tachycardia, defined as a mean heart rate>2SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5- to 4-hr time period or for children<1 yr old: bradycardia, defined as a mean heart rate<10th percentile for age in the absence of external vagal stimulus,beta blocker drugs, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5-hr time period.<br>●Mean respiratory rate >2SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anesthesia.<br>●Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or>10% immature neutrophils. |
| Sepsis | SIRS in the presence of or as a result of suspected or proven infection. |

* The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count. Modified from Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics*. Pediatric Critical Care Medicine. 2005;6(1):2-8.

and preexisting conditions. Also collected were interventions including a fluid bolus, antibiotic administration, timing of antibiotics and lactic acid level, if measured. A diagnosis of sepsis was determined based upon two separate reviews by critical care physicians utilizing the 2005 pediatric sepsis definition[10] (Table 2). For cases with a split decision, a third critical care physician reviewed chart to determine sepsis diagnosis.

Our hospital utilizes a validated, nurse-triggered PEWS system for inpatient pediatric patients.[11] PEWS range from 0-7 and includes behavior, cardiovascular and respiratory scoring. Any patient with a score of 4 or above triggers a rapid response team for further assessment. For all subjects in whom the BPA alert triggered, we calculated PEWS scores at the time of the BPA for comparison.

Continuous variables were presented as means, standard deviations, median, and interquartile ranges as appropriate. Categorical values were presented as values and proportions. Chi square test was used for comparison of categorical values. A multinomial logistic regression analysis was conducted to investigate how effective the pediatric sepsis tool is at identifying sepsis. The predictor variables (binary values; normal vs. abnormal), gender, heart rate, respiratory rate, systolic blood pressure, peripheral pulse strength, capillary refill time, level of consciousness, presence of preexisting condition, and age were tested a priori to verify there were no violations of the assumption of the linearity of the logit. Odds ratios and 95% confidence levels were generated. Alpha level of 0.05 was chosen for statistical significance.

## Results

The sepsis BPA triggered in 736 subjects. Of those subjects, 380 were male and 356 were female (Table 3). Of the 736, 517 subjects were white, 122 Native American, 55 African American and 38 Hispanic or other ethnicities. In 181 subjects, the sepsis tool triggered in the ED; 275 on the pediatric inpatient floor and 280 in the PICU. Median age was 4 years. According to expert opinion based on current

**Table 3. Patient demographics and characteristics.**

| Patient characteristics | Value |
|---|---|
| **Age (years)** | 4 [1,12][a] |
| **Gender** | |
| *Male* | 380 (52%)[b] |
| *Female* | 356 (48%) |
| **Ethnicity** | |
| *Caucasian* | 517 (70%) |
| *American Indian* | 126 (17%) |
| *Other* | 93 (13%) |
| **Patient Location** | |
| *Emergency department* | 181 (25%) |
| *Floor* | 275 (37%) |
| *PICU* | 280 (38%) |
| **Patients with pre-existing conditions** | 233 (32%) |

[a] Interquartile range
[b] Percentile of total

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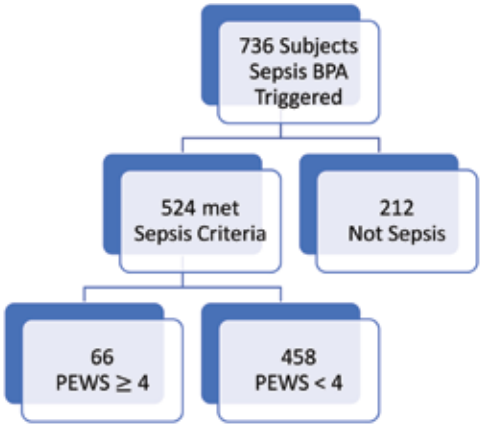
pediatric sepsis criteria, 524 of the 736 (71%) BPA activations were due to sepsis (Figure 1).

Of the 212 in whom did not have sepsis, etiologies of the triggers were identified. The most common false positive was erroneous temperature measurement. Inaccurately low measurements were found upon further chart review. Accidental and intentional overdose with anticholinergic or sympathomimetic medications accounted for other false positives with elevated temperature.

A logistic regression model was built with predictor values for elements of the BPA including gender, heart rate, respiratory rate, systolic blood pressure, peripheral pulse strength, capillary refill time, level of consciousness, presence of preexisting condition, and age. (Figure 2) Abnormal heart rate and systolic blood pressures were found to have contributed to the model. The odds of sepsis were 1.769 times higher with an abnormal heart rate versus normal heart rate [Exp (B) = 1.77, 95% CI (1.2, 2.61)]. The odds of sepsis were found to be 0.83 times lower with abnormal systolic blood pressure versus normal systolic blood pressure [Exp (B) = 0.21, 95% CI (0.11, 0.4)].

Figure 1. Results of sepsis trigger tool.



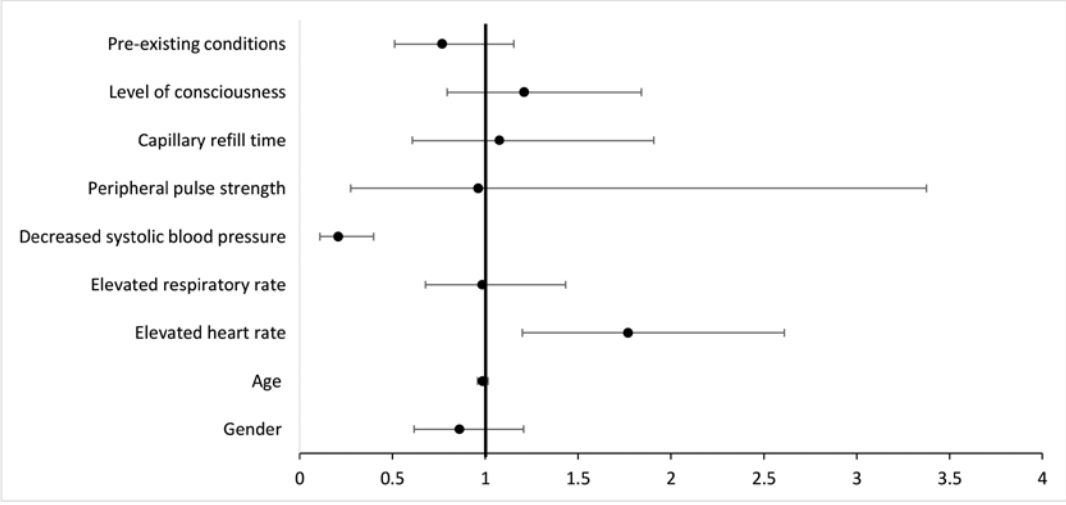

Subjects in whom the BPA triggered had a mean PEWS score of 2 (±1.98). Of those subjects in whom the BPA fired and were determined to have sepsis, 66 (13%) had a calculated PEWS 4. PEWS did not differentiate septic versus non-septic subjects (c2=0.43,p: 0.51).

## Discussion

Implementation of a characteristics-based electronic early sepsis warning system, including a combination of abnormal vital signs, physical examination findings, and preexisting conditions, is feasible. This early warning system accurately identified sepsis in 71% of subjects in this study.

Electronic alert systems offer the advantage of frequent, automated alerts that can combine vital signs, physical examination findings and clinical diagnosis. Also, these alerts do not rely on person to person conveyance of information and augment communication gaps within the care team.[13] Electronic alerts can contribute to alarm fatigue, which itself can contribute to poor patient outcomes and provider burnout.[14,15] There was a false positive rate of 29% in this current study, which upon further evaluation, suggests areas for improvement within the BPA. The most common etiology found was inaccurate temperature measurement, creating a quality improvement initiative for proper technique when measuring temperature. Intentional overdose with anticholinergics or sympathomimetics can cause similar symptoms to trigger the BPA. Our quality improvement team

Figure 2. BPA predictor values for sepsis.



is currently developing a correction to the tool to limit the false positive rate with re-evaluation planned in the future.

PEWS are a common tool utilized in children's hospitals as early recognition for a rapid response team evaluation or elevation to a higher level of care.[9] Although the EPOCH trial did not demonstrate a mortality benefit with implementation of an inpatient PEWS, other studies have shown improved timeliness of PICU transfer and shorter hospital length of stay.[16-18] Our hospital uses a validated, manual, inpatient PEWS tool.[11] In this study, a PEWS score ≥ than 4 (score that triggers a rapid response evaluation) was observed in 66 of 524 subjects (13%). Although this study was not designed to compare PEWS to the sepsis BPA, the sepsis specific warning system may be superior to general PEWS in detection of sepsis. This finding highlights the need for both the PEWS and early sepsis warning systems in children's hospitals.

Automated sepsis screening tools may be SIRS related or non-SIRS related.[13,19-21] Kurzcewski et al. implemented a SIRS-based early warning tool that required the presence of an abnormal white blood cell count or temperature and was able to show a shorter intervention time in the study group.[22] Similarly, we included abnormal temperature as a requirement for our BPA trigger. However, in addition to SIRS criteria, physical examination findings observed in septic shock such as peripheral pulse strength, capillary refill time, and level of consciousness have been included in this study as binary predictors (normal vs. abnormal). Although only heart rate and systolic blood pressures contributed to the model in our analysis (Figure 2), inclusion of those signs may help clinicians address and aggressively treat shock early in the disease process. Elevated heart rate increased the odds of sepsis in our model, which was expected. However, when grouped with low systolic blood pressure, elevated heart rate had a decreased odds of sepsis in our patient cohort. Although this finding was statistically significant, the effect was marginal.

There are limitations to this study. The data is from a single children's hospital and may not be generalizable at other institutions. Determination of pediatric sepsis heavily relies on SIRS criteria, which was shown to have low sensitivity and specificity in multiple studies.[23,24] Updated pediatric sepsis criteria, not using SIRS criteria or in addition to SIRS criteria could improve statistical analysis. The incidence of sepsis without septic shock or severe sepsis was unable to be determined by research methods to benchmark our findings. Due to this, the false negative rate was unable to be evaluated.

This study demonstrates successful implementation of a sepsis early warning system in a pediatric hospital. Within this warning system, elevated heart rate demonstrated the greatest odds of identifying sepsis. False positives are an area for future improvement. Best practice alerts can identify subjects with early sepsis and may be superior to PEWS at identifying sepsis.

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*Supplementary Figure, Pediatric Sepsis Early Response System, available at sdsma.org (member login).*

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# When Anticoagulation Matters: A Case of Large Left Atrial Thrombus After Left Atrial Appendage Ligation

Emmanuel Fohle, MD, MPH; Natale Wasef, MD; Filip Oleszak, MD; and Maria Stys, MD

**Abstract**

Atrial fibrillation (AF) is the most frequently encountered arrhythmia in the clinical practice and is associated with stroke. In clinical practice, CHAD2DS2-VASc score is used as a tool to decide whether anticoagulation is needed. In those patients with high bleeding risk or falls, surgical ligation of the left atrial appendage (LAA) or percutaneous closure devices are strategies used to mitigate these challenges. However, there is no guideline advising on what patient's specific factors should be considered in determining initiation or continuation of anticoagulation post LAA ligation. Herein, we report the case of a patient with surgical ligation who developed large atrial thrombus requiring emergent median sternotomy.

## Introduction

Oral anticoagulants (OAC) have been used for several years to reduce the risk of thrombus formation and stroke in patients with atrial fibrillation (AF). However, high bleeding risk/complications and nonadherence hinder their use. Surgical ligation of the left atrial appendage (LAA) or percutaneous closure devices are strategies used to mitigate the challenges of OAC.[1,2] Though there are guidelines for suture ligation of LAA at the time of cardiac surgery in patients with AF, there is no guideline advising on what patient's specific factors should be considered in determining initiation of anticoagulation post LAA ligation. Likewise, there is no screening for incomplete LAA closure following surgical intervention. We report a case of a patient with AF, bioprosthetic mitral valve, status post coronary artery bypass graft (CABG) and LAA ligation, who presented with near syncope and found to have a massive left atrial thrombus requiring urgent median sternotomy.

## Case

A 78-year-old female presented to the emergency department with generalized weakness/fatigue and near syncope. She has medical history notable for paroxysmal atrial fibrillation, severe mitral regurgitation status post 29 mm St. Jude Epic bioprosthesis, coronary artery disease status post bypass, status post LAA ligation, deep vein thrombosis status post IVC filter. Vitals were stable albeit bradycardia. Initial laboratory studies showed a normal complete blood count as well as chemistry panel. Troponin I was mildly elevated 0.014 (normal 0.000- 0.013 ng/mL), BNP 1,568 (normal 0-100 pg/mL). Chest X-ray showed enlarged cardiac silhouette with pulmonary vasculature congestion. Electrocardiogram (ECG) revealed atrial fibrillation (AF) with slow ventricular response (Figure 1). She was admitted and treated with IV diuretics. Transthoracic echocardiogram (TTE) showed left ventricular ejection fraction (LVEF) of 70-75%, severely dilated left atrium 74.17 ml/m$^2$ (normal <34 ml/m$^2$) with a fixed mass in the left atrial cavity attached to the left atrial wall suggestive of possible thrombus versus myxoma/tumors or vegetations (Figure 2). A bioprosthetic mitral valve was

Figure 1. ECG showing A-fib with slow ventricular response.

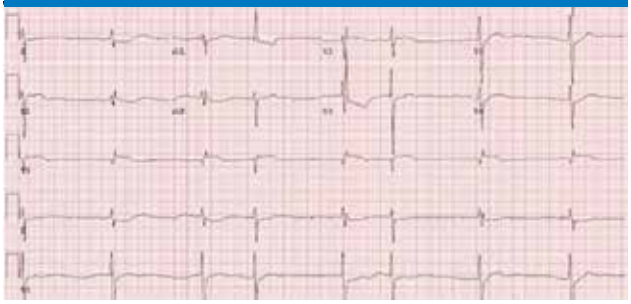

Figure 2. TTE showing left atrial thrombus.

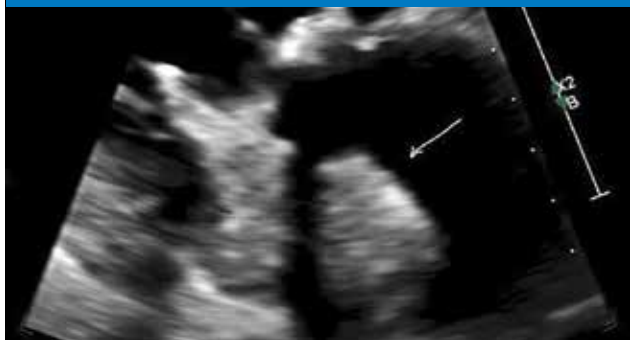

Figure 3. TEE showing left atrial thrombus.

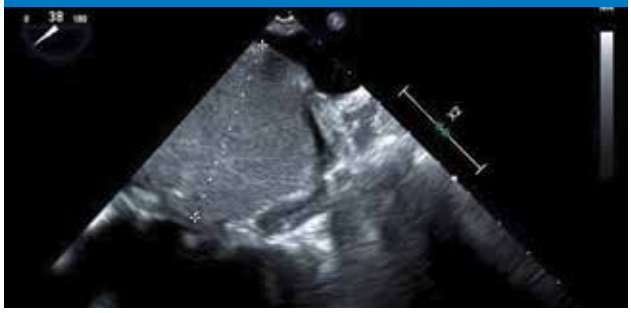

Figure 4. Resected left atrial thrombus.

in place with elevated gradient which was thought to be secondary to hyperdynamic circulation and some mild degree of valvular stenosis. The patient was systemically heparinized and underwent transesophageal echocardiogram (TEE) that confirmed a large 5 cm mass in the left atrium, mean gradient of 9 mmHg (heart rate [HR]= 86 bpm) and some communication with the left atrial appendage (Figure 3).

A multidisciplinary and patient centered discussion was held, and management options were discussed. These options included median sternotomy with possible repeat mitral valve replacement and extraction of the thrombus; IV thrombolytic therapy or systemic anticoagulation. Given the high risk for embolization with thrombolytics and given the size of the thrombus and its impact on the inflow of the left ventricle, urgent surgical extraction of the thrombus was pursued (Figure 4). In addition, she also had a repeat mitral valve replacement with 31 mm Abbott laboratories epic stented mitral valve bioprosthesis. However, re-ligation of the LAA was not attempted. The postoperative course was complicated by hypotension with multiorgan failure requiring escalating doses of inotropic and vasoactive agents. Given the amount and degree of organ system dysfunction, the patient's family elected for comfort care measures. Unfortunately, the patient expired 2 days after surgery.

## Discussion

The history of LAA occlusion or excision can be traced back to the mid-20th Century when cardiac surgery techniques were developed.[3] Because almost 91% of thrombi in nonvalvular AF tend to localize in LAA, there is a focus on occlusion or exclusion of the LAA for the prevention of embolic stroke alongside Maze procedure for the treatment of AF.[3,4] Current surgical techniques to exclude the LAA include resection, epicardial stapling, clip application, suture closure.[5] However, there have been multiple difficulties and mixed results from these surgical techniques.

To establish the prevalence of incomplete LAA ligation during mitral valve surgery, 50 patients underwent TEE post operation. Of these patients, 36% had incomplete LAA ligation on TEE testing and that 50% of those noted to have incomplete ligation had thrombus noted on follow up echocardiogram testing. Moreover, 22% had thromboembolic events at the time of echocardiogram assessment.[1] Another study evaluated 72 patients who underwent surgical LAA ligation in the setting of mitral valve surgery with postoperative assessment of LAA using computed tomography angiography (CTA). Incomplete surgical ligated LAA was noted in 24%. Ischemic stroke/systemic embolization occurred in 24% of patients with incomplete surgically ligated LAA as opposed to 2% in patients with closed LAA.[6] None of the patients who developed stroke or systemic embolization were receiving anticoagulation due to contraindication.

Incomplete surgical LAA ligation is a predictor of higher risk of development of ischemic stroke and systemic embolization.[6]

As shown in many studies, failure of LAA ligation is mostly derived from surgical technique rather than a gradual suture or staple dehiscence.[7] Incomplete occlusion carries a higher risk than no occlusion in relation to long-term thromboembolic events.[8] Prosthetic mitral valve material can limit the reach to the most distal edge of the LAA, leading to a large remnant.[9]

In our case, the patient had LAA ligation without maze procedure during coronary bypass and bioprosthetic MVR. The current guidelines by the Society of thoracic surgeons, LAA ligation during cardiac surgery is class IIa recommendation, whereas American College of cardiology/ American Heart Association recommends it as class IIb (Table 1).[10] Anticoagulation after bioprosthetic MVR is a class IIa recommendation for 3-6-months postoperative to minimize thrombus risk but there is a hospital variability on this practice. Our patient completed 3 months of anticoagulation

**Table 1. Summary of current clinical practice guidelines concerning surgical occlusion of the left atrial appendage.**

| Guideline | Recommendation | Class | Level of evidence |
|---|---|---|---|
| 2019 ACC/AHA/HRS Focused Update of the 2014 Guideline for the Management of Patients with AF | Surgical occlusion of the LAA may be considered in patients with AF undergoing cardiac surgery, as a component of the overall heart team approach to the management of AF | IIb | B (non-randomized) |
| STS 2017 Clinical Practice Guidelines for the Surgical Treatment of AF | 1. It is reasonable to perform LAA excision or exclusion in conjunction with surgical ablation for AF for longitudinal thromboembolic morbidity prevention. | IIa | C (limited data) |
| | 2. At the time of concomitant cardiac operations in patients with AF, it is reasonable to surgically manage the LAA for longitudinal thromboembolic morbidity prevention class IIA | IIa | C (expert opinion) |
| 2016 ESC/EACTS Guidelines for the Management of AF | Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery | IIb | B |

ACC – American College of Cardiology; AHA – American Heart Association; HRS – Heart Rhythm Society; AF – atrial fibrillation; EACTS – European Association of Cardio-thoracic Surgery; ESC – European Society of Cardiology; LAA – left atrial appendage; LAAO – left atrial appendage occlusion; STS – Society of Thoracic Surgeons

post bioprosthetic MVR. However, anticoagulation was discontinued soon after due to rectus sheath hematoma. She subsequently developed deep vein thrombosis and ended up having IVC filter due to bleeding risk.

The decision of timing and duration of anticoagulation for specific patients must be individualized given the mixed results with surgical LAA ligation and the lack of conventional consensus. It is this exact variability that results in marked differences within clinical practice and limits the utility of guidelines with respect to anticoagulation post LAA ligation. This patient had high risk factors that likely predisposed her for the formation of LA thrombus. These risk factors include the presence of AF, severely dilated LA, incomplete surgical LAA ligation, history of DVT. In retrospect, given these multiple risk factors, she may have benefited from close evaluation with TEE to guide decision regarding earlier systemic anticoagulation versus percutaneous LAA closure device implantation due to incomplete surgical ligation.

## Conclusion

Despite higher rate of unsuccessful surgical LAA closure, there is no consensus for the timing and duration for anticoagulation use. This case demonstrates continued risk despite surgical intervention. Decision for initiation or discontinuation of anticoagulation must be individualized considering thrombotic risk factors of the patient and careful review of the transesophageal echocardiogram should be carried out before interrupting oral anticoagulation.

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# Atypical Presentation of Severe Bullous Pemphigoid: A Case Report

Tinotenda ME Sekeramayi, MD; and Sara Ruter, MD

**Abstract**

Bullous pemphigoid (BP) is the most common autoimmune subepidermal blistering disorder. Typically, patients will present with tense bullae and intense generalized pruritus with a skin biopsy demonstrating subepidermal split with eosinophils and a direct immunofluorescence highlighting autoantibodies against the basement membrane zone. Prognosis varies, and treatment involves an assessment of the severity of disease to determine whether to initiate topical or systemic immunosuppressive agents. We present an atypical presentation of BP that presented as a 3-to-4-week duration of pruritic small vesicular lesions in the upper chest, scabbed circular lesions along the upper extremity and pinnas of bilateral ear. Initially thought to be herpes zoster infection initially treated with valacyclovir for a week following a prior concern of a concomitant superficial skin infection with cephalexin and prednisone. With no clinical improvement, tissue biopsy was performed that confirmed bullous pemphigoid and treatment with steroid taper, doxycycline, and triamcinolone acetonide 0.1% cream was started. The aim of this case report is to present an atypical presentation of BP and to highlight maintaining a high index of suspicion of BP in patients presenting with disseminated significantly pruritic lesions.

## Introduction

Bullous pemphigoid (BP) most commonly presents in elderly patients around ages 60 to 80 and is characterized by the presence of immunoglobulin G (IgG) autoantibodies specific for the hemidesmosomal bulbous pemphigoid antigens BP230 (BPAg1) and BP 180 (BPAg2).[1] A review article that investigates the role of BP antigen 2 (BP180) in the autoimmunity of BP noted that the structure and location of BP180 indicates that it acts as a core anchor protein that connects the intracellular and extracellular hemidesmosomal proteins and plays a key role in the pathogenesis of BP.[2] The exact role of bullous pemphigoid antigens in the pathogens is of bullous pemphigoid is not entirely clear in the literature albeit the pathophysiology is due to IgG autoantibodies binding at the basement membrane leads to complement activation and inflammatory cells that likely release proteases that degrade the hemidesmosomal proteins and lead to blister formation. Of note, drug-induced bullous pemphigoid can occur up to three months after starting the medication and includes, but not limited to: furosemide, spironolactone, NSAIDs, amoxicillin, PD-1/PD-L1 inhibitors, gliptins, and TNF-alpha inhibitors.[3] We present a case of a patient on furosemide for diastolic heart failure that had been prescribed in 2018 and well-tolerated. With no other known inciting medications.

## Case Presentation

An 81-year-old female with a past medical history of diastolic heart failure, late onset Alzheimer's disease, primary Parkinsonism, and hypothyroidism presented to clinic for an emergency department (ED) visit follow-up for a pruritic, disseminated vesicular rash. This rash was described by the patient as "small blisters" that "popped" and drained clear fluid and upon presentation to an outside clinic was started on cephalexin and prednisone. The rash did not improve so she presented three weeks later to the ED following diagnosis of herpes zoster (shingles) was prescribed valacyclovir 1,000 mg three times a day for a week and hydroxyzine four times a day for pruritus.

The pruritic nature of the rash improved but she continued to develop larger, tense blisters. This was complicated by a difficult history of events given patient's underlying dementia, but she continued to deny severe pain, pain rated at a 5/10, in the setting of bilateral ear pinnacle, bilateral shoulders, and left upper chest involvement of intact blisters with erythematous bases and scabbing and drying of other

Figure 1. Intact blisters with erythematous bases and scabbing and drying of other lesions in that same distribution.

lesions in that same distribution. The initial plan was to continue the course of valacyclovir with an alternative plan to biopsy the involved skin if no improvement in two weeks.

With no improvement in blistering lesions, there was higher suspicion for bullous pemphigoid although there was no obvious medication outside of daily furosemide (started in 2018 for diastolic heart failure) that could induce BP. Additional clobetasol was prescribed and then the case was discussed with a dermatologist who reviewed photos and agreed with plan for biopsy.

The biopsy obtained revealed complete loss of the epidermis with superficial dermal mixed inflammation composed of frequent neutrophils and eosinophils that raised suspicion for immunobullous disorder with possible subepithelial blister formation. Biopsy confirmed bullous pemphigoid. Patient started on prednisone taper, doxycycline 100 mg daily, and continued triamcinolone acetonide 0.1% cream. In addition, remaining open areas were covered with silvadene and telfa dressing to avoid itching and trimerization.

### Treatment and Outcome

The patient's diagnosis of bullous pemphigoid was treated with prednisone, doxycycline, and triamcinolone acetonide 0.1% cream to affected areas with eradication of blisters and marked improvement of erythema. Hydroxyzine was prescribed for pruritus with modest improvement in itching, so trial of over-the-counter anti-itch ointments was discussed with the patient. Complications associated with BP include increased susceptibility to staphylococcal and streptococcal skin infections, sepsis secondary to infection, adverse effects of treatment, and viral infections including herpes simplex or varicella-zoster.[1]

### Discussion and Conclusion

In BP, a patient will typically experience generalized pruritus either alone or associated with urticarial popular lesions that can later evolve to tense bullae within weeks to months.[4] However, initially, a patient may present with pruritus alone or with urticarial lesions, so the diagnosis relies on clinical suspicion and laboratory testing. The differential diagnosis can be broad including but not limited to: epidermolysis bullosa acquisita, bullous arthropod bite reaction, allergic contact dermatitis, bullous drug eruption, urticarial dermatoses, scabies, and other autoimmune disorders like BP such as pemphigus vulgaris. Of note, there have been case reports describing a bullous drug eruption with modafinil, which our patient had been prescribed about six months prior, thus making it the second drug after furosemide with known cutaneous reactions. However, the fixed drug reaction seen with modafinil usually presents within 30 minutes to 24-hours of drug exposure versus our patient's presentation around six months after starting modafinil and improvement of bullous lesions whilst still on modafinil.[5] We did not have the patient stop furosemide, another possible offending agent, as she started this medication in 2018 and subsequently had rapid improvement and full resolution of lesions with treatment. Current literature recommends stopping any offending medications primarily started within two to three months of symptom onset and starting steroids;[3] however, we did not stop the patient's furosemide since we did not believe furosemide, which has been well tolerated over the past five years, triggered drug-induced BP. The mainstay of treatment for bullous pemphigoid is systemic corticosteroids depending on the extent of the disease. If disease is more localized, less than 20% of body surface area, aim for potent topical steroids such as clobetasol or combine topical steroids with tetracycline, minocycline, or doxycycline.[6] For more extensive disease, current literature advises systemic prednisone at a dose of 0.5 to 1.0 mg/kg per day for approximately two weeks that can be slowly tapered over months,[6,8] for our patient we saw a role for concurrent use of oral and topical steroids for treatment given the localized nature of the severe lesions.

If symptoms are not controlled with steroids or there are contraindications for use of systemic steroids, alternative regimens include but are not limited to: azathioprine, mycophenolate mofetil, methotrexate, cyclophosphamide or for resistant case, rituximab.[7] Of note, BP often resolves spontaneously in a few months but can also remain active for up to five years.[1]

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# The Evolution of Renal Denervation for the Treatment of Hypertension: Insights from Trials and Prospects for Clinical Practice

Hammad Shabir Chaudhry, MD; Dawood Shehzad, MD; Mustafa Shehzad, MD; Logan Johnke, MD; Muhammad Asif, MD; Dawlat Khan, MD; and Wahab Jahangir Khan, MD

**Abstract**

Hypertension affects 1.3 billion adults globally, with severe health implications if left untreated. Despite efforts, research suggests only a fraction achieve adequate control. Renal denervation (RDN) therapy has emerged as a potential solution, particularly for treatment-resistant cases. RDN targets the dysregulated sympathetic nervous system activity frequently encountered in resistant hypertension. Recent FDA approval of advanced RDN catheter systems in 2023 signifies a pivotal advancement in hypertension management. As an adjunctive to pharmacotherapy, RDN holds promise as a therapeutic modality in achieving optimal blood pressure control and attenuating hypertension-related morbidity and mortality. Further research elucidating the nuances of patient selection, procedural standardization, and long-term outcomes is warranted to optimize the clinical utility of RDN in the management of hypertension. This manuscript compiles evidence for the use of RDN and reviews the long-term safety data from recent trials.

## Introduction

Recent worldwide estimates suggest that as many as 1.3 billion adults currently suffer from hypertension, with global prevalence continuing to rise each year.[1] According to the 2020 International Society of Hypertension Global Hypertension Practice Guidelines, hypertension is defined as a systolic blood pressure (SBP) of ≥140 mmHg and/or a diastolic blood pressure (DBP) of ≥90 mmHg.[2] Left untreated, hypertension can have severe consequences on health outcomes, leading to myocardial infarction, kidney disease, stroke, and even death.[3] Hypertension remains the leading risk factor for mortality globally, contributing to an estimated 19% of all deaths worldwide.[1]

Despite increased efforts to improve hypertension management in recent years, only an estimated 54% of individuals with hypertension have been diagnosed. Furthermore, of those diagnosed, only 21% have their hypertension adequately controlled.[1] About 10% of patients have resistant hypertension (BP ≥ 140/90 mmHg) despite being on 3 antihypertensive medications, one of which is a diuretic.[1,4] Current guidelines for hypertension management focus on lifestyle modifications and various medications; however, strict adherence to prescribed medications poses a significant challenge, with up to 50% of patients becoming non-adherent within the first year of starting therapy.[5,6] Increased sympathetic activity in the afferent and efferent pathways of the sympathetic nervous system that surrounds the renal vasculature contributes to the development of essential hypertension. This has become a target for modern catheter-based antihypertensive modalities.[7] Introduced over a decade ago, renal denervation (RDN) therapy has gained momentum as an adjunct therapy for patients with treatment-resistant hypertension with the first catheter gaining FDA approval in November 2023. With continuing success in clinical trials, utilization of renal denervation therapy is likely to continue to gain momentum in the coming years.

## Physiological Basis

The kidneys are innervated by afferent and efferent sympathetic fibers located in the adventitia of the renal arteries. Renal efferent nerve stimulation activates the renin-angiotensin-aldosterone neurohormonal cascade, promoting renin release from the juxtaglomerular apparatus, increasing sodium retention, and decreasing renal blood flow and glomerular filtration. Afferent renal sensory nerves project to the hypothalamic paraventricular nucleus in the brain to modulate sympathetic outflow to the periphery, including the heart, kidneys, and arterioles. The degree of efferent

and afferent sympathetic fiber innervation are collectively referred to as renal sympathetic nerve activity (RSNA). Chronically elevated RSNA signaling leads to an increased sympathetic tone and norepinephrine release. To obliterate the dysfunctional RSNA, catheters were developed to ablate the nerves in the main body of the renal artery.

### Evolution of Renal Denervation Catheters

The Symplicity Flex catheter was the first generation of an ablation system. It consists of a single unipolar electrode on a flexible (4-F) catheter, delivering radiofrequency energy to the perivascular space to ablate renal nerves. Catheter manipulation was difficult as the catheter had to be rotated helically to achieve circumferential denervation. This catheter was used in SYMPLICITY 1 and 2.

The Symplicity Spyral catheter was the next generation of ablation systems. It differs from the first-generation device by using a multielectrode, helical device with four simultaneous ablation electrodes allowing for near-complete circumferential ablation with minimal catheter manipulation and less procedure time (Figure 1). Like the Flex catheter, this device also utilized radiofrequency energy to create thermal ablative energy, which generated heat in the perivascular fat that contains the target nerves. Renal nerves including branch arteries as small as 3 mm can also be denervated with this device. The Spyral catheter was used in the SPYRAL HTN-ON MED and SPYRAL HTN-OFF MED trials.

### Procedure Used for the Actual Denervation

In both trials subjects in the denervation group underwent the renal artery denervation procedure following the Symplicity Spyral catheter Instructions for Use, Symplicity G3 generator User Manual, and sponsor-provided training (Medtronic). As per sponsor guidelines, ablations target all accessible renal arterial branch vessels with diameters between 3 and 8 mm, including accessory, branch, and main renal arteries outside of the renal parenchyma. Initial catheter placement, guided by fluoroscopic imaging, is just proximal to the renal parenchyma. Investigators were directed to perform multiple ablations within a segment, progressing from distal to proximal without overlapping treatment zones. Ablations were cautioned against in bifurcations and within 5 mm of areas with calcification, atheroma, or stented lesions.[8,9]

### Landmark Trials

In 2009, the inaugural publication investigating the impact of catheter-based renal denervation in humans revealed a noteworthy decrease in blood pressure, demonstrating

**Figure 1. Multielectrode, helical device with four simultaneous ablation electrodes allowing for near-complete circumferential ablation with minimal catheter manipulation and less procedure time.**

a reduction of 22 mmHg in systolic and 11 mmHg in diastolic blood pressure among patients with drug-resistant hypertension who were concurrently using an average of five antihypertensive medications.[7] A major drawback of this study was a lack of control group. A second study yielded similar statistically significant results; office blood pressure was reduced by 32 mm Hg systolic and 14 mmHg diastolic in the RDN group. This second trial included a comparative control group to account for some of the confounding factors.10 The same catheter was used for renal denervation in both studies. These trials were SYMPLICITY HTN-1 and 2.[10, 11]

Following the favorable outcomes of initial investigations, a subsequent trial was devised, (SYMPLICITY-3) which was the largest-to-date trial that incorporated a control group that underwent all procedures except for actual denervation, in direct comparison to the intervention group. Regrettably, this trial did not establish the superiority of catheter-based renal denervation (RDN) in the management of drug-resistant hypertension, the mean change in the office based systolic blood pressure was -14.13 mmHg in the RDN group compared to 11.74 mmHg in the sham procedure group. [12]

The conflicting outcomes in the SYMPLICITY trials cast doubts regarding the credibility of the initial findings. This led to a thorough exploration of the various factors that might have played a role in the inability to establish the superiority of RDN over the sham procedure. Numerous investigative paths were pursued. The catheter design, the technique employed for denervation, and patient-related factors like adherence to the medical therapy were implicated as possible confounders.[12]

One of the differences between the SYMPLICITY HTN

**Table 1. Trials.**

| Trial name | Date | Study design | Sample size RDN/control | Denervation system | Primary outcome | Primary outcome achieved? | Longest follow-up period | Long-term results at present |
|---|---|---|---|---|---|---|---|---|
| SYMPLICITY HTN –1 | 2009 | Open-label trial | 153/NA | SYMPLICITY FLEX | Change in office SBP at 12 months | Yes, SBP –22 mmHg (95% CI –32 to –12 mmHg), *p*-value < 0.001 | 36 months | SBP reduction of 32 mmHg in the treatment arm (p<0.001), DBP reduction of 14 mmHg (p<0.01) in the treatment arm |
| SYMPLICITY HTN-2 | 2010 | Randomized control trial, multicenter | 52/54 | SYMPLICITY FLEX | Change in mean office SBP at 6 months | Yes, RDN –32±23 mmHg vs control 1 ±21 mmHg, *p*-value < 0.0001 | 36 Months | At 36 months, SBP reduction of 33 mmHg (p <0.01), and DBP reduction of 14 mmHg (p<0.01) in the treatment arm |
| SYMPLICITY HTN-3 | 2014 | Randomized control trial, double-blinded, multicenter | 364/171 | SYMPLICITY FLEX | Change in office SBP at 6 months | No, RDN –14.1±23.9 mmHg vs sham –11.7±25.9 mmHg, *p*-value = 0.26 | 36 months | Office SBP was –26·4 mm Hg (SD 25.9) in the RDN group and –5·7 mm Hg (24.4) in the sham control group (adjusted treatment difference –22·1 mm Hg [95% CI –27·2 to –17·0]; p≤0·0001 |
| SPYRAL HTN-OFF MED | 2017 | Randomized control trial, sham-controlled | 166/165 | SYMPLICITY SPYRAL | Change in 24-h ambulatory SBP at 3 months | Yes, RDN –4.7 mmHg (95% CI –12.7 to –5.3 mmHg) vs sham –0.6 mmHg (95% CI –5.2 to 2.0 mmHg), *p*-value = 0.0051 | 3 months | |
| SPYRAL HTN-ON MED | 2018 | Randomized control trial, double-blinded, sham-controlled multielectrode | 38/42 | SYMPLICITY SPYRAL | Change in 24-h ambulatory SBP at 6 months | Yes, RDN –9.0 mmHg (95% CI –12.7 to –5.3 mmHg) vs sham –1.6 mmHg (95% CI –5.2 to 2.0 mmHg), *p*-value = 0.0051 | 36 months | At 36 months, adjusted treatment differences were –10 mmHg for the ambulatory SBP, –5.9 mmHg for mean ambulatory DBP, –11 mmHg for morning SBP, and –11.8 mmHg for night-time SBP, all demonstrating the superiority of the RDN procedure over the sham procedure |
| GLOBAL SYMPLICITY REGISTRY | 2012 | Prospective, multi-center, non-randomized trial | 3100 | SYMPLICITY FLEX or SIMPLICITY SPIRAL | N/A | N/A | 36 months | At 36 months, reduction in OBP by –18.5 and 24-hour SBP –9.2 mmHg |

-1,2 and 3 was using different denervation catheters. In SYMPLICITY-1 and 2, a fixed arch radiofrequency denervation catheter was used, providing fixed contact pressure to the arterial wall.[8,9] However, in the SYMPLICITY-3, a variable arch radiofrequency catheter was used, this catheter provided the operators to choose the tip contact pressure. Both these systems used unipolar electrodes.[10]

To overcome the contradictory results of the SYMPLICITY HTN trials, another group of trials named the SPYRAL HTN global clinical trial program was initiated. This program had initial pilot studies that reaffirmed the biological proof of principle that renal denervation had a significant blood pressure-lowering effect.[13-16]

The 2 trials of the SPYRAL HTN program focused on the effect of renal denervation using Simplicity Spyral multielectrode renal denervation catheter in hypertensive patients in the absence (SPYRAL HTN OFF- MED) and presence (SPYRAL HTN ON-MED) of antihypertensive medications, first pilot studies were conducted with n=80 and this was later followed by larger studies.[17]

These trials used the newer Symplicity Spyral multielectrode radiofrequency RDN delivery system (Medtronic, Galway, Ireland). This catheter system enables the delivery of radiofrequency treatment in a spiral fashion to the four quadrants of the renal artery and its branches between 3 mm and 8 mm in diameter.[18]

In the SPYRAL HTN OFF-MED trial the participating patients (n=331) were allowed a 3-4 weeks long drug washout period, this was followed by the 3-month efficacy and safety endpoint in the absence of the antihypertensive medications.20 At the 3-month mark, a significant disparity in the primary efficacy endpoint, namely the alteration in 24-hour systolic blood pressure from baseline, was observed between the renal denervation and sham procedure groups treatment difference of –3.9 mm Hg (95% CI –6·2 to –1·6). The secondary endpoint was the difference in 3-month changes in office systolic blood pressure between the two groups, the difference was significant and the endpoint was met (difference –6·5 mm Hg (95% CI –9·6 to –3·5).[18, 19]

The SPYRAL HTN ON-MED study required patients (n=337) to be treated with a consistent triple therapy antihypertensive regimen. The patients who received RDN and continued taking their prescribed anti-hypertensive medications were noted to have sustained statistically significant lowering of systolic and diastolic blood pressure at 24 and 36 months compared to their baseline blood pressures. At 36 months, the RDN group demonstrated a substantial reduction in ambulatory systolic blood pressure by -18.7 mm Hg surpassing the sham control group's reduction of -8.6 mm Hg. The adjusted treatment difference of -10.0 mm Hg (95% CI -16.6 to -3.3; p=0.0039) highlighted the efficacy of renal denervation. Additionally, notable treatment differences were observed at 36 months in mean ambulatory diastolic blood pressure (-5.9 mm Hg, 95% CI -10.1 to -1.8; p=0.0055), morning systolic blood pressure (-11.0 mm Hg, 95% CI -19.8 to -2.1; p=0.016), and night-time systolic blood pressure (-11.8 mm Hg, 95% CI -19.0 to -4.7; p=0.0017). Importantly, no safety concerns were identified in the short-term or long-term associated with renal denervation.[21] A summary of the landmark trials, with their primary outcome is tabulated above.

### Long-term Follow-up Results

As evident from the summarized randomized controlled trials, the radiofrequency RDN is successful in achieving short-term blood pressure reduction. However, the pivotal factor for widespread applicability lies in exploring the long-term effects of these therapies in sustained lowering of blood pressure. Managing hypertension is akin to a marathon, necessitating sustained, long-term control of blood pressure to effectively diminish the overall cardiovascular risk.

A meta-analysis of 1742 patients from the prospective, open-label, Global SYMPLICITY Registry, showed that at 3-year follow-up RDN with the Symplicity mono-electrode Flex catheter was associated with 24-h ambulatory SBP reduction of (-8.0 ± 20.0 mmHg; $P < 0.001$). Office BP readings were (-16.5 ± 28.6 mmHg, $P < 0.001$).[21]

A recent study examined the long-term outcomes (8.8 ± 1.2 years post-procedure) of 66 patients with resistant hypertension previously enrolled in various radiofrequency-based renal denervation trials. It found that ambulatory systolic blood pressure (BP) decreased by -12.1 ± 21.6 mm Hg (from 145.2 to 133.1; $P < 0.0001$), and diastolic BP decreased by -8.8 ± 12.8 mm Hg (from 81.2 to 72.7; $P < 0.0001$). The mean heart rate remained unchanged. In the long-term follow-up, participants were on one less antihypertensive medication compared to baseline ($P = 0.0052$). However, recruitment for this study depended on potential participants expressing their willingness to participate, which may be associated with their procedural success. Moreover, although 163 participants from previous trials were identified, 57 patients were lost to follow-up or were deceased. Despite the lack of evidence indicating an increased risk of cardiovascular or other adverse events following RDN, accurate data on the

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cause of death for participants is unavailable.[22]

Presently, the data suggests that RDN leads to a sustained reduction in blood pressure throughout the 24 hours for at least 9 years post-intervention, without evidence of adverse effects.

## Long-term Safety Data

### Procedural compilations

In the SYMPLICITY HTN-1 trial, 4 out of 153 patients studied experienced catheter-related complications. Three had femoral artery pseudoaneurysms, and one patient had a renal artery dissection. During the application of radiofrequency energy, 8 out of 153 patients had episodes of bradycardia that spontaneously resolved. There were no episodes of postoperative orthostatic hypotension, bradycardia, or vasovagal syncope.[7,11]

In the SYMPLICITY HTN-2, no serious device-related complications were noted. This trial had a control arm. Peri-operatively, there was one case of access site hematoma in the RDN group, and one case of renal artery dissection in the crossover group. Reported late complications included 2 cases of acute renal failure and 18 hospital admissions. 15 admissions were due to hypertensive crisis and 3 were due to hypotensive episodes.[25] Reported adverse events in the SYMPLICITY HTN-3 trial remained consistent with the previous two trials. Only 1 of 364 patients had complications related to the vascular access site.

### Renal Function

Currently, there is no evidence to suggest that RDN leads to a reduction in renal function over an extended monitoring period. The Global SYMPLICITY Registry, which assessed a 3-year follow-up of 2,237 patients post-RDN using the Symplicity mono-electrode Flex catheter, the estimated glomerular filtration rate (eGFR) exhibited a decline in line with the age-related rate, dropping from 71.1 to 61.2 mL/min per 1.73 m2 over 3 years.[26]

### Renal Artery Stenosis

A theoretical concern related to catheter-based RDN is the potential development of new-onset renal artery stenosis due to vascular injury. A comprehensive meta-analysis of 5,769 patients who underwent radiofrequency RDN, estimated an annual incidence of renal artery stenosis at 0.2% in this group.[27] This incidence is comparable to the occurrence of naturally developing renal artery stenosis in the context of arterial hypertension. [28]

### Post-Denervation Reinnervation

The peripheral nervous system has the potential for nerve regeneration after injury.[29] This leads to the question of possible renal sympathetic nerve reinnervation and the long-term efficacy of RDN in resistant hypertension control. One study looking at renal denervated normotensive, non-CKD sheep found that renal nerve regrowth and neural control of renal function were restored to levels of control sheep at 30 months. This suggested complete functional reinnervation. In the hypertensive-CKD sheep group, nerve regeneration was only partially restored. Renal nerve regrowth was assessed by measuring the degree of vascular contraction to nerve stimulation in the renal arteries and by measuring levels of renal tyrosine hydroxylase, calcitonin gene-related peptide, and norepinephrine levels in kidneys at 30 months after RDN.[30] To date, data on renal nerve regeneration is inconclusive but given the durable clinical effects observed in trials with human subjects, a substantial regeneration does not seem to occur.

## FDA Approval for the Symplicity Spyral Catheter

In light of the successful clinical trials with the RDN catheters, the FDA has recently approved the Symplicity Spyral renal denervation system. This catheter system got FDA approval on Nov. 17, 2023, and it is culmination of 14 years of research and development.

## Conclusion

Hypertension remains a challenging chronic medical condition that affects a large portion of the human population. With the approval of the new RDN system we now have a new modality to tackle medication-resistant hypertension. Of note, this newer modality may not eliminate the need for anti-hypertensive medications but surely will aid in better control of this morbid condition.

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# Acute Arthritis Presentations of Gonorrhea and Syphilis – A Concise Update

Randall Lamfers, MD, FACP; and Rachael Fanciullo, BA

**Abstract**

According to the 2021 CDC sexually transmitted disease surveillance report, national cases of syphilis and gonorrhea continue to rise. Currently, South Dakota ranks #1 in syphilis and #2 in gonorrhea cases per 100,000 population. The higher incidence increases the likelihood South Dakota clinicians will encounter different presentations of syphilis and gonorrhea. Recently, we have seen patients presenting with acute STI related inflammatory arthritis. This review discusses the acute arthritic presentations associated with gonorrhea and syphilis and its treatment.

## Introduction

Syphilis and gonorrhea cases are on the rise nationally, according to the 2021 CDC sexually transmitted disease surveillance report. Currently, South Dakota ranks #1 in syphilis and #2 in gonorrhea cases per 100,000 population. From 2017 to 2021, syphilis cases rose from 75 to 924, and gonorrhea cases rose from 1,290 to 3,258 in the state.[1] This higher incidence increases the likelihood that SD clinicians will encounter uncommon presentations of these two infections. In the hospital, we have identified cases of STI related inflammatory arthritis as the initial presentation. This concise review examines the acute arthritic presentations associated with gonorrhea and syphilis.

## Gonococcal Arthritis

*Neisseria gonorrhoeae* is a gram-negative diplococcus that most commonly presents as minor mucosal infections.[2,3] However, approximately 0.5 - 3.0% of cases are more severe, manifesting as disseminated gonococcal infection (DGI).[2,3,4,5] The development of DGI may be associated with various risk factors. In one series, DGI was found to be three to five times more likely in women.[6,7] In more recent case series, no difference in gender has been found.[8,9,10] Alternatively, the CDC 2021 treatment guidelines note an increase in men experiencing DGI. Other risk factors for DGI include HIV positivity, complement deficiency, SLE, IV drug use, menses, gonococcal strain characteristics, pregnancy, multiple sexual partners, low socioeconomic status, and asymptomatic mucosal infection.[11]

The complement pathway in the immune system is important for defense against *Neisseria* infections. In patients with recurrent DGI, it is recommended to test for complement deficiency. Eculizumab is a monoclonal antibody that targets complement 5 and is used in the treatment of neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria, and other diseases. Patients treated with this biologic agent are considered at risk for DGI.[12]

In the presence of DGI, gonococcal arthritis is the most common manifestation.[10] The arthritis presents in two distinct forms: arthritis-dermatitis syndrome and septic arthritis.[3,13,14] The more common presentation is arthritis-dermatitis syndrome, with features of polyarthralgia, tenosynovitis, and skin lesions.[3] The polyarthralgia is often asymmetrical and migratory, affecting knees, ankles, wrists, and elbow joints.[5,9,11] While most DGI patients with polyarthritis have asymmetrical involvement, we have encountered symmetrical presentations. In up to 75% of cases, skin manifestations may be found.[5,11,15] Lesions often appear on extremities in groups of 5-40 papules or pustules with hemorrhagic components.[5,15] In the septic arthritis presentation, joint involvement is mono-articular or oligo-articular and may affect the knees, wrists, ankles and fingers.[5,11,13] Genitourinary symptoms are atypical in cases of DGI.[6,8,10]

When gonococcal arthritis is suspected, it is recommended to obtain blood cultures, synovial cell count with culture, and mucosal cultures.[8] Given the specific growth requirements for *N. gonorrhoeae,* consultation with lab prior to obtaining samples will optimize culture results.[16] In DGI with arthritis presentations, blood and synovial cultures are positive approximately 50% of the time.[11,13,15] Cultures from mucosal sites are positive in approximately 80% of patients and provide the added benefit of acquiring antibiotic sensitivities.[11,13,15] A Nucleic Acid Amplification Test (NAAT) may be performed from synovial and mucosal

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sites to confirm diagnosis when cultures are negative. The sensitivity of NAAT on synovial fluid is 80%.[13] There may be varying specifications on NAAT collection depending on mucosal site tested and manufacturer, hence consultation with the lab is recommended for maximizing results.[16]

For treatment of gonococcal arthritis, the 2021 CDC STI treatment guidelines recommend third generation cephalosporins. Preferred regimen is ceftriaxone 1 g IM or IV every 24 hours for 7 days. An alternative is cefotaxime 1 g every 8 hours. For the arthritis dermatitis syndrome, the clinician can change to an oral antibiotic if antimicrobial sensitivities are available and there has been 1-2 days of significant clinical improvement. Total antibiotic treatment duration should be a minimum 7 days. If the patient is not improving with cephalosporin treatment after several days, consider the possibility of antibiotic resistance and consult infectious disease or the South Dakota State Health Department. Note the guideline recommends treating for chlamydia with doxycycline 100 mg po twice daily for 7 days if chlamydia has not been excluded.[16]

### Syphilis

While Gonorrhea is the more notable of the two infections to cause acute arthritic presentations, syphilis may present with inflammatory arthritis. Syphilis is caused by *Treponema pallidum* and occurs in distinct stages. According to Traczuk et al., in the primary stage a single painless ulcer occurs about 2-3 weeks at the site of the infection. This ulcer can last up to 3-6 weeks if untreated. Secondary syphilis can occur 2-8 weeks after resolution of untreated primary stage. In secondary syphilis most common symptoms are fever, rash (palms and soles), and malaise. During this stage, involvement in multiple organ systems may occur. if secondary syphilis is untreated, symptoms may resolve over a period of weeks and enter a period of latency where the patient is asymptomatic. Approximately a 1/3 of patients with latent syphilis will develop tertiary syphilis. In tertiary syphilis patients can experience neurological or cardiovascular or gummatous lesions.[17]

Inflammatory arthritis typically occurs in secondary syphilis approximately 3-12 weeks after resolution of the primary chancre.[17] Only about 2-12% of patients during this stage experience arthritis.[18] Inflammatory arthritis is a symmetrical non-migratory polyarthritis, most commonly affecting knees and the ankles. The inflammatory presentation is milder than that of gonococcal arthritis.[18] Mono-arthritis involving knee and ankle should not be excluded.[17,19] The arthritis is often accompanied by an erythematous maculopapular rash involving the palms and soles.[17,18] Other musculoskeletal manifestations include tenosynovitis in the hands and wrists and myositis. Periostitis and osteitis are rare.[17]

Charcot arthropathy, a manifestation of tabes dorsalis, is common in patients who develop tertiary syphilis.[17] The frequency of arthropathy in tabes dorsalis is estimated between 5-10%, and most commonly affects the knees and hips.[17,18] There often no associated pain, but swelling and deformity are likely. With the advancement of antibiotic therapy, neuropathic arthropathy has become less common.[20] However, tabes dorsalis secondary to syphilis should still be considered in patients with unexplained destructive, neuropathic arthropathy.[21]

The definitive diagnosis of syphilis requires darkfield examination and molecular testing to detect the presence of *T. pallidum* in involved tissues. This is not always practical, so a presumptive diagnosis utilizing serologic testing is most frequently employed. This strategy requires positive serologies on nontreponemal testing (Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagin (RPR)), and an additional positive treponemal test (*T. pallidum* Passive Particle Agglutination (TP-PA) or other available treponemal assays). If neurosyphilis is suspected, a combination of tests may be performed on CSF samples.[16]

Non-treponemal titers are used for monitoring disease, decrease with treatment, and eventually may become non-reactive. Treponemal tests remain positive for life in many patients even if they were successfully treated. This presents a challenge in the diagnosis of recurrent syphilis infection. In this situation, CDC STI guidelines recommend following changes in titers on nontreponemal testing to guide decisions on possible reinfection.[16]

Penicillin remains the preferred treatment for any stage of syphilis, however dose and frequency vary by stage and CNS involvement.[16] Treatment for secondary syphilis with inflammatory arthritis and no CNS involvement is Benzathine penicillin G 2.4 million units IM in a single dose. For those with penicillin allergy, doxycycline 100 mg twice daily for 14 days may be used.[16] Azithromycin had been effective in the past, but it is no longer recommended given resistance patterns.

### Other Management Considerations

In patients with either gonorrhea or syphilis it is recommended to test for other STIs. Remember that in South Dakota gonorrhea and syphilis are reportable to the

State Health Department. The South Dakota State Health Department has a STI Control Program that provides partner notification along with additional services including resources for health care providers. Information about the SD STI Control Program can be found at the following website: https://doh.sd.gov/topics/family-planning/sexually-transmitted-infection-control/.

### Conclusion

South Dakota is experiencing a significant increase in cases of syphilis and gonorrhea. The case increase has led South Dakota to #1 and #2 rankings in the nation per capita for these two infections. It is important for clinicians to recognize the systemic manifestations of these two sexually transmitted infections. Key points for the South Dakota clinician to remember in gonococcal arthritis are that it can present in two forms, remember to obtain cultures from not only blood and synovial fluid but also from mucosal sites, and the drug of choice is IV ceftriaxone. For syphilis key points to remember are it can present with symmetrical polyarthritis or a mono-arthritis, the arthritis is usually associated with a rash on the palms or soles, diagnosis is based on serological testing, and drug of choice is penicillin G. The website below takes the South Dakota clinician directly to the CDC STI treatment guidelines where there are options for a pocket guide, mobile app, or a pdf of the full 2021 STI treatment guidelines: www.cdc.gov/std/treatment-guidelines/provider-resources.htm.

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# Obesity: A Profoundly Under Recognized Chronic Disease; And Its Impacts on Cardiovascular Disease

Muhammad Asif, MD

**Abstract**

Obesity is a treatable chronic disease of high prevalence in the U.S. It has various direct and indirect adverse health effects in terms of morbidity and mortality. It not only increases cardiovascular mortality but is also associated with an increased risk of multiple cancers. However, unlike other chronic diseases, obesity diagnosis often misses patients' and providers' attention and historically has been undertreated. This article is written to highlight the impact of obesity on health with special reference to cardiovascular disease, stimulate the quest among the masses and primary care providers for the diagnosis and treatment of obesity, its complications, and benefits obtained from its treatment.

The Obesity Medicine Association (OMA) defines obesity as a chronic, progressive, relapsing, and treatable multifactorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences. Obesity is one of the profoundly under-recognized and untreated chronic conditions that have many direct and indirect adverse health outcomes. A body mass index (BMI) of ≥30 kg/m$^2$ is an easy and sensitive tool most used in clinical practice to screen people for obesity. In addition to measuring BMI, measuring waist circumference is helpful to assess abdominal obesity. A waist circumference of ≥40 in (102 cm) for males and ≥35 in (88 cm) for females is considered elevated and indicative of increased cardiometabolic risk. In children, the cutoff for this diagnosis is a BMI equal to or greater than the 95th percentile of the reference population in the same age and sex group.

As per CDC, the prevalence of obesity among U.S. adults as of 2017-18 is 42.4%, and that trend has been on the rise since 1999.[1] Contrary to many other chronic diseases, obesity is also significantly prevalent among minors, affecting 19.3% of children and adolescents between the ages of 2 to 19, of which 6.1% have severe obesity. There are many determinants of obesity, including epigenetics, genetic syndromes, endocrine disorders, psychiatric and sleep disorders, medications, food types, and psychosocial and behavioral variables.

Cardiovascular disease is the leading cause of death in the United States, followed by Cancers. Obesity is not only associated with an increased risk of cardiovascular disease (CVD) and cancers but many other diseases as well. These include diabetes mellitus type 2 (DM2 up to 80% of patients), chronic kidney disease (CKD), obstructive sleep apnea (OSA), obesity hypoventilation syndrome (OHS), asthma, hypertension (HTN), dyslipidemia (HLD), nonalcoholic fatty liver disease (NAFLD), osteoarthritis, venous thromboembolism, gall stones, gout, depression, and polycystic ovarian syndrome (PCOS) among others. Obesity is the second most preventable cause of cancer; among US adults, the proportion of cancers attributable to excess body weight is nearly 5% for men and 10% for a woman.[2]

Obesity has a multiprong contribution to cardiovascular disease (CVD). Its manifestations include increased risk of coronary artery disease and atherosclerosis, heart failure, arrhythmias including atrial fibrillation, stroke, and sudden death[3]. The management of CVD, and other obesity associated diseases puts a significant burden on limited healthcare resources. In addition to direct health care expenses incurred on the treatment of obesity related conditions, there is indirect cost too, including lost work, productivity, and lower household income. According to a study in 2016, direct health care cost for chronic diseases to which obesity is known to be a risk factor was $480.7 billion in US, moreover $1.24 trillion were estimated to be the indirect cost due to loss of economic productivity. The total cost of chronic diseases due to obesity and overweight was $1.72 trillion, equal to 9.3% of the U.S. GDP.[4]

The first step in limiting the morbidity and mortality caused by obesity is to recognize obesity as a serious disease both by the population and the healthcare providers. BMI should be

viewed as a sixth vital measure recorded and considered to be addressed on every primary care visit. Once diagnosed, obesity should be treated according to the standard guidelines using behavioral, pharmacological, and surgical treatments like any other chronic disease under the care of appropriate providers. The treatment of obesity is long-term and involves various components, including lifestyle modification, dietary changes, exercise, pharmacological treatments, and bariatric surgical procedures when indicated. Despite the significantly high number of overweight and obese people who qualify for obesity medications and bariatric surgery, according to various studies, only less than 2% received anti-obesity medications (AOMs),[5] or bariatric surgery.[6] There are multiple factors for this under treatment, including the social stigma associated with obesity, hesitancy, and lack of access to healthcare, nonuniform coverage of some anti-obesity medications (AOMs) and procedures by insurance companies, primary care providers' lack of experience in using new antiobesity medications, fear of side effects and unfamiliarity with the laws governing the use of AOMs.

Adults are advised to have at least 150 to 300 minutes a week of moderate-intensity or 75 to 150 minutes a week of vigorous-intensity aerobic physical activity; additional health benefits are gained by engaging in physical activity beyond this time. In 2020, as per CDC only 24.2% of the adults met these physical activity guidelines. There are many dietary plans available to meet the person's specific needs and preferences with common goal being net negative energy balance and promotion of healthy macronutrients, including ketogenic, low carb and low-fat diets or meal replacement. The FDA–approved AOMs include orlistat, phentermine/topiramate ER, naltrexone/bupropion ER, liraglutide, semaglutide and setmelanotide. Commonly performed metabolic bariatric surgical procedures include sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), bilopancreatic diversion with duodenal switch and a loop duodenal switch, and laparoscopic adjustable gastric band.

The importance of weight loss and obesity treatment cannot be overstated. The healthcare benefits from treating obesity start from as little as 2% loss of excess weight. The magnitude of benefits continues to rise proportionately with the amount of weight loss. For instance, by successive loss of excess body weight, one can not only decrease the need for medical treatment for medical conditions like DM2, HTN, HLP, OSA but also in many cases can achieve complete remission as well. According to one study, the estimated adjusted cumulative DM2 remission rates for patients who had RYGB and SG were 59.2% and 55.9%, respectively at 1 year, and 86.1% and 83.5% at 5 years post-surgery.[7] Other studies have reported better mood, quality of life, increased physical performance, and economic productivity.

The purpose of this writing is to raise awareness among readers about obesity as a significant disease so that they can appreciate the increased health-related risk factors associated with this condition and available treatment options with the associated benefits. However, for all practical purposes, the readers should refer to the latest diagnostic and treatment guidelines specific to pertinent patient characteristics before making any clinical decisions to manage obesity.[8]

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# Comprehensive Cardiac Care

## Across Nebraska, the Region and Beyond

*Content submitted by Children's Nebraska*

In the Dr. C.C. & Mabel L. Criss Heart Center at Children's Nebraska, pediatric cardiology and heart surgery teams specialize in treating a range of congenital heart defects and offer comprehensive cardiac care. From the Fetal Heart to Adult Congenital Heart Disease (ACHD) programs, Children's has the expertise to provide exceptional cardiac care in all stages of life. In addition to providing care in Omaha, Children's cardiologists conduct pediatric and congenital heart disease outreach clinics in 11 locations, providing the same standard of specialty care closer to home.

### CUTTING-EDGE CARE

Children's is dedicated to staying at the forefront of medical innovations, investing in state-of-the-art equipment and expert providers.

One such investment is to offer comprehensive interventional and diagnostic cardiac catheterization procedures. Our state-of-the-art cardiac catheterization suites double as full-service operating rooms if and when surgery is needed. The suites house ARTIS pheno, a robotic C-arm X-ray that provides swift, 360-degree images of even the tiniest hearts with limited exposure to radiation for patients. Children's was the first in the world to adopt ARTIS pheno in a pediatric setting.

Children's also houses a first-in-the-region Cardiac Care Unit (CCU), a floor exclusively dedicated to caring for the full spectrum of pediatric heart patients. Working alongside Children's pediatric specialists, the CCU team includes highly skilled nurses and advanced practice providers specially trained in providing care to pediatric patients with cardiovascular conditions.

### EXTENDING EXCELLENCE ACROSS THE REGION

Understanding the challenges that geographic distance can pose to families, Children's has established outreach clinics across Nebraska, Iowa and South Dakota. The outreach clinics bring the expertise and innovation of Children's pediatric cardiac care right to the communities we serve. Children's cardiology outreach clinics are offered in:

***Nebraska:*** Columbus, Grand Island, Kearney, Hastings, Lincoln, Norfolk and North Platte

***Iowa:*** Atlantic and Sioux City

***South Dakota:*** Rapid City and Sioux Falls

When visits to Children's main campus are necessary, patients and families traveling from more than 90 miles outside of Omaha can access the Rainbow House, a 56-room overnight guest house for a patient's immediate family.

### OUR PROGRAMS & SERVICES

Children's offers a range of cardiac programs and services to meet the needs of our patients and families. Our providers use a patient-centered approach to care, meaning each patient receives an individualized care plan tailored to their specific condition. Cardiac programs offered at Children's include:

- Adult Congenital Heart Disease
- Aortopathy Program
- Cardiac Rehabilitation
- Cardiothoracic Surgery
- Cardiovascular Genetics
- Diagnostic Testing & Advanced Cardiac Imaging
- Electrophysiology
- Fetal Cardiology
- Fontan Program, in partnership with Children's Adolescent Medicine and Gastroenterology, Hepatology & Nutrition
- Interventional Cardiology
- Pediatric Cardiology
- Pulmonary Hypertension Program, in partnership with Children's Pulmonology
- Single Ventricle Program
- 3D Visualization Lab

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Children's NEBRASKA

# Member News

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

## SDSMA President Welcomes MD Class of 2028

SDSMA President Jen Tinguely, MD, helped welcome 71 new students in the MD class of 2028 during USD Sanford School of Medicine orientation in Vermillion. On the first day of orientation on July 15, Dr. Tinguely provided an overview of the SDSMA and its benefits to medical students. On July 17, Dr. Tinguely led the Affirmation of the Physician during the White Coat Ceremony. Congratulations to the incoming class!


## The Issue Is...

### SDSMA Pushes for Congressional Action on Medicare Physician Payment

In light of the recently released CY2025 Medicare Physician Fee Schedule rule which proposes to cut Medicare physician payments by 2.8%, the SDSMA, AMA and 124 other medical associations sent a letter to congressional leadership.

The 2025 Medicare conversion factor is set to decrease for the fifth straight year by approximately 2.80% from $33.2875 to $32.3562. This cut is largely the result of the expiration of a 2.93% temporary update to the conversion factor at the end of 2024 and a 0% baseline update for 2025 under the Medicare Access and CHIP Reauthorization Act (MACRA). These cuts coincide with ongoing growth in the cost of practicing medicine as CMS projects the increase in the Medicare Economic Index (MEI) for 2025 will be 3.6%.

Physician practices cannot continue to absorb increasing costs with increasing inflation rates, while payment rates dwindle. Both the Medicare Payment Advisory Commission (MedPAC) and the Medicare Trustees have issued warnings about access to care problems for seniors and persons with disabilities if the gap between what Medicare pays physicians and what it costs to provide high quality patient care continues to grow. Committees of jurisdiction have started conversations on reforming MACRA, and the letter urges them to continue these negotiations in earnest given the cuts in the latest proposed rule and enact priority legislation. The letter urges leadership to act on bills or future legislation which reforms MACRA.

# American Medical Association Delegate Report – 2024 Annual Meeting

The 2024 Annual Meeting of the American Medical Association House of Delegates was attended by South Dakota's delegation in Chicago June 7-12 including Mary Carpenter, MD and Rob Allison, MD seated as delegates with Jen Tinguely, MD, MPH, and Robert Summerer, DO attending as alternate delegates. Barb Smith also represented the SDSMA in her role as CEO. Medical student attendees were Colton Carlson, Nathan Popp, Kianna Thelen and Sam Vassar. Here are some of the highlights of the meeting:

## RURAL HEALTH CRISIS

Ahead of his inauguration, now-AMA President Bruce Scott, MD (who last month spoke at the SDSMA's annual conference) outlined how to address the alarming inequalities that contribute to rural residents often living sicker and dying younger than their urban counterparts. Dr. Scott proposed five strategies that could help turn things around:

- Fix the Medicare payment system. Adjusted for inflation, Medicare physician payment has fallen 29% since 2001.
- Address workforce burdens that drive burnout and early retirements. This includes th e two hours physicians waste on administrative burdens such as prior authorization for every one hour they spend face to face with patients.
- Enact legislative fixes to grow the physician workforce, including expanding residency and graduate medical education slots, incentivizing physicians to work in rural communities and supporting an expanded role of international medical graduates.
- Permanently remove telehealth restrictions. The pandemic showed that removing restrictions is an essential tool to providing care, especially in rural areas where transportation can be challenging.
- Tackle chronic disease head-on. This includes bolstering health outreach and education to rebuild trust in science and medical institutions.

## MEDICARE PAYMENT REFORM

Medicare reform is a top priority for the AMA because it is crippling the sustainability of physician practices, threatening patient access to care, and choking the pipeline for future physicians. The House of Delegates (HOD) made clear the imperative to step up the pressure on the nation's lawmakers. Among the fixes is H.R. 2474, the Strengthening Medicare for Patients and Providers Act. This bipartisan legislation would provide physicians with an annual, permanent inflationary payment update in Medicare tied to the Medicare Economic Index.

## SCOPE CREEP

With several actions, delegates built upon the AMA's efforts to fight scope creep and defend the practice of medicine against scope of practice expansions that threaten patient safety. With direction from the HOD, the AMA will move to tackle the growing phenomenon of specialty switches among nonphysician providers. The HOD supported physician-led care in the emergency department, but rural physicians once again cautioned the House regarding staffing concerns in rural facilities. Additionally, AMA Immediate Past President Jesse Ehrenfeld discussed concerns with efforts to allow pharmacists to administer tests, diagnose conditions and prescribe medications, far exceeding their training and jeopardizing patient health. The South Dakota delegation attended the Scope of Practice session in which states present their efforts to limit scope creep. Some of the suggestions were to develop a coalition of medical societies that could work together with state legislatures. Another suggestion was to host a meeting between physician leadership and the legislators, or even sending personal postcards to legislators at the beginning of the session.

## NATIVE AMERICAN CONCERNS

Several resolutions addressed the concerns of Native people. These included payment options for traditional healing services, and raising awareness over water rights and the need for appropriate access to clean water with improvement of sanitation systems in Native communities. Physicians working for Indian Health Service (IHS) rank in the bottom-quartile within the U.S. Department of Health and Human Services for employee engagement and satisfaction. The AMA continues to support loan forgiveness programs for physicians working in the IHS. The HOD supported the expansion of IHS Youth Regional Treatment Centers, recognizing them as a model for culturally-rooted, evidence-based behavioral health treatment. Delegates passed policy on missing and murdered Indigenous persons. The policy states that the AMA supports emergency alert systems for American Indian and Alaska Native tribal members reported missing on tribal reservations and elsewhere. Delegates of the House also voted to support increased funding for IHS, Tribal, and Urban Indian Health Programs to provide cancer care to Native Americans.

## TELEHEALTH

Nearly 70% of physicians want to provide telemedicine services. Paying for telemedicine services means greater convenience for patients. But the regulatory flexibilities that enabled telemedicine to flourish during the COVID-19 public health emergency are set to expire this year. To strengthen advocacy supporting telehealth, delegates adopted policy to "support removal of the Dec. 31, 2024, 'sunset' date currently set for Medicare to cease reimbursement for services provided via telemedicine, such that reimbursement of medical services provided by telemedicine be continued indefinitely into the future, consistent with what would be determined" by the AMA's RUC Committee. The RUC is a unique multi-specialty committee dedicated to describing the resources required to provide physician services which the Centers for Medicare & Medicaid Services considers in developing relative value units (RVUs).

## MEDICAL STAFF AND AI TOOLS

The AMA has prioritized making technology work for physicians, ensuring that it is an asset — not a burden. AI tools are growing increasingly common in health care, but sometimes physicians and organized medical staffs are not given the proper say in how they are chosen or used. Given the promise of AI tools to improve care as well as their potential risks, delegates stated that this status quo is untenable. Accordingly, policy was adopted that modifies existing AMA principles for strengthening the physician-hospital relationship. The policy now states: "The organized medical staff and the hospital governing body are responsible for the provision of quality care, providing a safe environment for patients, staff and visitors, protection from interruption of delivery of care, and working continuously to improve patient care and health outcomes — including but not limited to the development, selection and implementation of augmented intelligence — with the primary responsibility for the quality of care rendered and for patient safety vested with the organized medical staff. These activities depend on mutual accountability, interdependence and responsibility of the organized medical staff and the hospital governing body for the proper performance of their respective obligations."

## PRIOR AUTHORIZATION

Prior authorization is a complex and often frustrating process that physicians face on a regular basis. Of particular concern is the lack of information included in denial letters. That is because appropriate information to understand or appeal the denial itself is not included. For example, patients and physicians may simply be informed that a medication has not been granted prior authorization. Beyond that, no justification as to why the denial took place or an alternative treatment option is provided. "Health-insurer denials must not be a mystery to patients and physicians," said AMA Trustee Marilyn J. Heine, MD. "Without clear information from an insurer on how a denial was determined, patients and physicians are often left to the frustrating guesswork of finding a treatment covered by a health plan, resulting in delayed and disrupted care. Transparency in coverage policies needs to be a core value, an essential principle to help patients and physicians make informed choices in a more efficient health care system." The AMA is working to fix prior authorization by challenging insurance companies to eliminate care delays, patient harms and practice hassles by pushing for payers to include detailed information in prior authorization denial letters and improve the use of real-time benefit tools.

Other Topics that may interest South Dakota Physicians:

- Maintenance of Certification: Scrutiny over the Continuing Board Certification process/Maintenance of Certification (MOC) has been discussed for several years. This year delegates reaffirmed the AMA's existing MOC policies, while asking the AMA to undertake a thorough review and analysis of the available information with a goal to re-examine and potentially update the accepted standards for continuing board certification, so the standards reflect the best manner to assess physicians' knowledge and skills necessary to practice medicine. Additionally, new policy was passed which states that MOC requirements should not be duplicative of continuing medical education requirements, and should not be used to determine or dictate hospital privileges, insurance network credentialing or hiring practices.
- BMI: Delegates voted to adopt policy that supports the removal of BMI as a standard measure in medicine and recognize the culturally-diverse and varied presentations of eating disorders
- Perinatal mental health condition: Delegates voted to pass amended policy that strengthens the AMA's position on screening of perinatal mental health conditions in physicians and medical students. The updated policy now includes referral to services, which expands it beyond screening. The AMA will continue to work with relevant stakeholders to identify ways to increase screenings, reduce stigma, and maintain privacy protections surrounding these diagnoses and treatments for physicians and medical students.
- Mental Health and Substance Abuse: The Board of Trustee's report offered support for Mental Health Courts. Additionally, the HOD resolved to continue efforts to bring about changes in how people with substance abuse disorders are handled and treated in the criminal justice system.
- Delegates opposed the Hospital Readmission Reduction Program.
- Dental Care as part of cancer care was strongly supported. It was noted that some dental care is important prior to certain oncologic treatments, and many treatments, especially radiation treatment result in dental loss and disfiguring conditions of the jaw and maxillary bones. It was stressed that restorative maxillofacial surgery should also be covered for these cancer treatments.
- Maternity care payment was addressed regarding bundling of care. Delegates advocated for separate payment systems for care not address by maternity global codes. They opposed inappropriate bundling of related services.
- Finally, there was a bit of drama regarding the war affecting Israel and Palestine. The delegates were protested outside the convention hotel, and there was heated debate regarding the AMA's response to the war. Many believed that it was outside of the AMA's purview, but all it was reaffirmed that healthcare workers and facilities should be protected in a wartime setting.

Robert L. Allison, MD, Delegate
Mary S. Carpenter, MD, Delegate
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Jennifer J. Tinguely, MD, MPH, SDSMA President

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