February 2024
Volume 77
Number 2

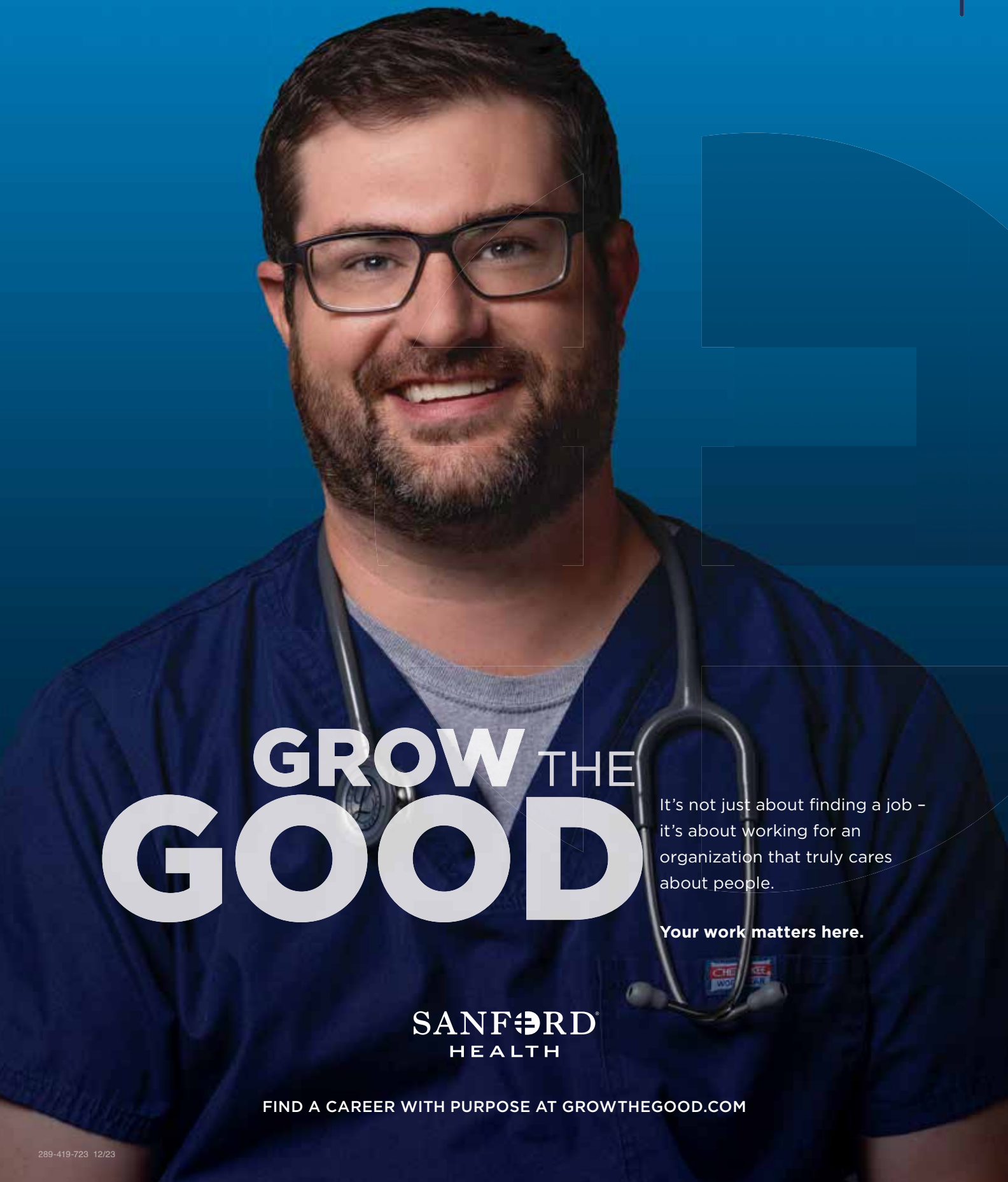
South Dakota medicine

THE JOURNAL OF THE SOUTH DAKOTA STATE MEDICAL ASSOCIATION

UDSSSOM Celebrates 50 Years of the Four-Year Medical School

CAREERS WITH PURPOSE

MATT, RN
A resilient and selfless nurse, Matt has added to the good for 15 years. He leads pulmonary patient care and often mentors new nurses.



GROW THE GOOD

It's not just about finding a job – it's about working for an organization that truly cares about people.

Your work matters here.

SANFORD HEALTH

FIND A CAREER WITH PURPOSE AT GROWTHEGOOD.COM

289-419-723 12/23

Contents

February 2024
Volume 77 | Number 2

Cover photo by Robert Seidel, MD

South Dakota medicine

The Journal of the South Dakota State Medical Association

Office of Publication
2600 W. 49th Street, Suite 100
Sioux Falls, SD 57105
605.336.1965
Fax 605.274.3274
www.sdsma.org

Editor
Keith Hansen, MD

SDSMA President
Denise S. Hanisch, MD

Chief Executive Officer
Barbara A. Smith

Staff Editor
Elizabeth Reiss, MS
–ereiss@sdsma.org, 605.336.1965

Advertising Representative
Elizabeth Reiss, MS
–ereiss@sdsma.org, 605.336.1965

South Dakota Medicine
(ISSN 0038-3317)
Published 12 times per year with one special issue by the South Dakota State Medical Association.

The SDSMA thanks the University of South Dakota Sanford School of Medicine for its financial contributions toward the production of *South Dakota Medicine*.

Subscription price: $50 per year domestic
$65 per year foreign, $8.95 for single copy

Periodicals postage paid at Sioux Falls, South Dakota and additional mailing offices.

Postmaster: Send address changes to
South Dakota Medicine
2600 W. 49th Street, Suite 100
Sioux Falls, SD 57105

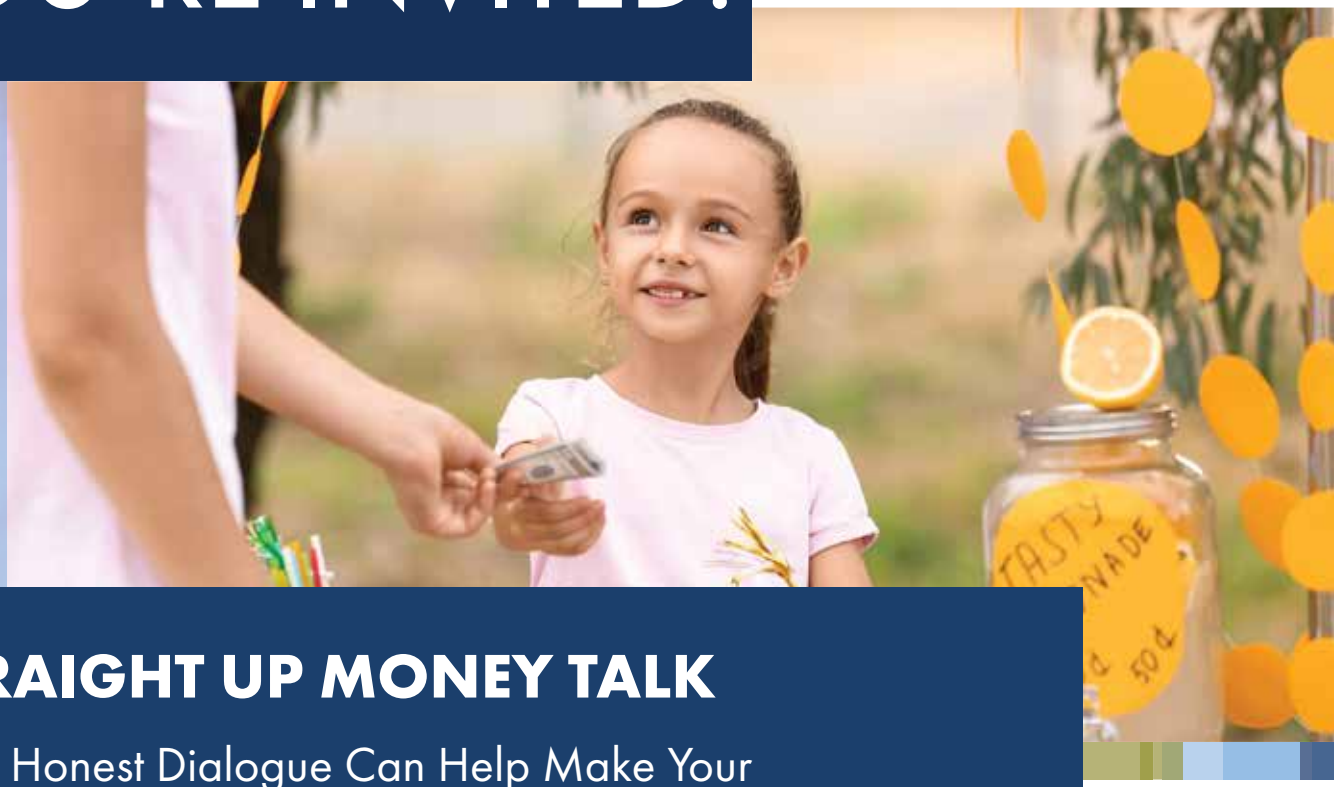
SDSMA Home Page: www.sdsma.org

AMA Home Page: www.ama-assn.org

Printer:
Walsworth
P.O. Box 370
Fulton, Missouri 65251-0370

YOU'RE INVITED!

FOSTER GROUP
Your Financial Life, Truly Cared For®



STRAIGHT UP MONEY TALK

How Honest Dialogue Can Help Make Your Children and Grandchildren Money Smart

Help your children or grandchildren grow up to be financially responsible adults. Join us for a complimentary webinar to learn why and how to have age-appropriate conversations about money with kids of all ages.

WEDNESDAY
FEBRUARY 28, 2024

11:30 A.M.
30 MINUTES

Space is limited.
Reserve your spot today!

RSVP to **FOSTERGRP.COM/SDSMAwebinar**
OR CALL **515-896-0003**

The team at Foster Group is dedicated to providing comprehensive financial life advice, helping clients turn their vision of success into reality.

14301 FNB Parkway, Suite 207 | Omaha, Nebraska | **fostergrp.com/sdsma**

Celebrate

By H. Bruce Vogt, MD, FAAFP

This February 23, the University of South Dakota Sanford School of Medicine (USDSSOM) will celebrate the 50th anniversary of the four-year MD-granting program. The need to expand the program to an MD-granting school became paramount by the early 1970s. Physician-shortage was worsening. In 1972, South Dakota was 50th in the nation in the physician-to-patient ratio. In addition, it had become increasingly difficult for students to transfer to a four-year school to complete MD training. A campaign promoting development of a "school without walls" emphasizing family medicine was led by Karl H. Wegner whose enthusiasm, sincerity, and personal integrity was key to the success.

On Feb. 13, 1974, Gov. Richard Kneip signed SB 30 into law, creating a degree-granting medical school for South Dakota. Onlookers included Sen. Harvey Wollman, second from left, and Dean Karl Wegner, center.

Photo credit: USD SSOM

Has the school been successful? I think the evidence is strong that it has. There are now 2,200 physicians in the state compared to the 588 at the time of approval of the four-year program. The school has grown from an initial inaugural class size of 40 to 71 today. Fifty-seven of first-year students are South Dakotans and 10 are non-residents but with ties. The 36 men and 35 women have graduated from 58 different South Dakota high schools. Thirty-two percent of the 2023 graduates plan to practice primary care, compared to 22% nationally, and over 60% indicate a strong desire to practice in our state. Consistent with the emphasis on rural primary care practice, the Frontier and Rural Medicine (FARM) program has increased from an initial six students in five communities to 13 in eight sites, and a new rural family medicine residency program has been developed in Pierre. Training opportunities in other specialties and subspecialties have also expanded significantly in the last several years. There are now nine residency and six fellowship programs. The significance of this is demonstrated by the fact that greater than 75% of our graduates who have completed residency training in South Dakota have stayed to practice in the state.

USDSSOM has made tremendous strides since institution of the four-year program. Physicians in South Dakota, the vast majority of whom teach our students, are owed a debt of gratitude for their teaching and support. We hope you will join us to celebrate "your" school's success on February 23.

REFERENCES

Dean's Office, USDSSOM.

About the Authors:

H. Bruce Vogt, MD, FAAFP, Professor Emeritus, Department of Family Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Stigma in Treating Chronic Pain: The Obstacles and Our Ethical Imperative

Denise Hanisch, MD
President, South Dakota State Medical Association

The words "crisis" and "epidemic" have both been used when discussing the controversy of opioid use in our country. We understand that the crisis began with overprescribing, but the introduction of fentanyl has drastically increased the death rates related to overdose. According to the Centers for Disease Control & Prevention, death rates due to prescription opioids remained the same from 2020-2021, while the death rate during the same time increased 22% with synthetic opioids.

Prescribing practices have changed in the past 15 years and that is a testament to a physician's willingness to learn and change to provide the best care for our patients. On the other hand, our understanding of the potential for abuse regarding pain medications makes it difficult to know what the right answer is for patients who suffer from chronic pain. People do experience chronic pain and that pain needs to be acknowledged. The American Medical Association reported that over 50 million adults in the U.S. suffer from chronic pain. They deal with pain daily but also must overcome the stigma that accompanies that pain. It was also reported that over 20 percent of outpatient visits are pain related. That is a large portion of our daily practice focused on pain management. The pendulum has swung, from freely prescribing opioids, to some that refuse to prescribe pain medications.

Recently, I had a patient that decided to move closer to family in another state. He had hypertension, diabetes, and severe peripheral vascular disease with edema. He had undergone multiple procedures with stent placements in his lower extremities. He had severe neuropathic pain. We tried all modalities possible to treat his pain including physical therapy, Cymbalta, Lyrica, and leg pumps that he used twice a day. He was compliant with all recommendations but still had pain that was intolerable at times. We had a discussion regarding the use of pain medications, and he understood the risks and benefits. He took 1-2 tablets of hydrocodone a day and he did have moments in his day when he was pain free. We sent all his records to the clinic he had chosen, only for them to refuse to take him as a new patient because of the diagnosis "chronic pain management". He is a patient that had multiple chronic illnesses, all of which need ongoing care, and he was turned away because of 1-2 hydrocodone a day. He was judged and stigmatized before learning his story.

As physicians, we have an obligation to care for all patients. People have all types of illnesses that are difficult to treat. I have people with diabetes who are non-compliant, but I would not refuse to care for them. Mental health and drug addiction issues are escalating and difficult to treat, but turning our back and denying care is not the answer. Acknowledging that these conditions are real, without patronizing or being dismissive, is paramount in making steps forward to improve the health and wellbeing of people who are suffering.

I often fall into the trap of believing that because we live and practice in South Dakota, we are isolated from "big" issues, such as drug addiction and gun violence, that affect the rest of the country. While researching this topic, I read a study published by the American Farm Bureau Federation that made it clear we do not live in an area that is protected against threats to our communities.

In 2017, The American Farm Bureau Federation surveyed over 2,000 farmers and ranchers in rural areas and found that rural residents have higher rates of opioid misuse than people residing in urban areas. The survey also found that 74% of farmers and farm workers have "been directly impacted by the opioid epidemic." Even more surprising, three out of four farmers admitted that it would be "easy for someone in their community to access a large amount of prescription opioids or painkillers without a prescription." The opioid crisis is in our backyard, and we need to be aware because rural residents often do not have reasonable access to care, drug treatment programs or mental health services.

We, as physicians, need to understand that drug addiction, opioid use disorder and mental health are illnesses just as dangerous as heart disease or diabetes. I am aware of how difficult it is to provide medical care for this population but, ignoring these patients or continuing to stigmatize chronic pain and drug use, prevents us from treating the "whole patient."

PHYSICIANS
VEIN CLINICS

WE CHECK ALL THE BOXES

- ☑ Office procedures keep **COSTS DOWN** for patients.
- ☑ Back to work SAME DAY.
- ☑ NO sedation procedures.
- ☑ In-office. NO hospital stay needed.
- ☑ We are an extension of YOUR practice.
- ☑ Accepts most insurances.
- ☑ Better results for YOUR patients.
- ☑ Certified by the American Board of Venous and Lymphatic Medicine.

HEALTHY LEGS. HEALTHY LIFE.

1-888-PVC-VEIN *(782-8346)*

physiciansveinclinics.com

Locations across South Dakota, Iowa, North Dakota, and Minnesota

Lornell Hansen II,
MD, DABVLM, RPhS, FAVLS

Darren Chester,
MD, DABVLM, RPhS

A Case of Chagas Disease in South Dakota: Diagnosis and Treatment

Lillian Schulte, MS III; and Jean Lageson, MD

Abstract

Chagas disease is a chronic, systemic parasitic infection caused by the protozoan *Trypanosoma cruzi*. The primary mode of transmission to humans is by the Reduviid insect, endemic to South America. Recent migration of the vector has led to increased cases in the southern United States and has prompted increased surveillance and blood donation screening. It is unusual to diagnose and treat individuals with Chagas disease in the northern United States. This case describes an immigrant female from El Salvador that was informed she had Chagas disease from a blood bank screening. Confirmation and treatment of the disease were performed by her South Dakota primary care provider thus demonstrating the importance of identifying Chagas disease in the immigrant population in regions where Chagas disease infection is uncommon.

Introduction

The World Health Organization (WHO) estimates between 6 and 7 million people are infected with *Trypanosoma cruzi* worldwide, with the majority living in Latin America.[1] Most individuals infected experience absent or mild initial symptoms. The parasite can remain dormant for many years and later cause chronic infection in 30-40% of infected individuals. Chronic infection can manifest as severe cardiac and gastrointestinal complications.[2]

The primary form of infection follows scratching at the site of a Reduviid bug bite with preceding nearby Reduviid defecation containing *Trypanosoma cruzi* protozoa. Skin excoriation leads to the potential inoculation of an individual with nearby fecal matter containing the protozoan. Figure 1 demonstrates *T. cruzi* lifecycle and infection pattern. Other emerging transmission routes include consumption of contaminated food products, vertical transmission, contaminated blood or organ product, and laboratory accidents.[1] Due to the risk of contaminated blood products, the Food and Drug Administration (FDA) approved a serological test for *T. cruzi* blood screening that started being used widely in the United States in January of 2007.[3]

While a growing number of local acquisitions of Chagas disease has occurred in the southern U.S., the disease is largely restricted to the immigrant population in northern states. The South Dakota Department of Health does not routinely report Chagas disease as a part of their infectious disease surveillance program.[4] Rare, reported cases in the state are seen predominantly in people with a travel history to South America. The immigrant population in South Dakota was reported to be 35,175 individuals in 2018. Immigrants from South America have grown to make up a large portion of the state's immigrant population.[5] The increasing South American immigrant population and increasing local spread in the southern United States highlight the importance of identifying and treating Chagas disease infection in local communities.

Case Report

A 31-year-old female from rural El Salvador first presented to the Sioux Falls Avera Medical Group (AMG) Health Care Clinic in June 2018 to establish care and to complete her annual well-woman exam. While giving her past medical history she stated that during a blood donation in February 2017 in Florida she screened positive for Chagas disease. She had received a letter detailing that she was advised not to donate blood or organs in the future and that she should seek treatment. Due to her uninsured status while living in Florida, she was unable to be seen for evaluation and treatment. She moved to Sioux Falls, South Dakota, in 2018 and was seen at the AMG clinic where patients are provided access to healthcare regardless of insurance status. At her initial encounter, she denied chest pain, tightness, pressure, or palpitations. She denied dyspnea on exertion, pedal edema, or orthopnea. She notes occasional abdominal bloating but

It's time to REALLY LIVE

Quitting tobacco can make all the difference.

With South Dakota QuitLine, patients can choose the best FREE way for them to put out the last cigarette, let the vape pen die and close that chewing tobacco tin for good. Choose from enhanced phone and video coaching, the self-driven Kickstart Kit, hybrid coaching through text and phone or the comprehensive Quit Guide. Patients CAN leave tobacco in the past and live more **good** years.

Did you know that Chantix is available to the public at **NO COST** with a prescription?

Encourage patients ages 13+ to call the QuitLine today!

1-866-SD-QUITS

1-866-737-8487 | SDQuitLine.com

SOUTH DAKOTA QuitLine

Brought to you by the South Dakota Department of Health and the South Dakota QuitLine.

Figure 1. *Trypanosoma cruzi* lifecycle and human infection cycle.

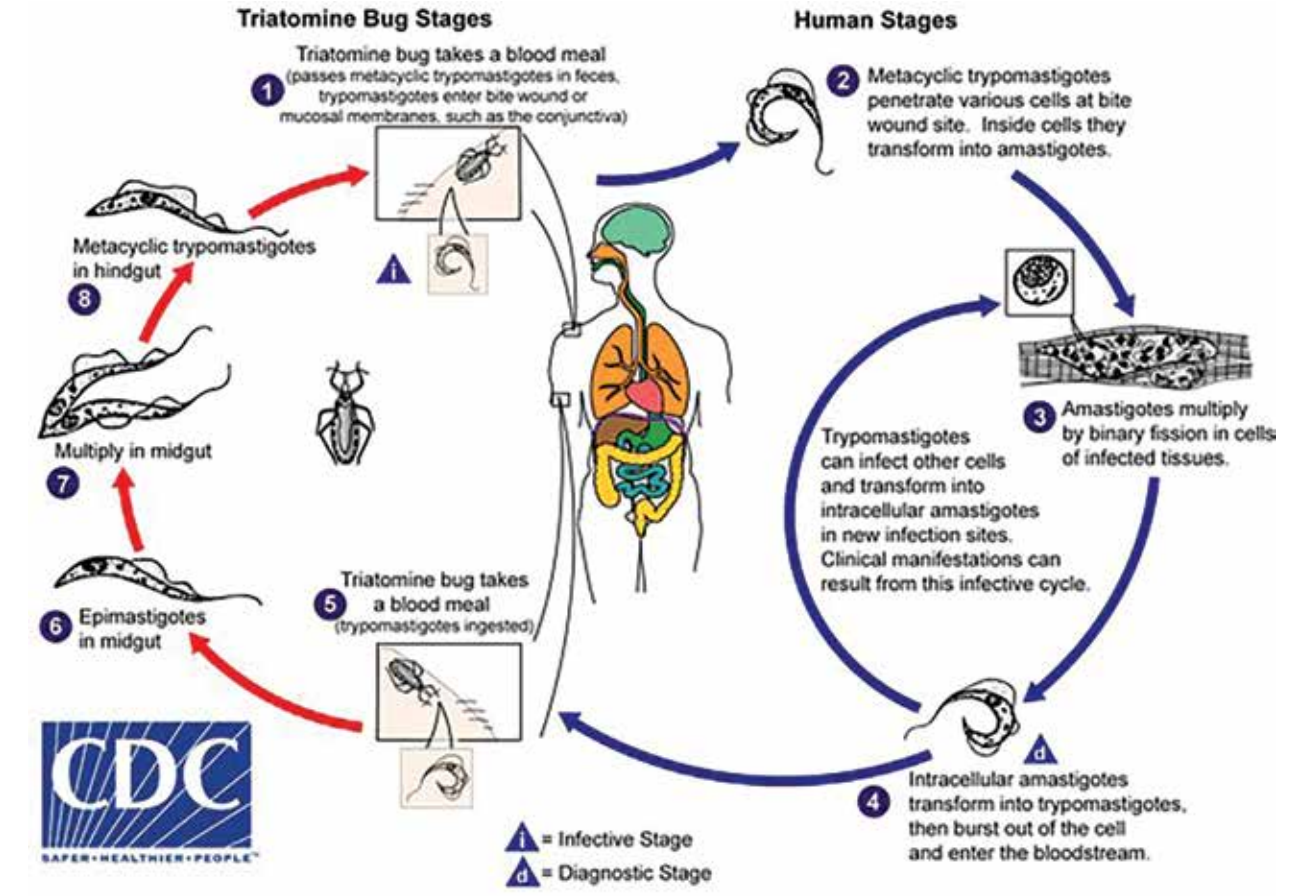
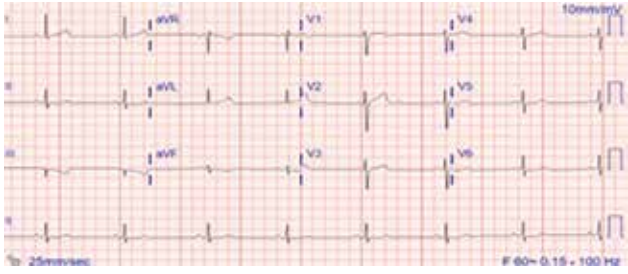


Image courtesy of the Center for Disease Control and Prevention Public Health Image Library ID#3384.

denied diarrhea, constipation, nausea, and vomiting. No melena or hematochezia was noted. An eletrocardiogram (EKG) completed at her initial encounter showed sinus bradycardia with borderline T abnormalities in the inferior leads (Figure 2). Initial history and exam deemed the patient as asymptomatic. The patient's uninsured status at the time of initial exam did not allow for further echocardiogram or cardiac workup. The patient's cardiovascular health was assesed with EKG readings at subsequent appointments. No concerning changes from her original EKG were noted on subsequent EKG tracings.

Figure 2. The patient's EKG shown was obtained in June 2018 demonstrating sinus bradycardia and borderline T abnormalities. Subsequent EKG tracings show no substantial change to this preliminary EKG. Consent to use images from the patient's medical record has been provided.



Due to the rarity of Chagas disease encounters in South Dakota, her primary care provider collaborated with a Center for Disease Control and Prevention (CDC) Chagas disease expert for guidance on current diagnosis and treatment protocol. CDC parasitic disease prevention contact information is provided in Table 1. Following consultation, the patient was advised to provide a blood sample to send to the CDC for further confirmatory testing. The CDC completed a *Trypanosoma cruzi* antibody immunoblot assay. Current CDC guidelines state that a reactive test has an optical density (OD) > 0.330.[6] The patient's OD was 2.486 indicating a positive test consistent with a *T. Cruzi* infection.

At a follow-up appointment scheduled to deliver confirmatory

Table 1. CDC Parasitic Disease Inquiries hotline phone number and email contact information.

Center for Disease Control and Prevention Parasitic Disease Inquiries	
Phone Number	404-718-4745
Email	chagas@cdc.gov

Information obtained directly from Center for Disease Control and Prevention Parasitic Disease Inquiry Contact Resources.[6]

test results and to discuss treatment, the patient notified her primary care provider that she is pregnant. Due to the teratogenic effects of approved trypanocidal medication, treatment was deferred until after delivery. While pregnant, the patient's healthcare was covered by Medicaid and she transferred care to the local obstetrical care team who were also provided with positive Chagas disease test results. The patient was assessed at routine prenatal appointments and had no concerning changes in cardiac or gastrointestinal function related to Chagas disease during pregnancy. In January 2019 the patient met with an infectious disease specialist. The specialist recommended that she receive an echocardiogram six weeks post-partum to evaluate cardiac function before starting treatment. The treatment recommendation given is to complete a minimum of 60 days of 100 mg benznidazole three times a day (TID). The patient was advised to avoid pregnancy during treatment and three months following treatment. It is recommended to have the newborn, post-delivery, and existing children tested for *T. cruzi* infection due to the risk of vertical transmission of Chagas disease. Testing and treatment of the patient's children, following the CDC's recommended Chagas disease pediatric dosing guidelines, was completed by the children's pediatrician. The specific details of the patient's children's disease course and treatment are not further expanded on in this discussion due to their minor status and receiving consent solely from the adult patient.

The patient remained asymptomatic post-delivery and was nursing at the time of her post-partum visit. She was cautioned that it is not safe to nurse while taking benznidazole. The patient discontinued nursing to begin treatment. The medication was obtained from the state's patient assistance program. Unfortunately, due to the patient's uninsured status post-partum, she could not receive the recommended echocardiogram before treatment initiation. Subsequent chest X-rays and EKGs did not demonstrate any concerning cardiac features, so the patient was instructed to begin treatment. She began a 90-day treatment of 100 mg of benznidazole TID in April 2019. One month into treatment, the patient experienced a pruritic rash on her hands and face that subsequently spread to the rest of her body. There was concern that this was an adverse reaction to the medication. Discontinuation was advised, but due to a communication error, she continued the benznidazole regimen. The rash subsequently improved with medication adherence. The patient completed treatment without any further complications. The patient continues to receive follow-up care and routine screening from the clinic.

Discussion

Chagas disease is predominantly asymptomatic or mild in many acutely infected individuals but poses a risk for severe chronic disease. Between 30 and 40% of infected individuals will develop cardiomyopathy, digestive megaesophagus, megacolon, or both.[2] The risk of cardiac and digestive complications emphasizes the importance of preventing infection, identifying the disease in infected individuals, and implementing appropriate treatment.

The chronic gastrointestinal Chagas disease manifestations are a result of enteric nervous system injury caused by *T. cruzi* infection, and nearly one-third of patients with Chagas disease develop dilation of their gastrointestinal tract.[7] Matsuda et al. found, in an evaluation of 1,708 chagasic chronic post-mortem examinations, megacolon was the most frequent gastrointestinal manifestation followed by megaesophagus. Other gastrointestinal findings include megasmall intestine, megagallbladder, megacholedochus, achalasia of the cardia, changes in gastric receptive relaxation, fast gastric emptying of liquid meals, delayed gastric emptying of solid meals, altered small intestine transit, impairment of colon and gallbladder motility, hypertrophy of the salivary glands, and increased rate of peptic gastric lesions when in conjunction with *H. pylori* infection.[7]

Chagas heart disease is another major cause of morbidity and mortality for those infected by *T. cruzi*. The cardiovascular pathophysiology is influenced by parasite persistence in conjunction with an inflammatory response which leads to chronic fibrosing myocarditis, ventricular remodeling, and damage to the electrical conduction system.[8] Figure 3 illustrates a magnified heart tissue sample that has been infected with *T. cruzi* amastigotes in their leishmanial form.[9] This disruption of cardiac tissue can lead to patients presenting with bradyarrhythmia, tachyarrhythmia, cardioembolic events, heart failure, and sudden death. An elevated 10-year mortality rate, ranging from 10% in the low-risk group to 84% in the high-risk group with sudden cardiac death being the primary mode of death for those with Chagas heart disease.[8]

Figure 3. Heart tissue sample magnified 1125x demonstrating *T. cruzi* amastigote clusters in their leishmanial form. Micrographic finding that is seen in Chagas heart disease.

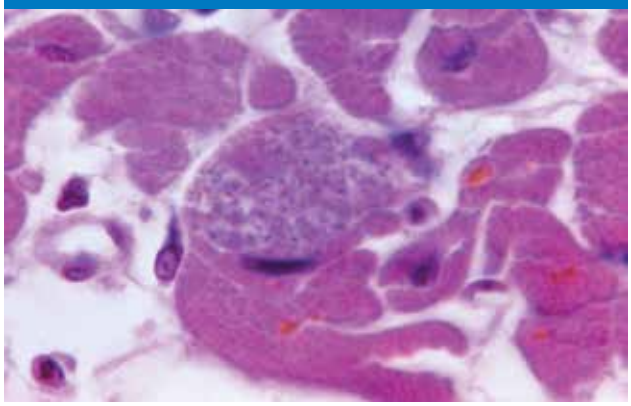


Image courtesy of the Center for Disease Control and Prevention Public Health Image Library ID#21123.

Currently, Chagas disease is endemic in 21 countries, with the vast majority being in Central and South America.[10] Those at highest risk are individuals from rural settings where exposed wood in walls and roofs and dirt floors increases chance of reduviid insect exposure.[6] As immigration continues to rise, between three hundred thousand and one million people in the United States have chronic Chagas disease. Most are unaware of their condition but are at risk of developing Chagas's heart disease.[8] Improvements in Chagas disease detection and management include large-scale vector control programs, effective trypanocidal drugs, and blood donor screening. With the increased vector and human migration, Chagas disease has begun to emerge as a health problem in non-endemic regions where early detection and treatment protocols are not widely practiced.[2]

The U.S. FDA approved a Chagas disease blood screening test in 2007. Between 2007 and 2019 the Association for the Advancement of Blood & Biotherapies Chagas Biovigilance Network (AABB) reported 15,999 blood donors screened positive with an initial reactive test result for Chagas disease.[11] Figure 4 shows the United States' graphical distribution of confirmed positive screenings. Of note, our patient's positive screening was conducted in Florida and is not represented in the South Dakota portion of Figure 4. Individuals screening positive would receive notice to discontinue donating blood or organ products in the future and a recommendation to further follow-up for confirmatory testing and treatment with a primary care provider. Additionally, individuals with a known risk due to travel or migration from the endemic region can present to their primary care provider and request screening testing.

Many reported cases in non-endemic regions are in the immigrant population. In 2018, South Dakota reported 35,175 foreign-born individuals composing 4% of the state's population. Another 4% of the state's population had at least one immigrant parent. The top countries of origin for immigrants residing in South Dakota include Guatemala, the Philippines, and Mexico.[5] Guatemala and Mexico are both regions where Chagas disease is endemic in the population. With an increasing immigrant population from regions with endemic disease, providers in South Dakota need to remain

Figure 4. Distribution of confirmed positive Chagas disease blood donations in the United States 2007-2019.

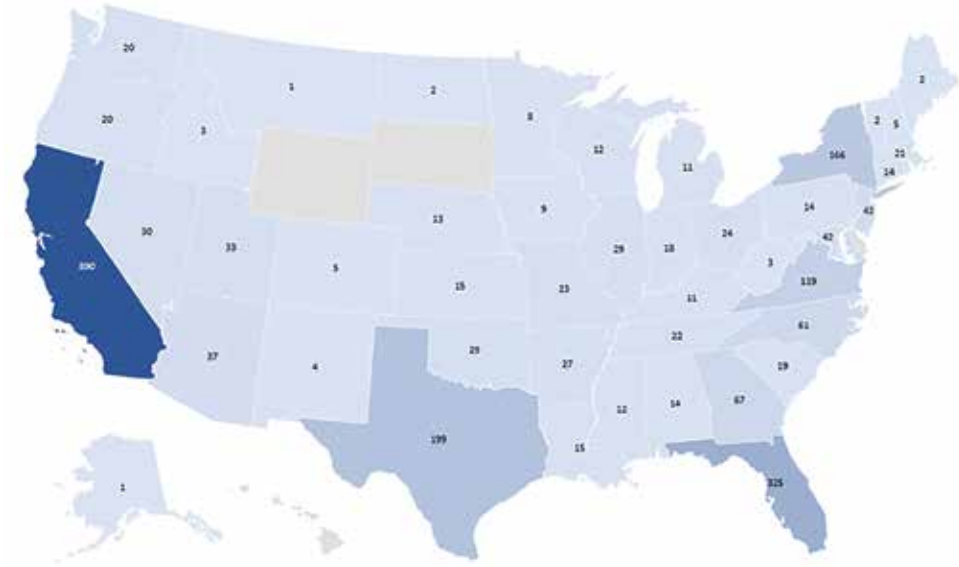


Photo courtesy of the Association for the Advancement of Blood & Biotherapies Chagas Biovigilance Network.

QUIT BIG QUIT FOR KEEPS.

Making a big change takes guts.

It takes being unafraid of shifting your normal. It takes the confidence to know you can do it... you ***should*** do it. When it comes to quitting tobacco, procrastination is the enemy — don't let putting it off... ***take years off.***

Varenicline

Your patients have options — and with free prescriptions* to varenicline (generic Chantix) available, it's easier than ever to remove the barriers to quitting, particularly if their quit journey has hit bumps in the past.

Want to find out more about free-of-charge varenicline options for your patients?

Contact us at 1-866-SDQUITS today.

QuitTobaccoSD.com

*Receiving a free prescription of varenicline or bupropion requires a prescription from a provider, which may include an office visit charge or copay, depending on insurance status. The medication itself can be offered at no charge when you enroll in coaching with the South Dakota QuitLine.

Paid for by the South Dakota Department of Health.

Help Shape the Future of Medicine in South Dakota

The South Dakota State Medical Association Foundation, the philanthropic arm of the South Dakota State Medical Association, is a tax-exempt 501(C)(3) non-profit corporation, was established to assist and support medical research, medical teaching and medical education at the Sanford School of Medicine.

On average, medical students graduate with $130,000 in debt. Contributions to the South Dakota State Medical Association Foundation provide financial assistance to students at the Sanford School of Medicine and are all designated for scholarships, grants and low-interest loans for students.

Any amount can be donated at any time throughout the year. If you have questions or want more information, please call 605.336.1965.

Send Your Contributions Today To:
South Dakota State Medical Association Foundation
2600 W 49th St Ste 100, Sioux Falls, SD 57105
Or contribute online at www.sdsma.org

SOUTH DAKOTA
State Medical Association Foundation
Shaping the Future of Medicine in South Dakota

vigilant for signs of the disease and educate patients with increased risk on screening options.

The current CDC standard approach to the serological diagnosis of Chagas disease is to apply two or more tests that use different techniques to detect antibodies to varying antigens associated with Chagas Disease. The most widely used diagnostic techniques are the enzyme-linked immunosorbent assay and an immunofluorescent antibody test.[6] Patients who subsequently screen positive on two or more tests should receive trypanocidal drugs, such as benznidazole. Patients undergoing treatment should be counseled on the potential risks of benznidazole such as genotoxicity, carcinogenicity, embryo-fetal toxicity, and hypersensitivity skin reactions.[12]

This case demonstrates a positive blood-bank screening resulting in patient identification and treatment for Chagas disease in a non-endemic region. The patient in this case underwent subsequent testing from the CDC and was counseled on treatment options due to pregnancy at the time of confirmatory diagnosis. Providers in South Dakota and other non-endemic regions should be able to recognize at-risk patient populations and formulate appropriate diagnostic and treatment options. There are currently no formal screening processes in place for individuals at high risk of Chagas disease infection. Women of childbearing age from rural endemic regions are at higher risk of infection and subsequent transmission to future children. This case indicates that further exploration into formal screening recommendations may be important.

REFERENCES

1. World Health Organization. Chagas disease (American trypanosomiasis). 2019. Retrieved from www.who.int/news-room/fact-sheets/detail/chagas-disease-(american-trypanosomiasis).
2. Rassi A Jr, Rassi A, Marin-Neto JA. Chagas disease. Lancet. 2010;375(9723):1388–1402.
3. Bern C, Montgomery SP, Katz L, Caglioti S, Stramer SL. Chagas disease and the US blood supply. Current Opinion in Infectious Diseases. 2008;21(5):476–82.
4. Clayton J. Infectious Disease Surveillance – South Dakota Department of Health. 2022. Retrieved from https://doh.sd.gov/statistics/surveillance/.
5. Immigrants in South Dakota. American Immigration Council. 2022. Retrieved from www.american-immigrationcouncil.org/research/immigrants-in-south-dakota.
6. Centers for Disease Control and Prevention. Chagas disease - resources for health professionals. 2022. Retrieved from www.cdc.gov/parasites/chagas/health_professionals/dx.html#:~:text=In%20December%202006%2C%20the%20U.S.%20Food%20and%20Drug.
7. Matsuda NM, Miller SM, Evora PRB. The chronic gastrointestinal manifestations of Chagas disease. Clinics. 2009;64(12):1219-24.
8. Saraiva RM, Mediano MFF, Mendes FS, Sperandio da Silva GM, Veloso HH, Sangenis LHC, Silva PS, et al. Chagas heart disease: an overview of diagnosis, manifestations, treatment, and care. World Journal of Cardiology. 2021;13(12):654-75.
9. Green. Details - public health image library (phil). Centers for Disease Control and Prevention. 1968. Retrieved from https://phil.cdc.gov/Details.aspx?pid=21123.
10. Jannin J, Villa L. An overview of Chagas disease treatment. Memórias Do Instituto Oswaldo Cruz. 2007;102(suppl 1):95-8.
11. Chagas Biovigilance Network. 2019. Retrieved from www.aabb.org/news-resources/resources/hemovigilance/chagas-biovigilance-network.
12. Food and Drug Administration. Highlights of prescribing information-benznidazole tablets. 2017. Retrieved from www.accessdata.fda.gov/drugsatfda_docs/label/2017/209570lbl.pdf.

About the Authors:

Lillian Schulte, MS III, University of South Dakota Sanford School of Medicine.

Jean Lageson, MD, Avera Medical Group Health Care Clinic, Sioux Falls, South Dakota; Clinical Associate Professor, Department of Internal Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

The Coyote Clinic: A Student-Run Free-Clinic

Cole D. Tessendorf, MS III; Tiffany Bender, MPH, MS III; Joseph Reynen, MS II; Sydney Bormann, MS IV; and Mark N. Beard, MD

Mission: *To increase access to quality healthcare, promote health equity, and enhance the well-being of Sioux Falls community members through teaching, innovation, and compassion.*

Vision: *To enhance the community's well-being by providing free healthcare and public health outreach services to underserved individuals through an interdisciplinary collaboration led by Sanford School of Medicine medical students.*

The Coyote Clinic is a student-run clinic that provides free health care services to underinsured and uninsured members of the Sioux Falls community. Successfully blending public service and experience-based training for medical students, the Coyote Clinic has empowered medical students to serve in a primary care role for underserved patients for almost two decades. What began in 2006 as a small group of students holding a monthly clinic night has evolved into a well-known Sioux Falls resource spearheaded by an 18-person steering committee.

The 100% volunteer-based clinic has now grown to offer weekly internal medicine clinic nights, monthly psychiatry clinic nights, and a bi-monthly pop-up clinic at the Bishop Dudley Hospitality House. Other key moments of growth included adding pre-medicine undergraduate students to the volunteer pool in 2018 and implementing an on-call model in 2022 where patients can present for walk-in acute care services during clinic nights without scheduled appointments. More recently in 2023, USD nursing students were integrated to provide additional interdisciplinary partnership opportunities.

The Coyote Clinic has also fostered a commitment to community service and acted as an opportunity for medical students to develop as leaders. In addition to the clinic nights, student committee members oversee and implement several research and quality improvement projects. Many of these efforts have been presented at national conferences and published in peer-reviewed journals, such as the *Journal of Student Run Clinics*. The committee also conducts outreach events across South Dakota, including flu shot drives and screening events at local food shelters, the Health Connect Fair, Turner County Fair, and Feria de Salud.

The Coyote Clinic is overseen by a steering committee of 18 medical students. The steering committee is further specialized into sub-committees that oversee the various functions of the clinic. Figure 1 is a visual representation of the clinic leadership organization. While the student steering committee conducts the majority of the clinic's day-to-day operations, Dr. Mark Beard, Dr. Mary Schmitz, and Dr. Mamoon Ahmed serve as faculty advisors. They are available for administrative and legal guidance, while also regularly volunteering at clinic and outreach events.

Patient Care Services

The internal medicine clinic occurs every Tuesday night at the Avera Downtown Clinic, in which services in primary care, acute care, and sports physicals may be provided. Appointments are scheduled between 5:30 p.m. and 7 p.m., and patients may be self-scheduled or referred by other clinics or Coyote Clinic outreach events. All necessary labs can be collected on site and physician supervisors may write prescriptions as needed. Prescription cost assistance is offered as needed via partnerships with local HyVee and Lewis pharmacies.

On a typical clinic night, the team consists of an attending physician, an internal medicine resident, Coyote Clinic steering committee members, medical student volunteers, nursing students, a nursing faculty supervisor, a pre-medicine undergraduate student, and Avera Downtown Clinic staff members.

Nursing and undergraduate students room the patient and obtain vitals, allergies, medications, and other past medical

EM PROVIDERS NEEDED

Help build healthier Native American communities

We're looking for **EM physicians, PAs, and nurse practitioners** to cover gaps in Indigenous healthcare. As part of our Quick Response Force, you will:

- Commit to a standing call schedule (10-14 shifts/month)
- Deploy as needed to IHS emergency departments
- Make an immediate impact you can measure
- Earn $150K salary + $250/hr shift pay (MD) or $100K salary + $100/hr shift pay (PA/NP)

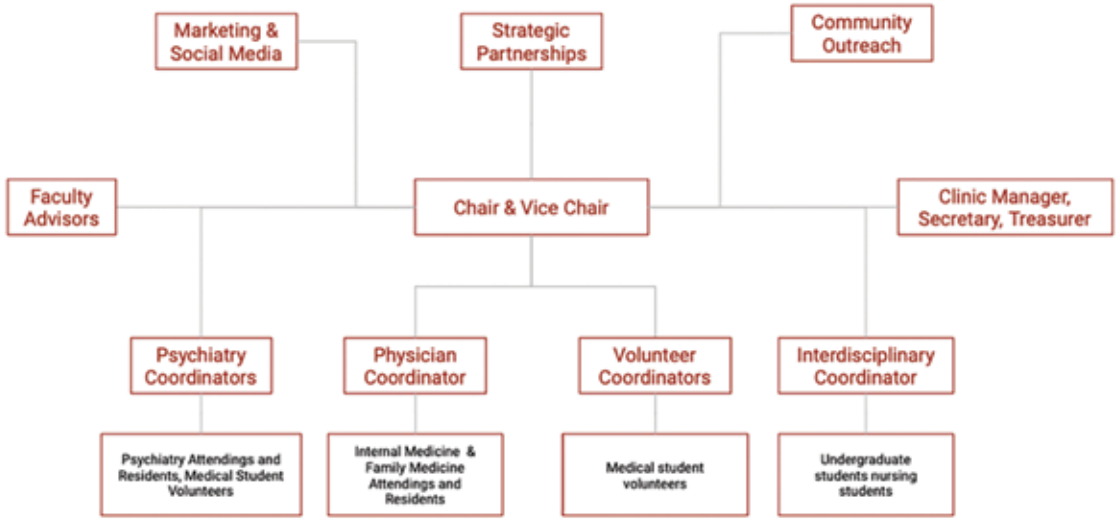
Join the leading provider network in Native health – and embark on what our physicians have called

"the most rewarding chapter in my career."

To get started, email:
Arthur Sakakihara-Chavarria MS-APA, PA-C
art@tribalhealth.com

TRIBAL HEALTH

Figure 1. Organizational chart of Coyote Clinic leadership.



history. Because many patients are non-English speaking, the nursing and undergraduate students also facilitate translator services. They present the patient to a medical student team who will then see and assess the patient, and afterward present their assessment and plan to the attending physician and/or resident physician. Nursing and undergraduate students are encouraged to be involved in the medical decision-making discussion.

In 2019, the Coyote Clinic partnered with psychiatrists from Avera Behavioral Health to address psychiatric care for both adolescents and adults. The psychiatry clinic occurs the first Wednesday of each month at the Avera Downtown Clinic, and the workflow is similar to the internal medicine clinic night.

The Bishop Dudley Hospital House (BDHH) is a non-profit organization founded in 2015 that provides support services, resources, and shelter to low socioeconomic status and homeless community members of Sioux Falls. Recognizing that transportation, physical access, and healthcare costs are major barriers for residents of BDHH, the Coyote Clinic instituted a satellite clinic on-site at BDHH in February 2022. The BDHH clinic is set up as a triage service open from 6:30 p.m. until 8:00 p.m. on the first and third Monday of the month. If the diagnosis is more complex or additional testing is needed, patients are referred to the Coyote Clinic's internal medicine or psychiatry clinics. This outreach clinic holds bimonthly pop-up clinic nights, and it is currently the only scheduled clinic night outside the walls of the Avera Downtown Clinic.

Community Outreach

Outreach programs and events are a large component of Coyote Clinic's mission to provide care for all community members in need. The Community Outreach Coordinator works closely with public health organizations across the state to identify events where Coyote Clinic can perform health screenings and health education.

A hypertension screening program was developed at The Banquet, a local food shelter in Sioux Falls. Each year, four medical students volunteer to conduct weekly blood pressure screenings at two Banquet locations. Banquet guests who screen positive for hypertension or who need other healthcare services are referred to Coyote Clinic for further care. And every fall, the clinic conducts a flu shot drive at the two Banquet locations in Sioux Falls. Over the years, this opportunity has allowed medical students to administer hundreds of vaccinations under the supervision of physician volunteers.

The Coyote Clinic also conducts free health screenings at various health fairs and events across the state including the Feria de Salud, Turner County Fair, Health Connect Festival, and Connecting Caregivers event. The Feria de Salud is a health fair for the Latino community that offers free onsite health screenings for heart disease, cancer, and diabetes. Coyote Clinic volunteers provided hypertension and blood glucose screening at the event. The Turner County Fair is a local county fair in Parker, South Dakota, where Coyote Clinic volunteers provide skin cancer and sun protection awareness and distribute educational materials to fairgoers.

for baby's sake

SOUTH DAKOTA DEPARTMENT OF HEALTH

safe sleep for SD INFANTS

In South Dakota, from 2018-2022:

There were **97 infant deaths** related to sleeping or the sleep environment

Of the 97 sleep-related deaths:

Over half (66%) of infants **were sharing a sleep surface*** with another adult and/or child when found

53% of infants were **bed-sharing in an adult bed** with another adult and/or child when found

84% of these sleep-related deaths were **potentially preventable**

*Sleep surfaces - couch, chair, bed, floor, mattress

SOURCE: Child Death Review, South Dakota, 2018-2022

Factors that increase risk when bed-sharing or surface sharing:

VERY HIGH RISK

*More than **10X** the baseline risk of parent-infant bed-sharing*

- Sleep surface is soft, such as a waterbed, old adult mattress, couch, or armchair
- Adult is very tired, taking medication that makes them drowsy, using substances like alcohol, or whose ability to respond is affected in some way.
- Adult smokes cigarettes or uses tobacco products (even if they do not smoke in the bed)

HIGH RISK

***5-10X** the baseline risk of parent-infant bed-sharing*

- Baby is younger than 4 months old (regardless of adult smoking or sleep surface)
- Adult is not the baby's parent, but is another caregiver, such as a grandparent or sibling

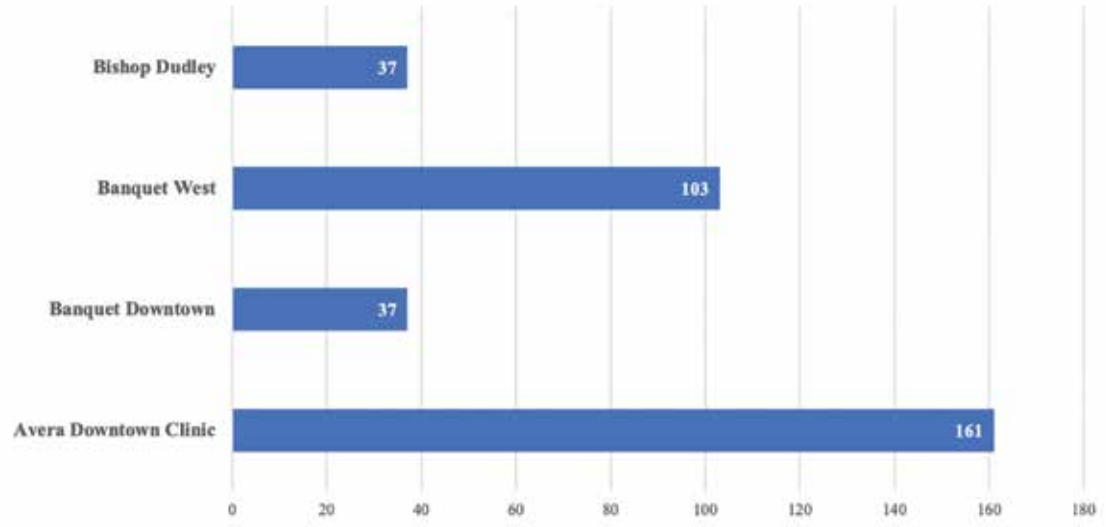
HIGHER THAN AVERAGE RISK

***2-5X** the baseline risk of parent-infant bed-sharing*

- Baby was born preterm (before 37 weeks) or born at a low birth weight
- Sleep area includes unsafe items, such as pillows or blankets

SOURCE: Safe to Sleep® Safe Sleep for Your Baby booklet.

Figure 2. Patient encounters by location, November 2022-October 2023.



This year at the Health Connect Festival, an annual event in Sioux Falls where families can learn more about health and safety, Coyote Clinic volunteers played an educational anatomy game and taught youth attendees healthy habits. In conjunction with the South Dakota Department of Health, the Coyote Clinic has also conducted several STI screening events at the downtown clinic location to help combat the rise of STIs in South Dakota.

Coyote Clinic by the Numbers

The steering committee utilizes Research Electronic Data Capture (REDCap), a secure web-based application in which patient information can be entered and utilized for research and health quality improvement projects. All patients seen at internal medicine and psychiatry clinic nights, the BDHH pop-up clinic night, and The Banquet hypertension program were logged into REDCap. In addition, patients seen at the Avera Downtown location for internal medicine and psychiatry clinic nights were also documented in Avera's electronic medical record system, but these records were not used for research purposes.

From November 2022 to October 2023, 161 patients were seen at the Avera Downtown location. This includes internal medicine and psychiatry clinic night appointments, as well as walk-ins. Of these patients, 80 presented for sports physicals. Currently, patient information in REDCap has only been recorded by location, so it was unable to determine internal medicine versus psychiatry appointments.

The hypertension referral program that takes place at the Banquet Downtown and Banquet West locations successfully screened 37 and 103 patients, respectively, for a total of 140. The BDHH pop-up clinic successfully triaged and documented 37 patients. However, the steering members endorse inconsistencies in correctly documenting all patients seen at BDHH. Patient numbers seen are likely greater than shown. Effective as of October 2023, the steering committee designated a committee member as the BDHH Coordinator with the goal of mediating documentation inconsistencies. Patient encounters for all locations can be seen in Figure 2.

Other notable statistics from patient encounters were the

Figure 3. Age of patients seen, November 2022-October 2023.

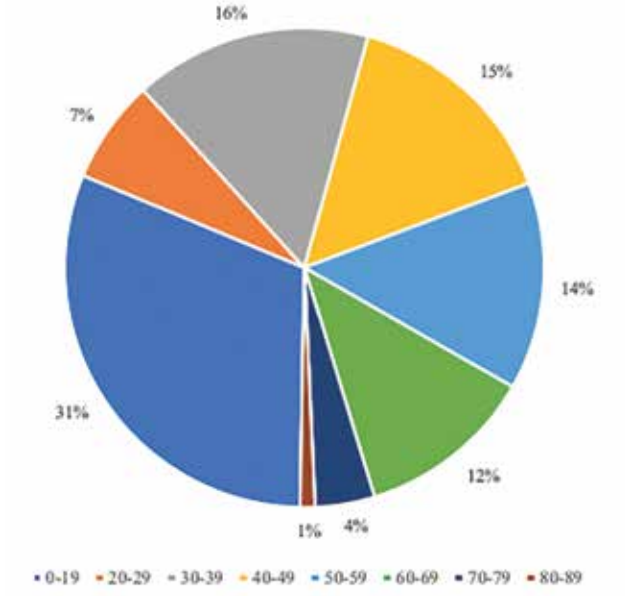
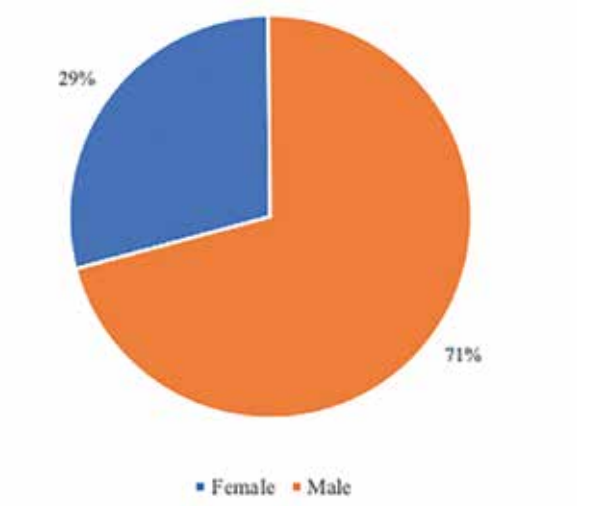


Figure 4. Sex of patients seen, November 2022-October 2023.



ages, gender, and primary languages. As seen in Figure 3, 31 percent of patients seen were 19 years or younger. In contrast, 31 percent of the patients were aged 50 and older. Seventy-one percent of patients were male, as seen in Figure 4. Primary languages of the patients were also obtained. Of all patients seen at the four locations, 45 percent of patients identified English as their primary language. Fifty-one percent of patients identified Spanish as their primary language, and the other 4 percent listed neither English or Spanish as their primary language.

About the Authors:
Cole D. Tessendorf, MS III, University of South Dakota Sanford School of Medicine.
Tiffany Bender, MPH, MS III, University of South Dakota Sanford School of Medicine.
Joseph Reynen, MS II, University of South Dakota Sanford School of Medicine.
Sydney Bormann, MS IV, University of South Dakota Sanford School of Medicine.
Mark N. Beard, MD, Sanford USD Medical Center, Sioux Falls, South Dakota; University of South Dakota Sanford School of Medicine.

Formation of a Pseudoaneurysm after a .22 Caliber Bullet Embolized to the Left Femoral Artery: A Case Report

Kahlen R. Morris, MS IV; Joseph C. Rath, MS IV; and Robert E. Miller, MD

Abstract

Bullet embolization is a rare and potentially life-threatening complication of gunshot wounds, particularly in low-powered and small-caliber bullets. When these small bullets enter a large elastic vessel, they have the potential to leave a small entrance hole that can form a traumatic pseudoaneurysm. These pseudoaneurysms, which may be life-protecting at first, may rupture and lead to exsanguination if not found. We report an interesting case of an 18-year-old male gunshot victim where a bullet formed an aortic pseudoaneurysm and subsequently embolized and present a review of the literature regarding bullet embolization and traumatic pseudoaneurysms.

FIntroduction

Bullet embolization is a rare and potentially life-threatening complication of gunshot injuries. Venous embolization is more common than arterial, with the portal vein and paradoxical emboli – the transformation of venous to arterial embolization bypassing pulmonary circulation – being exceedingly rare.[1,2] Small caliber bullets are more commonly embolized in part due to their size combined with a lower relative velocity.[1,3,4] A projectile traveling at a relatively slower velocity could be slowed enough by the impact to stop within an artery or vein and be swept downstream by blood flow. These emboli have the possibility of presenting asymptomatically thereby risking life and limb.

In a review of 7,500 gunshot wounds during the Vietnam War, there was a 0.3% incidence of bullet emboli.[3,4] Bullet embolism is a rare phenomenon, and the true incidence of noncombat bullet emboli is currently unknown.[2] In certain situations there should be a high suspicion of bullet embolization. For example, patients who become hemodynamically unstable with injuries where the final location of the bullet does not match the entrance trajectory or the number of entrance and exit wounds don't match. Radiologic imaging may also not correlate to the clinical and historical picture (e.g., a patient is shot in the chest but on x-ray, the bullet is found in the popliteal fossa). Situations like these could suggest a bullet has embolized and possibly left a pseudoaneurysm that ruptured causing a drastic change in hemodynamics.[2,5,6]

The purpose of this manuscript is to present an interesting case of bullet embolization from the abdominal aorta to the left femoral artery, as well as discuss bullet embolization and the formation of traumatic pseudoaneurysms.

Case Presentation

Initial Presentation

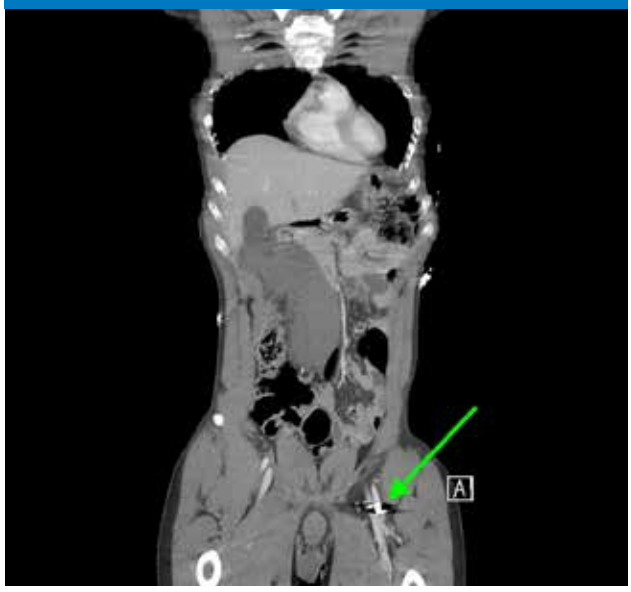
A previously healthy 18-year-old male was transferred via ambulance to our emergency department from a rural facility as a level one trauma status post accidental gunshot wound to the right upper flank approximately 1.5 hours before arrival. The patient was transferred due to the need for a higher level of care. The patient was briefly seen at the outside facility where he received a bolus of tranexamic acid, Zofran, Ancef, and fentanyl, and began receiving intravenous (IV) fluids, and 1 unit of O- blood. During the 32-mile transfer to our facility, the patient finished receiving 1 unit of blood and 1.5 liters (L) of saline.

Upon arrival at our facility, the patient's vitals were 36.5° C (97.7° F), 96 beats per minute, 21 respirations per minute, blood pressure 141/103, and 100% SpO_2 on 2.5 liters/min of supplemental oxygen via nasal cannula. Physical examination confirmed a posterior right flank gunshot entry wound approximately four inches above the posterior iliac crest. There was no exit wound. Peripheral pulses were intact bilaterally. It was noted at the outside facility that the patient's left leg had started to look mottled but motor function and femoral pulse remained intact bilaterally. The patient was awake, alert, and agitated. Plain films from the transferring facility confirmed a .22 caliber projectile in the left groin.

The patient was urgently taken to CT and trauma

surgery initiated massive transfusion protocol. CT scans demonstrated a central posterior abdominal major vessel injury. Other CT scan findings included: a grade III right inferior lateral liver laceration, shattered contained right kidney, central retroperitoneal and central abdominal major arterial/venous injury, and the supposed projectile directly adjacent to the left common femoral artery (Figure 1, arrow). As a result, the patient was taken emergently to the operating room, and emergent surgery was performed by the trauma surgery team (TS), vascular surgery team (VS), and urology.

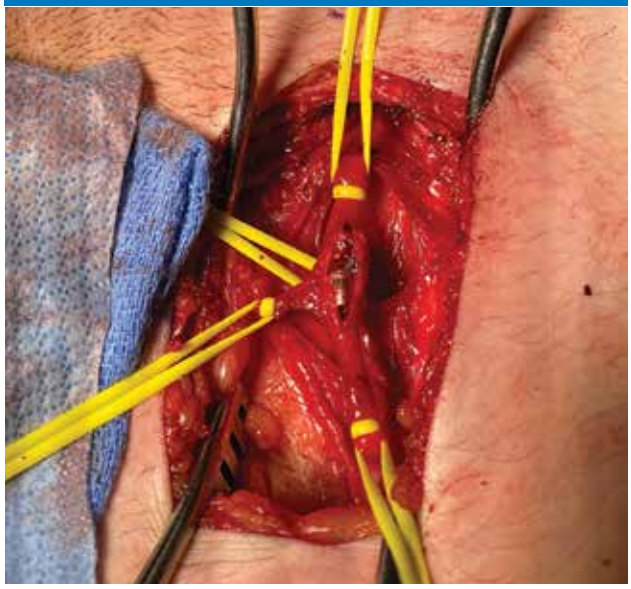
Figure 1. Coronal CTE slice of the abdomen.



Upon emergent exploratory laparotomy TS and VS proceeded to explore the abdomen. A grade III inferior liver laceration was identified and packed by the TS team. Two 19 Fr Blake drains were placed superior and inferior to the traumatic liver injury. Further abdominal exploration revealed a contained hematoma within the right kidney as well as injury to the central retroperitoneum. Para-aortic and inferior vena cava (IVC) dissection by VS identified bleeding posterior lumbar branches of both major vessels. These were suture ligated for hemostatic control. Urology proceeded with right kidney exploration and nephrectomy. Further abdominal exploration revealed no gastrointestinal tract injuries.

The patient was hemodynamically stable, and it was elected to explore the left groin to retrieve the .22 caliber projectile bullet thought to be adjacent to the left femoral artery. Unexpectedly, exploration revealed the .22 caliber bullet was contained within the femoral artery and was thus an embolus from a now apparent upstream injury. Simple closure of the left femoral artery was done subsequently to the extraction of the .22 caliber bullet (Figure 2). Afterward, the patient was immediately systemically heparinized for thrombus prevention. Fogarty balloon catheter thrombectomy of the left femoral-popliteal system retrieved arterial clots and vascular flow was re-established to the left lower extremity.

Figure 2. Gross dissection of the left femoral artery.



Re-evaluation of the aorta at this time revealed an occult right grade IV posterolateral infrarenal aortic traumatic injury approximately 5 mm deep to a small pseudoaneurysm. VS repaired the aortic injury with simple 3-0 proline closure. No further vascular injuries were identified and there was no evidence of bile or unexpected bleeding from the drains.

During the procedure, the patient lost approximately 5,000 milliliters (ml) of blood that was replaced with 1,690 ml of crossmatched packed red blood cells (PRBC), 906 ml fresh frozen plasma (FFP), 400 ml platelets, and 200 ml cryoprecipitate.

Postoperatively, the patient was transferred to the ICU for critical post-op monitoring and recovery.

Complications

The patient developed an acute kidney injury (AKI), likely a result of ischemic acute tubular necrosis (ATN). On the postoperative day (POD) #4, the patient developed a low-grade fever and cellulitis of the left lower extremity. The patient was already on a prophylactic antibiotic, Ancef, due to the trauma and bullet/gunshot wound. The empiric antibiotic regimen was broadened from Ancef to Zosyn and Vancomycin for better anaerobe and methicillin-resistant

staphylococcus aureus (MRSA) coverage. The patient was systemically heparinized after he developed a partial compartment syndrome of the left anterior calf and venous ultrasound of the left upper extremity demonstrated a basilic and cephalic vein clot. The partial compartment syndrome resolved without lower extremity fasciotomy.

Resolution

The 3M ABThera system was utilized during the first-week post-op before complete abdominal closure to prevent abdominal compartment syndrome. The patient returned to the OR for three exploration and washout procedures and one irrigation and debridement procedure over the next 10 days. On the 10th day after the initial surgical encounter, TS was able to primarily close the abdominal wall without mesh. The patient's AKI resolved on POD #18 with his creatinine stabilized to 0.95 mg/dl, which was within normal limits and approximately his baseline. Additionally, on POD #18 the patient was extubated and found to be awake, alert, and well-orientated. He was subsequently transported to the non-critical inpatient unit with close follow-up with Surgical and Medical services. He was discharged from the hospital on POD #33. Upon discharge, the patient continued apixaban 10mg twice daily for a right upper extremity DVT. The patient began outpatient home health with physical therapy. The patient has followed up at 3 and 6 months and remains healthy.

Discussion

The first bullet embolism was reported in 1834 by Thomas Davis.[3] A study done on gunshot wounds during the Vietnam War revealed an incidence of 22 cases out of 7,500 (0.3%).[3] From 1834 through 1996 there were only 160 cases within the literature.[3,4] The most common demographic where bullet emboli occur are young males (average age of 26) with single gunshot wounds.[2] Injuries most commonly originate in the thorax (39%) and the abdomen (23%). [2]

There are three different types of bullet embolism: arterial, venous, and very rarely paradoxical.[1] In a systematic review of missile emboli from 1988 to 2018, Anderson et al. found that emboli of venous origin are 56% of all bullet emboli followed by arterial origin (27%). Emboli of cardiac origin, which can be either arterial, venous, or paradoxical depending on the bullet trajectory make up 15%. Emboli of the portal venous system make up less than 1%.[1,2] It is estimated that 70% of arterial emboli occur through penetrating injuries to the aorta. The most common stopping points for bullet emboli in the venous and arterial systems are the IVC and the femoral arteries, respectively. There is a preponderance of bullet migration to the lower vessels most likely due to gravity.[1,3,4] There is a three times more frequent embolization to the left than the right lower extremity, likely due to the lesser angle of the left common iliac artery from the aorta – 30 degrees for the left and 45 degrees for the right.[3-5]

Bullet emboli are more commonly seen in civilian gunshot wounds compared to combat scenarios due to the make and caliber of the usual suspect bullets. In the United States in 2016 there were 11,004 fatal gunshot victims and 116,414 nonfatal gunshot injuries. With such a high incidence of gunshot wounds in the civilian setting, there is a need for clinical consideration of bullet emboli in gunshot wound evaluations.[2] The true incidence of bullet emboli in the civilian setting is unknown.[2,7,8]

The .22 caliber bullet is the most commonly (55%) embolized slug due to its low velocity, low power, blunted tip, and tumbling trajectory.[3,6,9] This is in comparison to the high-powered rifles that fire bullets with full metal jackets which do not lose enough kinetic energy as they travel through a body to stop and embolize.[1,10] The small .22 caliber bullets lose their already lower kinetic energy passing through tissue and amazingly have just enough energy to penetrate a vessel wall but not enough to exit the vessel. If the bullet is small enough it will be taken by the flow of blood and migrate to a point where the bullet will become lodged in a smaller diameter vessel, particularly at areas of bifurcation.[3,4] When these small bullets enter a large elastic vessel such as the abdominal aorta they have the potential to leave very small entrance holes that can form traumatic pseudoaneurysms.[11] Additionally the elastic nature of the artery can act to prevent exsanguination via a tamponade effect.[5,9,11]

Pseudoaneurysms (also called false aneurysms) are outpouchings of arteries that are only bounded by the tunica adventitia of the vessel. True aneurysms on the other hand are contained by all three layers of the arterial wall.[11,12] Abdominal aortic pseudoaneurysms are rare, accounting for only 1% of abdominal aneurysms, with infrarenal aneurysms being quite rare.[11,12] Pseudoaneurysms are often caused by penetrating trauma or aortic surgery. The vessel intima and media are disrupted but the vessels tunica adventitia and subsequent hematoma formation maintain vessel integrity.[12] Some signs and symptoms of pseudoaneurysm include a painful pulsing mass at the site of injury, a buzzing sensation, and a bruit on auscultation. Hemorrhage of the vessel may be stopped or slowed by a tamponade effect, particularly in the retroperitoneum.[11,12] Rupture of the abdominal aorta by any mechanism often leads to exsanguination and death

and is a major cause of mortality en route to the emergency department.[3,11] The formation of the pseudoaneurysms can be lifesaving, however, their rupture can cause death at any time.[3,12]

Bullet emboli should be suspected in cases when the location of the bullet does not match the trajectory, the clinical picture does not match imaging, or the patient remains hemodynamically unstable.[2,3,4] Hemodynamic instability may be due to the rupture of a previously stable occult pseudoaneurysm. Other signs or symptoms that may indicate a bullet embolus include signs of peripheral vascular ischemia, decreased peripheral pulses, cold extremities, limb weakness, decreased sensation, or paresthesia.[1,3,13] However, patients may be asymptomatic 70% of the time.[4]

In our case, the patient was stable, and in only mild distress when presenting to the emergency department. The physician from the outside facility emergency department noticed and documented the patient's left leg appeared mildly mottled, but the femoral pulses were palpated and intact bilaterally. This presentation disguised the severity of his injuries. Figure 1 illustrates the CT scan findings. Figure 2 further confirms the embolization within the left femoral artery. Failure to recover a bullet embolus may result in complications that include acute extremity ischemia or infarction, proximal or distal clot formation, septicemia, vessel erosion, and possibly death.[3,4]

In a 22-year literature review, Shannon et al. found that a tamponade effect could be made by a hematoma in the retroperitoneum, mediastinum, or hemopericardium, thus preventing exsanguination.[11] Exsanguination en route to the ED is a common cause of death in patients with thoracic or abdominal aortic gunshot wounds but a pseudoaneurysm may prevent death. However, these pseudoaneurysms are only temporary.[3] In this patient's case, re-evaluation of the right posterolateral aorta revealed a unilateral 5mm traumatic projectile injury deep to a small pseudoaneurysm. Although we can't say for certain, finding and repairing the pseudoaneurysm was likely lifesaving.

Biswas et al. describe a case in which a .22 caliber bullet entered the thoracic aorta from a gunshot wound to the upper abdomen and embolized to the right popliteal artery. The traumatic pseudoaneurysm and bullet resting in the popliteal artery remained asymptomatic and thus unknown while the patient underwent an exploratory laparotomy in which repairs were made to the cardia and one small enterotomy. The patient was transferred to the post-anesthesia care unit in critical, but stable condition. Over the next 5 hours, the patient's acidosis, HCO3, and base deficit began to improve. However, at approximately 5 hours post-op the pseudoaneurysm spontaneously ruptured and the patient rapidly exsanguinated and died despite resuscitation efforts.[3] This case described by Biswas et al. demonstrates that unless repaired, these pseudoaneurysms can rupture and lead to exsanguination as quickly as a few hours post-op.[3]

In summary, an 18-year-old male presented with a right flank gunshot wound. The .22 caliber bullet lacerated the liver, shattered the right kidney, penetrated the abdominal aorta, and embolized to the groin in the left femoral artery. All the while, his vitals were stable, and he was only in mild distress. Our patient survived and 33 days post-op he was discharged from the hospital. A literature review on PubMed by KM and JR utilized keywords such as "pseudoaneurysm", "embolization", "bullet emboli", "gun-shot-wound", "0.22 caliber", "arterial embolization", "venous embolization", and "paradoxical embolization". A Systemic Cochrane Review was not utilized. After the review, we believe this case is one of the first reports where an embolized bullet from the abdominal aorta was located and removed, the pseudoaneurysm was repaired, and the patient survived.

Conclusion

Bullet embolization is a rare and potentially life-threatening complication of gunshot injuries. Small caliber bullets can enter large arteries forming pseudoaneurysms that temporarily stabilize patients. The formation of the pseudoaneurysm and the embolized bullet has the potential to cause severe complications with the eventual rupture of the pseudoaneurysm and occlusion of downstream vessels. A high degree of suspicion for bullet emboli is necessary in the case of small caliber low-powered gunshot injuries when the clinical picture is not congruent with bullet trajectory, radiologic imaging, or hemodynamics. In these cases, retrieving the bullet is worthwhile as it may reveal a bullet embolus and, with subsequent repair of previously unknown pseudoaneurysms, may prevent postoperative morbidity and mortality.

Acknowledgments – The authors would like to thank Michael J. Statz, MD, and Kalyan Vunnamadala, MD, for their trauma and vascular surgical expertise.

REFERENCES

1. Belghith M, Lejeune J, Blum A, Marchand E, Martrille L. Unusual bullet embolism in the brachial artery: Case report and literature review. Legal Medicine. 2022;55:102024.

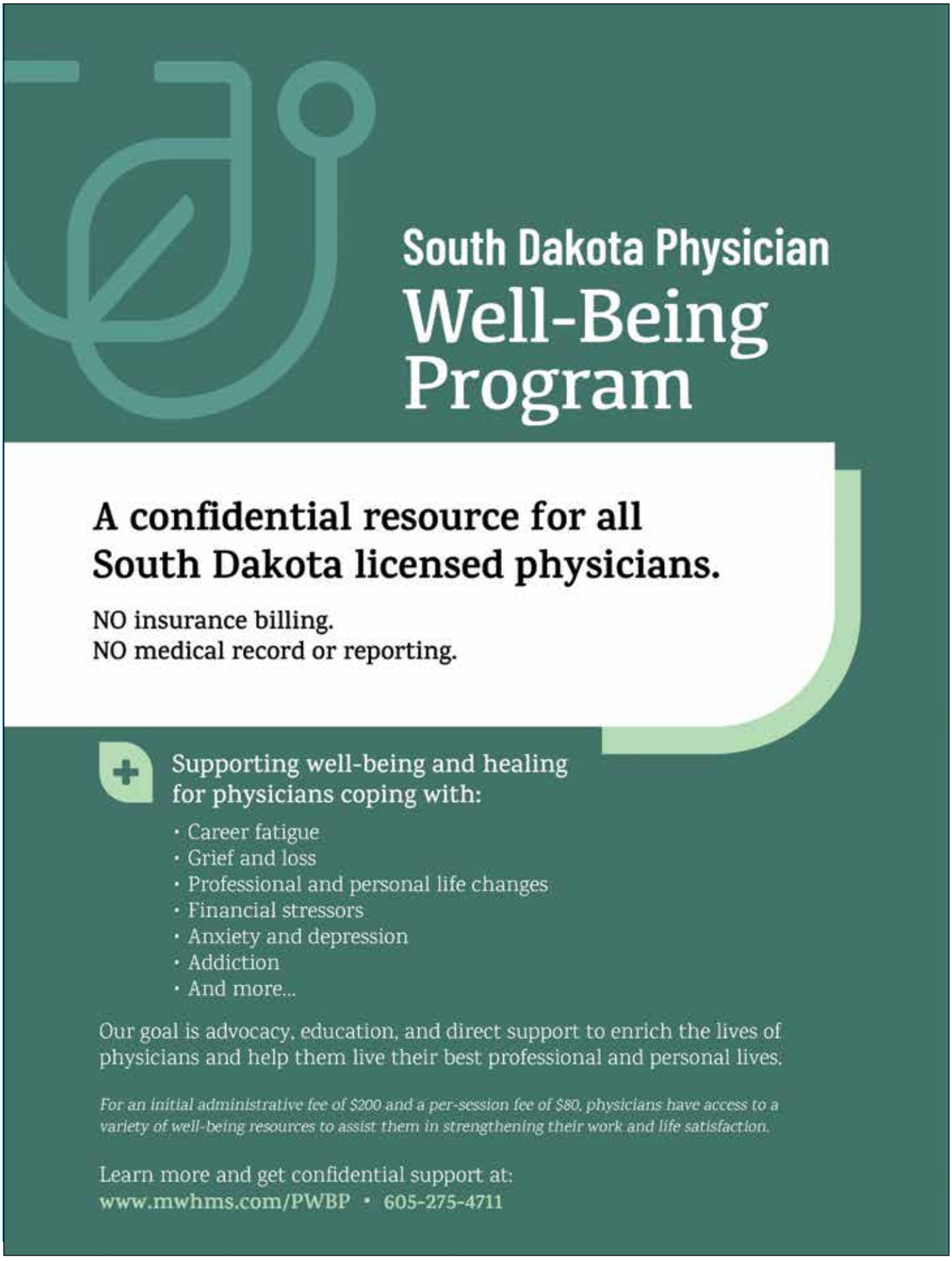
Please note: Due to limited space, we are unable to list all references. You may contact South Dakota Medicine at ereiss@sdsma.org for a complete listing.

About the Authors:

Kahlen R. Morris, MS IV, University of South Dakota Sanford School of Medicine.

Joseph C. Rath, MS IV, University of South Dakota Sanford School of Medicine.

Robert E. Miller, MD, Clinical Associate Professor, Department of Surgery, University of South Dakota Sanford School of Medicine; Rapid City Medical Center, Rapid City, South Dakota.


South Dakota Physician
Well-Being
Program
A confidential resource for all
South Dakota licensed physicians.
NO insurance billing.
NO medical record or reporting.
Supporting well-being and healing
for physicians coping with:
• Career fatigue
• Grief and loss
• Professional and personal life changes
• Financial stressors
• Anxiety and depression
• Addiction
• And more...
Our goal is advocacy, education, and direct support to enrich the lives of physicians and help them live their best professional and personal lives.
For an initial administrative fee of $200 and a per-session fee of $80, physicians have access to a variety of well-being resources to assist them in strengthening their work and life satisfaction.
Learn more and get confidential support at:
www.mwhms.com/PWBP • 605-275-4711

Depressive Disorders in Children and Adolescents: Evaluation and Management

Brendan Brodersen, DO; Vivek Anand, MD; and Shawn Van Gerpen, MD

Abstract

Depressive disorders among children and adolescents impact the practice of many providers, in many specialties. These disorders contribute to illness and disability throughout the world, and they are a significant risk factor for suicide. Depression in these age groups can differ from those in adults, and early recognition along with proper treatment can lead to improved outcomes. It is important for clinicians to differentiate depression from other possible diagnoses such as anxiety disorders, attention deficit hyperactivity disorder (ADHD), and other mood disorders. Once the diagnosis of depression is established, the severity should be assessed to determine the most appropriate level of treatment. Outpatient treatment often starts with therapy, and if medications are indicated, the use of selective-serotonin reuptake inhibitors (SSRIs) tend to be first-line.

Introduction

According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Text Revision (DSM-5-TR)*, depressive disorders constitute presence of sad, empty or irritable mood, accompanied by cognitive and somatic changes, which significantly impair the individual's functionality.[1]

There are ongoing efforts to develop interventions to prevent, screen, diagnose, and effectively treat mental health conditions in children and adolescents. Although many mental health disorders affect this population, the prevalence and effect that depression has on today's youth can have long lasting, and devastating results, if not identified and addressed. Depressive disorders affect millions of people around the world, and are associated with increased suicide risk.[2]

Major depressive disorder (MDD) is characterized by depressed mood or loss of interest occurring most of the day, over a 2 week period. In children or adolescents, this may be irritable mood rather than depressed mood. Additional symptoms include sleep problems, fatigue, significant weight loss or gain, feelings of worthlessness, psychomotor agitation or retardation, trouble with concentration, or thoughts of self-harm. The prevalence of MDD in the U.S. in those ages 3-17 years is estimated to be around 4.4%, and 20.9% of adolescents ages 12-17 years have experienced a major depressive episode.[3] The most serious consequence of depression is the risk of suicide. Suicide is the second leading cause of death in children and adolescents ages 10-19 years.[4] In South Dakota, approximately 23% of high school students have seriously considered attempting suicide.[5]

Persistent depressive disorder is a consolidation of chronic major depressive disorder and dysthymic disorder. This is defined by depressed mood for most of the day, for more days than not, for at least 1 year. The individual has not been without symptoms for more than 2 months, and depressed (or irritable) mood occurs along with 2 or more other symptoms including: appetite problems, sleep problems, low energy levels, low self-esteem, poor concentration and hopelessness. Prevalence in the U.S. is around 0.5%. [1]

Disruptive mood dysregulation disorder (DMDD) is characterized by severe, recurrent temper outbursts (verbal or physical), often occurring out of frustration. The temper outbursts are inconsistent with the developmental level and occur 3 or more times a week in different settings, for at least 1 year. The prevalence of DMDD ranges from 2% to 5%.[1]

In premenstrual dysphoric disorder (PMDD), at least five symptoms must be present during the last week before the start of menstruation, and individuals improve a few days after the onset of menstruation. PMDD is characterized by affective lability, irritability or anger, depressed mood, or anxiety, along with somatic symptoms. The prevalence of PMDD is estimated to be around 1.3 to 1.8% of women in the United States. Substance/medication-induced depressive disorder is characterized by depressive disorder symptoms induced by the use or withdrawal of a substance, and

prevalence in the U.S. is estimated to be 0.26.[1]

The DSM-5-TR indicates that symptoms seen in response to a significant loss may be similar to those in a major depressive episode. In these situations, the clinician may need to obtain additional history to determine if the symptoms are attributed to grief, or if a major depressive episode is occurring.[1] Depressive disorders can occur due to medical comorbidity, and may be associated with recurrent episodes, anxious distress, mixed features of mania or hypomania, or psychotic symptoms. Depressive disorders can be associated with catatonic features, occur in the context of pregnancy or childbirth, or have seasonal patterns.

Methods

Studies utilized as references primarily included children and adolescents up to age 18. The majority of references related to diagnosis and treatment are from 2001 to present, though references prior to 2001, which describe etiology and psychological theories, were also included. PubMed database was used for literature search, including search terms 'adolescent depression diagnosis,' 'adolescent depression treatment,' as well as corresponding terms for 'child' and 'pediatric' depression. DSM-5-TR and corresponding references were also utilized.

Etiology and Risk Factors

Various biological and psychological factors contribute to depressive disorders. For children and adolescents, having a parent with depression increases their depression risk 3 to 4 times, and twin studies estimate heritability to be between 30-50%.[6,7] Genetic predisposition to excessive amygdala response to stress during early childhood may trigger development of stress-related depressive disorder.[8] Serotonin, a monoamine with connections to adrenaline, norepinephrine, and dopamine, is linked to brain functions like sleep, appetite, and social behaviors which underlie many psychiatric pathologies. Serotonin plays an important role in neuroplasticity, which may contribute to the physiopathology of depression.[9,10] A reduction in neuronal density and hippocampal volume in depression has been attributed to changes in serotonergic neuroplasticity.[11] Furthermore, genetic polymorphisms and reduced serotonin transporter expression has been correlated with greater vulnerability to development of depressive disorders.[12] Epigenetic effects

Table 1. Key features of *DSM-5 -TR* depressive disorders.

Major depressive disorder	5 or more symptoms during the same 2 week period, at least one of which is either depressed mood or loss of interest (may be irritable mood in children and adolescents)
Persistent depressive disorder (dysthymia)	Depressed mood, more days than not, for at least 2 years (1 year in children and adolescents)
Disruptive mood dysregulation disorder	Severe, recurrent temper outbursts that are grossly out of proportion in intensity or duration to the situation or provocation; outbursts occur 3 or more times per week on average; mood in between temper outbursts is persistently irritable or angry; age of onset is before 10 years
Premenstrual dysphoric disorder	In the majority of menstrual cycles, at least 5 symptoms are present in the week before the onset of menses, and start to improve within a few days after the onset of menses; at least one symptom must be affective lability, marked irritability or anger, marked depressed mood or hopelessness, or marked anxiety or tension
Substance/medication-induced depressive disorder	Prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities; there is evidence the symptoms developed during or soon after substance intoxication/withdrawal/exposure or the involved substance/medication is capable of producing the symptoms
Depressive disorder due to another medical condition	Prominent and persistent period of depressed mood or markedly diminished interest/pleasure; there is evidence the disturbance is the direct pathophysiological consequence of another medical condition
Other specified depressive disorder	Applies when symptoms do not meet full criteria for any of the depressive disorders (e.g., recurrent brief depression for 2-13 days per month for 12 consecutive months, short-duration depressive episode of 4-13 days; depressive episode with insufficient symptoms
Unspecified depressive disorder	Applies when symptoms do not meet full criteria for any of the depressive disorders, and clinician chooses not to specify the reason the criteria are not met; includes situations in which there is insufficient information to make a more specific diagnosis

related to the social environment around children and adolescents may influence the development and activity of neural systems, thereby contributing to depression.[13]

Medical conditions including epilepsy, chronic headaches, neurometabolic diseases, and intracranial tumors are associated with higher rates of depression. Adolescents with epilepsy have a prevalence of depression between 8-35%, and 14% of adolescents with type 1 diabetes have experienced a major depressive episode within the last year.[15,16] Endocrine alterations during puberty and related hormonal or physical changes are associated with increased rates of depressive disorders, and depression has been correlated with alterations in secretion of nocturnal growth hormone secretion, nocturnal cortisol, thyroid stimulating hormone, melatonin, and prolactin.[17-22] Insomnia has also been indicated as a risk factor for the development or recurrence of depression.[23] Children and adolescents with depression have been found to have both longer sleep duration and trouble sleeping.[24] Treating sleep disturbances may reduce depression severity and accelerate recovery.[25] Over-activity of the hypothalamic–pituitary–adrenal (HPA) axis related to chronic stress and reduced neuroplasticity, along with smaller hippocampus, amygdala, and frontal lobe volumes have also been proposed to have biological underpinnings for depressive disorder.[26-28]

Table 2. Tests to evaluate for child and adolescent depression which are self-administered.[11,55,56]

Name	Target age group (years)	Psychometric characteristics	Number of items
Children's Depression Scale (CDS)	8–16	Alpha = 0.92–0.94	66
Children's Depression Inventory (CDI)	7–17	Alpha = 0.75–0.90; Sensitivity = 0.81–0.95; Specificity = 0.64–0.96;	27
Center for Epidemiological Studies Depression Scale for Children (CES-DC)	12–18	Alpha = 0.86–0.89; Sensitivity = 0.71–0.82; Specificity = 0.62–0.90	20
Depression Self-Rating Scale for Children (DSRS)	8–14	Alpha = 0.86; Test-retest reliability = 0.80; Sensitivity = 0.67; Specificity = 0.77	18
Patient Health Questionnaire-9 (PHQ-9)	18 and over	Alpha = 0.89; Sensitivity = 0.88; Specificity = 0.88; (statistics including adult population)	9
Patient Health Questionnaire-Adolescents (PHQ-A)	13 and over	Alpha = 0.83-0.88	9
Reynolds Adolescent Depression Scale (RADS)	13–17	Alpha = 0.92; Sensitivity = 0.86; Specificity = 0.49	30
Reynolds Child Depression Scale (RCDS)	7–13	Alpha = 0.85–0.91; Sensitivity = 0.79; Specificity = 0.87	30
Beck Depression Inventory (BDI-II)	13 and over	Alpha = 0.92–0.94; Sensitivity = 0.74–0.88; Specificity = 0.70–0.92	21
Revised Child Anxiety and Depression Scale—RCADS	8-18	Alpha = 0.78; Sensitivity = 0.74; Specificity = 0.77	Two versions: with 47 and 30 items
Kutcher Adolescent Depression Scale (KADS)	6–18	Alpha = 0.84; Sensitivity = 0.89; Specificity = 0.90	16 (long), 11 (short), and 6 (brief)

Various psychological theories have been connected to the development of depressive disorders. Attachment theory (relationship with caregiver during childhood), maternal depression after birth, and peer attachment can all have an impact.[29-32] Cognitive theory (cognitive distortions) and learned helplessness can be implicated in depression, while other concepts of childhood depression assume children internalize depressive attributional style and self-control problems from family or other surrounding social interactions. The self-control model connects depression to deficits in evaluting and monitoring one's own experiences and behaviors.[33-37] The interpersonal theory suggests close relationship between interpersonal functioning and depressive symptoms.[38]

Studies have implicated stressful life events during childhood and adolescence, including exposure to suicide, parental divorce, or loss of loved ones as risk factors for depression.[39]

Screening and Diagnosis

Several evaluation instruments are available to screen for child and adolescent depression. The

U.S. Preventive Services Task Force recommends screening for depression in all individuals between the ages of 12 to 18 years.[40] The patient health questionnaire-9: Modified for Teens (PHQ-A) was developed for adolescents, and includes additional questions about experiencing depression any time during the past year as well as questions about suicidal thoughts and attempts. The Children's Depression Inventory 2 (CDI 2) can be utilized for patients between ages 7 to 17, and the questions are written at a 2nd grade reading level. The CDI 2 has 28 items with each containing 3 statements, and the patient selects the statement which most accurately relates to their feelings. There are also parent and teacher versions of the CDI 2 available.[41] While these screening instruments can be utilized in an office visit, some other rating scales such as the Child Behavior Checklist (CBCL) or Behavior Assessment System for Children 3 (BASC-3) may be used in psychiatric settings or in schools to assist in screening for other psychiatric conditions. A clinical interview with the child or adolescent, along with collateral information from a caregiver, provides the most helpful information when diagnosing pediatric depression. Table 3 outlines the DSM-5-TR criteria for establishing a diagnosis of major depressive disorder.

Treatment

When the diagnosis of depression has been established, treatment may include medication management, psychotherapy or combination treatment. The treatment for adolescents with depression study (TADS), published in 2007, was a 9 month randomized control trial studying

Table 3. *DSM-5-TR* criteria for major depressive disorder.

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning	At least one of the symptoms is either: (1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (Note: In children and adolescents, can be irritable mood.) (2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.	Other symptoms: (3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain.) (4) Insomnia or hypersomnia nearly every day. (5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down). (6) Fatigue or loss of energy nearly every day. (7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick). (8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others). (9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without specific plan, or a suicide attempt or a specific plan for committing suicide.
C. The episode is not attributable to the physiological effects of a substance or to another medical condition. Note: Criteria A-C represent a major depressive episode.	
D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.	
E. There has never been a manic episode or a hypomanic episode. Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance induced or are attributable to the physiological effects of another medical condition.	

treatment options for moderate to severe depression. Participants were randomized to receive placebo, fluoxetine, cognitive behavioral therapy (CBT), or fluoxetine along with CBT. Benefit was noted in all groups, though the group receiving fluoxetine along with CBT showed better response than either treatment alone. This study led to the recommendation for combination treatment of an SSRI with psychotherapy, specifically CBT, for moderate to severe depression in adolescents.[42] Other studies have also replicated these findings.[43]

Both cognitive behavioral therapy and interpersonal therapy have been shown to be beneficial for adolescent depression.[44] Rather than using a child or adolescent's age to determine appropriate therapy recommendations, consideration of factors such as their cognitive and emotional developmental level can help achieve optimum outcomes. Assessment of any co-occurring intellectual disability or specific learning disorder is helpful to personalize therapy appropriately. Prior to referring for CBT, it is helpful to assess the patient's ability to describe their symptoms and contributing stressors. This helps identify areas of focus for future therapy sessions. During CBT sessions, individuals are taught cognitive and behavioral skills to develop more positive beliefs about themselves, others, and their surroundings. Interpersonal psychotherapy (IPT) can help identify connections between relationships and depression, and can help develop social skills and strategies to improve relationships. In younger children, having their guardian involved in the therapy process can be helpful, including utilizing play therapy if the child's cognitive and emotional developmental stage is not appropriate for CBT or IPT. Family therapy and group therapy can also be options if working on social dynamics is important. The American Psychological Association also identifies self-control therapy, cognitive behavioral analysis system of psychotherapy, behavioral activation, and problem-solving therapy as being rigorously studied for depression.[45]

Depending upon the severity of symptoms and level of impairment, medication may be considered. The child or adolescent and their guardian should have appropriate counseling on the potential risks, benefits, and expectations for medications. Selective serotonin reuptake inhibitors (SSRI) are typically considered first-line medication options. Fluoxetine has FDA approval for the treatment of depression in ages 8 and older, and escitalopram has FDA approval for depression treatment in ages 12 and older. The efficacy of fluoxetine 20 mg/day in children and adolescents (N=315 randomized; 170 children ages 8 to <13 yrs, 145 adolescents ages 13 to ≤18 yrs) was studied in two 8- to 9-week placebo-controlled clinical trials in depressed outpatients where fluoxetine produced a statistically significantly greater mean change on the Childhood Depression Rating Scale-Revised (CDRS-R) total score compared to placebo.[46] The efficacy of escitalopram as an acute treatment for major depressive disorder in adolescent patients was established in an 8-week, flexible-dose, placebo-controlled study that compared escitalopram 10-20 mg/day to placebo in outpatients 12 to 17 years of age. In this study, escitalopram showed statistically significant mean improvement on the Children's Depression Rating Scale - Revised (CDRS-R) compared to placebo.[47] Typical starting dose for fluoxetine would be 10 mg (may be started at 5 mg in younger children), and escitalopram is typically started at 5 to 10 mg daily depending upon the age and circumstances. A network meta-analysis including 34 randomized placebo-controlled trials to investigate 14 antidepressants among children and adolescents for major depressive disorder concluded that, of all included antidepressants, only fluoxetine was more effective than placebo. In terms of tolerability, children and adolescents were more likely to discontinue treatment on imipramine, venlafaxine, and duloxetine as they were significantly less well tolerated compared with placebo. In regards to rates of suicidal behavior or ideation, venlafaxine was associated with a significantly increased risk of suicidal behavior or ideation when compared with placebo.[48] Treatment with tricyclic antidepressants and monoamine oxidase inhibitors is not recommended in childhood and adolescence due to no benefits compared to placebo along with major side effect profile including cardiotoxicity, interactions with other medications and dietary restrictions. When the initial SSRI does not provide significant benefit, evidence indicates a switch to another SSRI can be helpful. Serotonin-norepinephrine reuptake inhibitors (SNRIs) have also been shown to be beneficial, though SSRIs tend to be better tolerated as initial treatment options.[49]

Due to the hepatic metabolism of SSRIs, clinicians must be cognizant of potential drug-drug interactions. For example, fluoxetine, an inhibitor of CYP2D6, should be used cautiously with other medications metabolized by CYP2D6 (such as atomoxetine for ADHD). Caution must also be taken when prescribing SSRIs in individuals also taking other serotonergic medications, such as tramadol or sumatriptan, due to the increased risk of serotonin syndrome. SSRIs tend to be well-tolerated, but some of the common side effects to monitor for include: abdominal pain, behavioral activation, restlessness, diarrhea, headache, nausea, and sleep changes.

Most of these side effects tend to resolve within 1-2 weeks or with reduction of medication dose.[50] It is important to discuss with the patient and their parents that antidepressants do carry a black box warning to monitor for increase in suicidal ideation in children and adolescents. The black box warning was issued by the FDA in 2004. This warning was related to a meta-analysis in which there was found to be an increased risk of suicidal thinking or behaviors in adolescents treated with antidepressants (4%) compared to adolescents treated with placebo (2%).[51] This 2% increased risk did not involve completed suicides, as there were no completed suicides in any of the trials. A follow-up meta-analysis in 2007 did not find statistically significant differences in the rate of suicidal thinking in adolescents taking antidepressant medications for major depressive disorder compared with those treated with placebo.[52] While it is important to monitor suicidal thoughts in all children and adolescents being treated with antidepressants, it is also important to discuss the risk of untreated depression with patients and their families.

Prognosis

It is important for patients and their caregivers to know that antidepressants should be taken for 4-6 weeks before determining effectiveness, unless there are concerns for adverse effects. While benefits may be noticeable prior to this, it is difficult to rule out a medication prior to this time period. Patients should be monitored frequently, and the dose of medication may be adjusted every 4 weeks if it is well-tolerated.[50] The response rate to adolescent depression with SSRI treatment has been found to range between 40-70%. While the placebo response rate also tends to be high in children and adolescents, the number needed to treat to get one response attributed to active treatment has been found to be 10.[50] Factors which may contribute to a lower rate of response to treatment include younger age, history of abuse, family conflicts, co-morbid psychiatric diagnoses, longer duration of depression, and severe depressive symptoms at baseline.[53]

Effectiveness of treatment is defined by: response (reduction or no symptoms for at least 2 weeks), remission (more than 2 weeks but less than 2 months with few symptoms), and recovery (2 months or greater without more than 1-2 symptoms). The rate of relapse can be high, ranging between 40-70%, with the greatest risk being in the first 4 months following improvement in symptoms. Studies demonstrate continuation of SSRIs through this period to be effective at decreasing the risk of relapse of depression, and for this reason it is recommended to continue medication treatment for 6 to 12 months after there has been a response.[50,54] If the medication is discontinued after this time period, it is helpful to plan for a time with as few stressors as possible (e.g., summer break from school). For individuals with severe depression or multiple depressive episodes, clinicians may consider recommending treatment beyond 12 months after symptoms have improved in order to further decrease the risk of relapse.[50]

Referral to child and adolescent psychiatry services can be helpful if there are questions about the diagnosis, concerns for other co-occurring psychiatric diagnoses, or to identify other potential treatment options. Individuals should be assessed for suicidal ideation and safety concerns at each visit. Inpatient hospitalization should be considered when there are safety concerns, declines in level of functioning, or concerns for self-harm.

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (5th ed., text rev). Arlington, VA. 2022.
2. World Health Organization (WHO) (2017). Depression. Fact sheet. Available online at: http://www.who.int/mediacentre/factsheets/fs369/en/
3. Bitsko RH, Claussen AH, Lichtstein J, Black LJ, Everett Jones S, Danielson MD, et al. Surveillance of children's mental health – United States, 2013 – 2019 MMWR. 2022;71(Suppl-2);1–42.
4. Centers for Disease Control and Prevention, National Center for Health Statistics. National Vital Statistics System, Mortality 1999-2020 on CDC WONDER online database, released 2021. Retrieved from http://wonder.cdc.gov/ucd-icd10.html.
5. South Dakota Suicide Prevention. Youth risk behavior survey. South Dakota Department of Health. 2019. Retrieved from https://sdsuicideprevention.org/data/.
6. Thapar A, Collishaw S, Pine DS, & Thapar AK. Depression in adolescence. Lancet. 2012;379(9820):1056-67.
7. Rice F. Genetics of childhood and adolescent depression: insights into etiological heterogeneity and challenges for future genomic research. Genome Medicine. 2010;2(9):68.
8. Dean J, Keshavan M. The neurobiology of depression: an integrative view. Asian J. Psychiatry. 2017;27:101-11.
9. Nique S, Fournis G, El Hage W, Nabhan-Abou N, Garré JB, Gohier B. Transporteur de la sérotonine, troubles ansieux et dépression: revue de la littérature. Eur. Psychiatry. 2014;29, 544-5.
10. Kraus C, Castrén E, Kasper S, Lanzenberger R. Serotonin and neuroplasticity – links between molecular, functional and structural pathophysiology in depression. Neurosci Biobehav Rev. 2017;77:317-26.
11. Bernaras E, Jaureguizar J, Garaigordobil M. Child and adolescent depression: a review of theories, evaluation instruments, prevention programs, and treatments. Frontiers in Psychology. 2019;10:543.
12. Caspi A, Hariri AR, Holmes A, Uher R, & Moffitt TE. Genetic sensitivity to the environment: the case of the serotonin transporter gene and its implications for studying complex diseases and traits. The American Journal of Psychiatry. 2010;167(5);509-27.
13. Curley JP, Jensen CL, Mashoodh R, Champagne FA. Social influences on neurobiology and behavior: epigenetic effects during development. Psychoneuroendocrinology. 2011;36(3):352-71.
14. Narbona J. Fenomenología depresiva al inicio de enfermedades neuropediátricas [Depressive phenomenology at the outset of neuropaediatric diseases]. Revista de Neurologia. 2014;58 Suppl 1:S71-5.
15. Coppola G, Operto FF, Matricardi S, Verrotti A. Monitoring and managing depression in adolescents with epilepsy: current perspectives. Neuropsychiatric Disease and Treatment. 2019;15:2773-80.
16. Hood KK, Rausch JR, & Dolan LM. Depressive symptoms predict change in glycemic control in adolescents with type 1 diabetes: rates, magnitude, and moderators of change. Pediatric Diabetes. 2011;12(8):718-23.

Please note: Due to limited space, we are unable to list all references. You may contact South Dakota Medicine at ereiss@sdsma.org for a complete listing.

About the Authors:

Brendan Brodersen, DO, Psychiatry Residency Program, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Bryan Health, Lincoln, Nebraska.

Vivek Anand, MD, Associate Professor, Department of Psychiatry, University of South Dakota Sanford School of Medicine; Avera Medical Group Behavioral Health, Sioux Falls, South Dakota.

Shawn Van Gerpen, MD, Associate Professor, Department of Psychiatry, University of South Dakota Sanford School of Medicine; Avera Medical Group Behavioral Health, Sioux Falls, South Dakota.

Strengthen the voice of **South Dakota physicians**

Your membership in the South Dakota State Medical Association and the American Medical Association (AMA) ensures you have powerful allies amplifying your voice and advocating for the needs of South Dakota patients and physicians—in your community and across the country.

AMA | MEMBERSHIP MOVES MEDICINE™

SOUTH DAKOTA STATE MEDICAL ASSOCIATION
Values. Ethics. Advocacy.

"The AMA and SDSMA help me "filter out" all the noise in my practice, which allows me to focus on the issues that are most important to me—my patients, the practice of medicine and my fellow physicians."

Robert Allison, MD

AMA MEMBER SINCE: 1991
South Dakota
AMA House of Delegates

"Every locality has a different perspective on what is most important for providing excellent health care. Everyone must be represented when policy is being crafted."

Mary Carpenter, MD

AMA MEMBER SINCE: 1982
South Dakota
AMA House of Delegates

Gout: A Rapid Review of Presentation, Diagnosis and Management

Mashood Badshah, MD; Ifrah Nadeem, MD; Ibrahim Ahmed, MD; Touba Naim, MD; and Joseph Fanciullo, MD

Abstract

Gout is inflammatory arthritis caused by monosodium urate crystal deposition in articular and non-articular structures. Acute gout flares are often monoarticular/polyarticular involving lower extremity joints characteristically involving 1st metatarsophalangeal joint. However, gout flares can also be polyarticular, involving upper extremity joints, especially in patients with multiple comorbidities and contraindications to urate-lowering therapies (ULT). Risk factors exacerbating gout flares include obesity, high alcohol and purine-rich food consumption, and the use of diuretics. Diagnosis requires synovial fluid analysis with direct visualization of monosodium urate crystals. Acute flares are managed with steroids, non-steroidal anti-inflammatory drugs, or colchicine. Long-term management includes lifestyle modifications including a heavy emphasis on weight loss, avoidance of alcohol, purine-rich foods, and diuretics. ULT is indicated in patients with ≥2 gout flares/year, tophi, or radiographic evidence of gouty arthropathy. Although allopurinol is the first-line ULT agent, it does carry a risk of inducing severe cutaneous adverse reactions, especially in patients with chronic kidney disease and patients harboring the HLA-B*5801 allele. Other ULT agents include febuxostat and probenecid. ULT is usually titrated to achieve goal serum uric acid (SUA) levels below <6 mg/dL. However, in patients with tophi, a lower SUA target of <5 mg/dL should be implemented for prompt urate crystal dissolution.

Introduction

Gout is a crystal deposition disease resulting from urate crystal saturation in articular and non-articular structures. Although acutely presenting as intermittent flares, it can also develop into gouty arthropathy and tophaceous gout. This review will highlight the gout presentations, risk factors, and diagnosis and shed light on the optimal acute and chronic management of gout.

Risk Factors of Gout

Hyperuricemia (serum uric acid [SUA] >7 mg/dL) serves as the primary risk factor (RF) for gout.[1] Increased alcohol intake particularly if consumed within 24 hours increases the risk of a recurrent gout flare.[2,3] Other RFs include an animal-derived purine intake, a high fructose diet, loop and thiazide diuretics, and cyclosporine.[4-7] Recent vaccinations and hospitalizations increase the risk twice and four-fold respectively.[8,9] Cardiometabolic factors including ischemic heart disease, hypertension, and renal failure are also associated with the risk of gout.[10]

Clinical Presentation

Gout Flare

A typical gout flare is frequently monoarticular/oligoarticular and involves lower extremities with significant aggravation in 24 hours and resolution by two weeks.[11,12] The first metatarsophalangeal (MTP) joint involvement is characteristic due to local tissue hyperuricemia, prior degenerative changes, and reduced blood flow propelling joint inflammation.[11,13] The joint inflammation results in intense, unrelenting, and throbbing pain which compromises ambulation and aggravates insomnia.[11,14] Gout flares typically occur at night/early morning, possibly due to joint dehydration, reduced temperature, and low body cortisol stimulating urate crystallization.[15]

Gout flares may also present as a polyarticular disease which if severe, can be accompanied by fevers, chills, and delirium imitating septic arthritis.[16] Polyarticular gout flares typically occur in resistant cases with multiple cardiac and renal comorbidities and contraindications to long-term urate-lowering therapy (ULT).[17] Gout can also involve the upper extremities including the joints of the wrists and hands.[18] Gout flares frequently involve joints previously affected by osteoarthritis (OA) with the probability increased by diuretic use in the elderly.[19,20] Although the elderly population experiences fewer acute flares, they frequently develop chronic polyarticular disease involving the upper extremities.[21] The

gout risk in the elderly is compounded by cardiac and renal failure managed with aspirin and diuretics.[21]

Inter-critical Period

The inter-critical period is characterized by the complete resolution of symptoms despite the initial severity of the gout flare. The presence of an inter-critical period is unique to gout, pseudogout, and palindromic rheumatism. While the patient remains asymptomatic, urate deposition, tophi formation, and chronic arthropathy continue during this phase. Without ULT, most patients experience a recurrent gout flare, with the risk increased with worsening SUA levels.[22] Without therapy, each subsequent gout flare lasts longer and merges with subsequent flares while decreasing or abolishing inter-critical periods.[23]

Tophaceous Gout

Chronic untreated hyperuricemia leads to tophaceous gout characterized by monosodium urate (MSU) crystals surrounded by chronic inflammation.[24] Common tissues affected include joints, tendons, bursae, skin, viscera, bones, and nerves.[25,26] The tophi can involve diverse body locations including the helix of the ear, olecranon bursae, and interphalangeal joints.[25] The risk of chronic tophi is characteristically aggravated in women, transplant recipients, and elderly patients.[26] In cases involving tendons and ligaments, the Achilles tendon is most frequently involved followed by the peroneal tendon.[24] Severe hand gouty arthritis can present similar to dactylitis (in psoriatic arthritis or sarcoidosis) or digital osteomyelitis leading to erroneous digital amputation.[27] Tophi can also be the initial manifestation of gout, particularly in elderly females with chronic kidney disease (CKD) who are being treated with diuretics.[28,29] Other chronic gout involvement sites include sacroiliac joints, shoulder joints, and spinal column including intervertebral discs.[30-32] Without therapy, the spinal column involvement can lead to myelopathy and cord compression.[33]

Evaluation and Diagnosis

Active gout is most definitively diagnosed by observing MSU needle-shaped negatively birefringent crystals in the synovial aspirate or tophi.[34] Synovial fluid analysis should include cell count, gram stain, and culture to rule out septic arthritis if joint inflammation is accompanied by fevers and leukocytosis. Although MSU crystal detection diagnoses gout, it cannot completely rule out concurrent septic arthritis. In rare cases, the joints have been affected by gout, pseudogout, and septic arthritis concurrently.[35] Clues suggesting pseudogout may include cartilage calcification on radiographs (chondrocalcinosis) or rhomboid-shaped, positively birefringent calcium pyrophosphate crystals.

SUA levels may be misleading and normal in up to 49% of gout cases during an active flare.[36-39] Measuring SUA levels two weeks after the flare should be done and is often revealing. If synovial fluid aspiration is not available or crystal diagnosis is not achieved, a clinical diagnostic rule (including 7 variables) can be employed to estimate gout flare likelihood (Table 1).[40]

Table 1. Clinical diagnostic rule to estimate gout flare likelihood (weightage in brackets).

1. Male sex (2 points)
2. Previous patient-reported arthritis flare (2 points)
3. Onset within one day (0.5 points)
4. Joint redness (1 point)
5. First metatarsal phalangeal joint involvement (2.5 points)
6. Hypertension or at least one cardiovascular disease (1.5 points)
7. Serum urate level greater than 5.88 mg/dL (3.5 points)

Score:

Low probability (≤ 4 points) rules out gout.

High probability (≥ 8 points) >80% risk for active gout

Intermediate probability (>4 to <8 points) requires joint aspiration and imaging including US and/or DECT for further evaluation.[40]

Since podagra may present similar to dactylitis and advanced polyarticular gout can mimic rheumatoid arthritis, imaging is frequently pursued to aid in diagnosis. Plain radiographs can show subcortical bone cysts, juxta-articular punched-out erosions, and over-hanging edges in chronic gout. Ultrasound (US) imaging can reveal double contour sign (DCS) due to reflecting MSU crystal deposition on articular cartilage, hyperechoic cloudy area (HCA) due to chronic tophi, and snowstorm appearance due to synovial hyperechoic foci. Meta-analysis of diagnostic performance indicates modest sensitivity (65%, [62-68.2]) and excellent specificity (89%, [86.6–91.1]) of the US for the assessment of gout.[41] However, US imaging requires significant operator expertise. Dual-energy computed tomography (DECT) is a newer technology available in specialized centers. It has high accuracy for MSU deposit detection. However, the performance is frequently affected by artifacts increasing false-positive interpretation.[42,43] Due to limited technical expertise and imaging facilities, US and DECT should only be pursued if the initial synovial studies and plain radiograph results are unrevealing.

Gout Flare Treatment

The basic foundation of acute gout flare management involves prompt initiation of therapy to control joint pain and inflammation, leading to shorter taper requirements.[44] The three first-line agents' corticosteroids, non-steroidal anti-inflammatory drugs (NSAID), and colchicine demonstrate comparable efficacy.[45-48]

Glucocorticoids, one of the first-line therapies can be instituted by oral, intravenous (IV), intramuscular (IM), or intra-articular (IA) routes.[49] Although preferred in moderate/severe renal insufficiency, steroids should be used with caution in patients with heart failure, hypertension, and brittle diabetes. Steroids in comparison to NSAIDs (indomethacin) offer a better side-effect profile while ensuring similar efficacy.[46,47] Oral glucocorticoids are used in a polyarticular (greater than 2 joints) flare or when IA steroid therapy is unavailable. Generally, oral steroids require a 7-10-day taper but a prolonged 14-21-day taper may be necessary for patients with recurrent flares or when treatment initiation is delayed. IA steroids are typically employed for gout flares involving 1-2 joints. IM/IV steroids are used in polyarticular gout flares when patients are unable to take oral medications. IM/IV steroids are the preferred parenteral agents in polyarticular gout flares since they provide more swift pain control with fewer adverse events when compared to NSAIDs.[49,50]

NSAIDs are typically used as alternative agents to corticosteroids usually in younger patients (<60 years). NSAID use is limited by multiple contraindications including CKD (glomerular filtration rate (GFR) <60 mL/minute per 1.73 m^2), heart failure, hypertension, active peptic ulcer disease, and concurrent use of anticoagulants. Although all NSAIDs provide similar efficacy in gout flares, indomethacin should be avoided particularly in the elderly due to the worst side effect profile.[51-53] NSAIDs in comparison to colchicine offer similar pain control with a lower risk of diarrhea and headaches.[45]

Colchicine is less desirable for acute flares but may have a role when patients develop intolerance or contraindications to steroids and NSAID therapy.[49] Colchicine is most effective within 24 hours of flare onset and generally avoided after 36 hours due to diminished efficacy. The low-dose regimen (1.2 mg followed by 0.6 mg one hour later) is preferred since it offers comparable efficacy to the high-dose regimen (4.8 mg over 6 hours) with a superior safety profile.[54] Due to the narrow therapeutic spectrum, colchicine toxicity can occur with renal or hepatic insufficiency or if the patient takes P-glycoprotein 1 (p-gp1) inhibitors, CYP3A4 inhibitors, or combined pgp1/CYP3A4 inhibitors (e.g cyclosporine, verapamil, erythromycin, clarithromycin).[55] Colchicine dose should be reduced or avoided altogether in the setting of renal/hepatic impairment, p-gp1 inhibitor, or CYP3A4 inhibitor intake. Due to cost concerns, second line agents including Interleukin 1 inhibitor anakinra should only be considered when other first-line therapies are inadequate, not tolerated, or contraindicated.[49,56] Adjunctive therapies including topical ice also show significant improvement in pain scores.[49,57]

Long-Term Gout Management

Lifestyle Modification and Medication Changes

Weight loss should be strongly emphasized due to the dose-response relationship between obesity and the risk of gout.[49,58,59] Weight loss by physical exertion or bariatric surgery leads to a significant reduction of SUA levels ranging from -0.5 mg/dL to -2.82 mg/dL.[60] SUA levels and subsequent gout flares may transiently increase for the first one to three months after bariatric surgery followed by a downtrend.[61,62] Dietary approaches to stop hypertension (DASH) and Mediterranean diets are associated with decreased gout risk and should be advised.[63,64] Decreasing alcohol intake is recommended due to increased gout flare risk with alcohol, particularly with beer.[3,65] High fructose intake and animal-derived high-purine diet also increase gout flare risk and should be reduced.[4,7,66]

Losartan and calcium channel blockers (amlodipine and nifedipine) are preferred in patients with hypertension and gout due to their urate-lowering properties.[67,68] Thiazide diuretics in contrast increase the gout risk and should be switched to another first line antihypertensive if possible.[49,69] Despite urate retention effects, low-dose aspirin (75 mg) should be continued in patients with appropriate cardiovascular indications.[49,70] Though fenofibrate significantly reduces SUA levels and gout events, it should be avoided solely for SUA reduction due to worse side effects.[49,71] In patients with indications for statins, atorvastatin is recommended due to its urate-lowering properties with a mean SUA reduction of -0.57mg/dL.[72] Recent data also suggests decreased gout risk in patients with type 2 diabetes started on sodium-glucose cotransporter 2 inhibitors.[73]

Urate Lowering Therapy

The American College of Rheumatology (ACR) recommends ULT initiation in patients with ≥2 gout flares/year, tophi, or radiographic evidence of gouty arthropathy.[49] However, ULT may be considered after the first gout flare in CKD ≥ 3,

SOUTH DAKOTA STATE MEDICAL ASSOCIATION
Values. Ethics. Advocacy.

Thank You

Thank you to these organizations for working with the SDSMA on group billing for physician membership. You help bring unparalleled member benefits to your physicians, providing them with access to an extensive array of benefits. Together, we strengthen the practice of medicine.

- Anesthesia Physicians
- Anesthesiology Associates
- Avera
- Avera Cancer Institute – Yankton
- Avera Medical Group – Dell Rapids
- Avera Medical Group – Dermatology Mitchell
- Avera Medical Group – Flandreau
- Avera St. Benedict CHR Clinic – Parkston
- Black Hills Dermatology & Laser Surgery Centre
- Black Hills Orthopedic & Spine Center
- Black Hills Pediatrics & Neonatology
- Black Hills Plastic Surgery at Rapid City Medical Center
- Black Hills Regional Eye Institute
- Black Hills Surgical Hospital
- Black Hills Urgent Care
- Brookings Health System
- Center for Family Medicine
- Clinical Laboratory of the Black Hills
- CNOS
- Community Health Center of the Black Hills
- Creekside Medical Clinic
- Dakota Dermatology
- Dakota Radiology
- Dakota West Radiation Oncology
- Douglas County Memorial Hospital
- ENT Consultants
- Fall River Health Clinic
- Horizon Health Care
- Huron Regional Medical Clinic
- James Valley Imaging
- Lewis & Clark Behavioral Health Services
- Madison Regional Health System
- Medicine Arts Clinic at Rapid City Medical Center
- Midwest Ear, Nose & Throat Associates
- Mitchell Clinic
- Mobridge Medical Clinic
- Monument Health
- Monument Health Family Medicine Residency Clinic
- North Central Heart Institute
- Ophthalmology, LTD
- Orthopedic Institute
- Philip Health Services Clinic
- Physicians Laboratory
- Pioneer Memorial Hospital
- Plastic Surgery Associates of South Dakota
- Prairie Lakes Healthcare System
- Rapid City Emergency Services
- Redfield Clinic
- Sanford Clinic – Chamberlain
- Sanford Clinic – Hospitalists
- Sanford Clinic – Orthopedics & Sports Medicine
- Sioux Falls Urgent Care
- Slingsby & Huot Eye Associates
- Surgical Institute of South Dakota
- University of South Dakota Sanford School of Medicine
- Urology Specialists
- Vance Thompson Vision
- Vermillion Medical Clinic
- West River Anesthesiology Consultants
- Yankton Anesthesiology
- Yankton Medical Clinic
- Yankton Surgical Associates

To learn more about SDSMA group billing, please contact membership@sdsma.org.

SUA > 9mg/dL, or urolithiases.[49] A treat-to-target approach with target SUA <6 mg/dL is strongly recommended for patients requiring ULT.[44,49] In severe gout (gouty arthropathy, tophaceous gout, or frequent attacks), a lower SUA target of 5 mg/dL is suggested for prompt urate crystal dissolution.[44] With structured nurse-led monitoring, the treat-to-target SUA strategy leads to higher ULT adherence, lower gout flares, and overall, improved quality of life.[74] ACR recommends starting ULT during an acute flare for improving patient compliance without increasing the risk of additional gout flares.[49,75] However, other experts usually wait two weeks after the gout flare since early ULT initiation can preclude accurate SUA measurements after the flare without improving long-term outcomes. Gout flare prophylaxis with low-dose colchicine (0.6 mg daily) or NSAIDs (naproxen 250mg BID) should be prescribed and continued for at least 3-6 months after ULT initiation.[49,76,77]

The first-line ULT agent is Allopurinol, a purine-based xanthine oxidase inhibitor (XOI) preventing urate production.[49] It should be initiated at 100 mg daily with glomerular filtration rate (GFR) ≥60 mL/minute and the dose should not exceed 1.5 mg per mL/minute of GFR in patients with CKD≥3 due to a higher risk of severe cutaneous adverse reaction (SCAR).[78,79] Allopurinol is usually up-titrated slowly in 100 mg increments per month (50 mg in patients with CKD≥3) until the target SUA level is achieved.[80] Although the maximum approved dose is 800 mg daily, most patients achieve SUA≤ 6 mg/dL with a mean allopurinol of around 400 mg daily.[80] Although the most common adverse effects include rash, allopurinol should be immediately stopped with any rash since this may be the initial harbinger of SCAR. SCAR usually involves Stevens-Johnson syndrome/toxic epidermal necrolysis, acute kidney injury, hepatitis, and eosinophilia and is strongly associated with the HLA-B*5801.[81-84] The risk of SCAR is increased in African Americans, Asians, and Native Hawaiians/Pacific Islanders.[85] Due to the strong association between the SCAR and HLA-B*5801 allele, and the higher incidence of the SCAR in African Americans and Asians, HLA-B*5801 should be tested in all high-risk populations.[86] Patients should be switched to alternate ULT if they are positive for HLA-B*5801.[86] Additional risk factors for SCAR include female sex, age ≥60 years, CKD, and initial allopurinol dose >100 mg/day.[85] Allopurinol should not be used with azathioprine (AZD) or 6-mercaptopurine (6-MP) since it inhibits the metabolism of AZD and 6-MP compounding the risk for myelotoxicity and immunosuppression.[87,88] However, if combined use is inevitable, the dose of AZD or 6-MP should be reduced by at least 67% with regular blood count monitoring to mitigate the risk of cytotoxicity.[89]

Febuxostat, a non-purine XOI is a second-line ULT agent.[49] It is available in 40 mg and 80 mg with a 40 mg dose similar in efficacy to 300 mg allopurinol.[90] Similar to allopurinol, febuxostat initiation requires gout flare prophylaxis.[49] However, febuxostat in comparison to allopurinol is associated with a higher risk for gout flares while on prophylaxis.[91] Liver function tests (LFT) abnormalities and rash are common with febuxostat and require regular monitoring. Severe hypersensitivity reactions including the Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) more commonly occur in CKD patients who previously developed SCAR with allopurinol.[92] Febuxostat received a Black Box warning after an initial trial between febuxostat and allopurinol showed increased all-cause and cardiovascular mortality in the febuxostat group (Hazard ratio [HR] 1.22 [95% CI, 1.01 to 1.47] and HR 1.34 [95% CI, 1.03 to 1.73] respectively).[93] However, over 56.6% of patients discontinued treatment prematurely, and 45% discontinued follow-up, affecting result accuracy.[93] A more recent trial of 6128 patients, aged >60 years with at least one cardiovascular risk factor however, showed similar all-cause mortality and cardiovascular mortality between febuxostat and allopurinol.[94] Since febuxostat being an XOI also inhibits the metabolism of AZD and 6-MP, the concurrent use of these medications is strictly contraindicated by the manufacturer.

Probenecid, the only available uricosuric agent in the United States function by promoting renal clearance of urate. Probenecid can be used in cases of intolerance to XOI or in combination with XOI, although XOI should be up-titrated to the maximum dose (e.g. allopurinol to 800 mg) before considering combination therapy.[95] Probenecid inhibits the renal clearance of many medications (e.g penicillin and ampicillin) necessitating dose reduction of these medications. Probenecid also increases the risk of urate and calcium urolithiasis and requires higher fluid intake (typically 2L/day) for prevention.[1,96] Probenecid is contraindicated in patients with previous urolithiasis and CKD ≥3 due to lack of efficacy.[49]

Pegloticase, a pegylated recombinant uricase enzyme available as a fortnight infusion converts urate into soluble allantoin. Although highly effective, the long-term efficacy is marred by anti-drug antibodies requiring methotrexate to improve therapeutic response and pre-infusion SUA levels for monitoring.[97-99] Given the significant cost, twice monthly infusions, and severe allergic reactions, pegloticase should

only be considered in patients who have failed XOI and uricosuric agents with active disease (≥2 flares/year) or who have non-resolving tophi. [49]

Conclusion

Although gout flares usually involve 1st MTP joints, patients can also develop polyarticular flares involving upper extremity joints. Diagnosis requires MSU crystal demonstration in synovial fluid or tophi. However, in unclear cases, imaging including radiographs, US, and DECT can be used to rule out alternate etiologies. Gout management requires steroids, NSAIDs, or colchicine for acute gout flares, lifestyle and medication changes, and consideration of ULT for optimal long-term control.

REFERENCES

1. Dalbeth N, Gosling AL, Gaffo A, Abhishek A. Gout. Lancet. May 15 2021;397(10287):1843-55.
2. Zhang Y, Woods R, Chaisson CE, et al. Alcohol consumption as a trigger of recurrent gout attacks. Am J Med. Sep 2006;119(9):800.e13-8.
3. Neogi T, Chen C, Niu J, Chaisson C, Hunter DJ, Zhang Y. Alcohol quantity and type on risk of recurrent gout attacks: an internet-based case-crossover study. Am J Med. Apr 2014;127(4):311-8.
4. Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study. Bmj. Feb 9 2008;336(7639):309-12.
5. Hunter DJ, York M, Chaisson CE, Woods R, Niu J, Zhang Y. Recent diuretic use and the risk of recurrent gout attacks: the online case-crossover gout study. J Rheumatol. Jul 2006;33(7):1341-5.
6. Lin HY, Rocher LL, McQuillan MA, Schmaltz S, Palella TD, Fox IH. Cyclosporine-induced hyperuricemia and gout. N Engl J Med. Aug 3 1989;321(5):287-92.
7. Zhang Y, Chen C, Choi H, et al. Purine-rich foods intake and recurrent gout attacks. Ann Rheum Dis. Sep 2012;71(9):1448-53.
8. Yokose C, McCormick N, Chen C, et al. Risk of gout flares after vaccination: a prospective case cross-over study. Ann Rheum Dis. Nov 2019;78(11):1601-4.
9. Dubreuil M, Neogi T, Chen CA, et al. Increased risk of recurrent gout attacks with hospitalization. Am J Med. Dec 2013;126(12):1138-41.e1.
10. Rothenbacher D, Primatesta P, Ferreira A, Cea-Soriano L, Rodríguez LA. Frequency and risk factors of gout flares in a large population-based cohort of incident gout. Rheumatology (Oxford). May 2011;50(5):973-81.
11. Taylor WJ, Fransen J, Jansen TL, et al. Study for updated gout classification criteria: identification of features to classify gout. Arthritis Care Res (Hoboken). Sep 2015;67(9):1304-15.
12. Hadler NM, Franck WA, Bress NM, Robinson DR. Acute polyarticular gout. Am J Med. May 1974;56(5):715-9.
13. Simkin PA. The pathogenesis of podagra. Ann Intern Med. Feb 1977;86(2):230-3.
14. Singh JA, Herbey I, Bharat A, et al. Gout self-management in african american veterans: a qualitative exploration of challenges and solutions from patients' perspectives. Arthritis Care Res (Hoboken). Nov 2017;69(11):1724-32.
15. Choi HK, Niu J, Neogi T, et al. Nocturnal risk of gout attacks. Arthritis Rheumatol. Feb 2015;67(2):555-62.
16. Ho G, Jr., DeNuccio M. Gout and pseudogout in hospitalized patients. Arch Intern Med. Dec 27 1993;153(24):2787-90.
17. Pascart T, Lioté F. Gout: state of the art after a decade of developments. Rheumatology (Oxford). Jan 1 2019;58(1):27-44.
18. Raddatz DA, Mahowald ML, Bilka PJ. Acute polyarticular gout. Ann Rheum Dis. Apr 1983;42(2):117-22.
19. Roddy E, Zhang W, Doherty M. Are joints affected by gout also affected by osteoarthritis? Ann Rheum Dis. Oct 2007;66(10):1374-7.
20. Lally EV, Zimmermann B, Ho G, Jr., Kaplan SR. Urate-mediated inflammation in nodal osteoarthritis: clinical and roentgenographic correlations. Arthritis Rheum. Jan 1989;32(1):86-90.
21. Fam AG. Gout in the elderly. Clinical presentation and treatment. Drugs Aging. Sep 1998;13(3):229-43.
22. Shiozawa A, Szabo SM, Bolzani A, Cheung A, Choi HK. Serum Uric Acid and the Risk of Incident and Recurrent Gout: A Systematic Review. J Rheumatol. Mar 2017;44(3):388-96.
23. Shoji A, Yamanaka H, Kamatani N. A retrospective study of the relationship between serum urate level and recurrent attacks of gouty arthritis: evidence for reduction of recurrent gouty arthritis with antihyperuricemic therapy. Arthritis Rheum. Jun 15 2004;51(3):321-5.
24. Dalbeth N, Kalluru R, Aati O, Horne A, Doyle AJ, McQueen FM. Tendon involvement in the feet of patients with gout: a dual-energy CT study. Ann Rheum Dis. Sep 1 2013;72(9):1545-8.
25. Grassi W, De Angelis R. Clinical features of gout. Reumatismo. Jan 19 2012;63(4):238-45.
26. Forbess LJ, Fields TR. The broad spectrum of urate crystal deposition: unusual presentations of gouty tophi. Semin Arthritis Rheum. Oct 2012;42(2):146-54.
27. Rousseau I, Cardinal EE, Raymond-Tremblay D, Beauregard CG, Braunstein EM, Saint-Pierre A. Gout: radiographic findings mimicking infection. Skeletal Radiol. Oct 2001;30(10):565-9.
28. Bieber A, Schlesinger N, Fawaz A, Mader R. Chronic tophaceous gout as the first manifestation of gout in two cases and a review of the literature. Semin Arthritis Rheum. Jun 2018;47(6):843-8.
29. Wernick R, Winkler C, Campbell S. Tophi as the initial manifestation of gout. Report of six cases and review of the literature. Arch Intern Med. Apr 1992;152(4):873-6.
30. Alarcón-Segovia DA, Cetina JA, Díaz-Jouanen E. Sarcroilaic joints in primary gout. Clinical and roentgenographic study of 143 patients. Am J Roentgenol Radium Ther Nucl Med. Jun 1973;118(2):438-43.
31. Gamala M, Jacobs JWG, Heggelman BGF, Klaasen R. An unexpected manifestation of gout. Rheumatology (Oxford). Apr 1 2020;59(4):810.
32. Das De S. Intervertebral disc involvement in gout: brief report. J Bone Joint Surg Br. Aug 1988;70(4):671.
33. Saketkoo LA, Robertson HJ, Dyer HR, Virk ZU, Ferreyro HR, Espinoza LR. Axial gouty arthropathy. Am J Med Sci. Aug 2009;338(2):140-6.
34. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yü TF. Preliminary criteria for the classification of the acute arthritis of primary gout. Arthritis Rheum. Apr 1977;20(3):895-900.
35. Colaco C, Dotel R. Coexisting polyarticular septic arthritis, gout and pseudogout. BMJ Case Rep. Oct 28 2018.
36. Urano W, Yamanaka H, Tsutani H, et al. The inflammatory process in the mechanism of decreased serum uric acid concentrations during acute gouty arthritis. J Rheumatol. Sep 2002;29(9):1950-3.
37. Logan JA, Morrison E, McGill PE. Serum uric acid in acute gout. Ann Rheum Dis. Nov 1997;56(11):696-7.
38. Park YB, Park YS, Lee SC, Yoon SJ, Lee SK. Clinical analysis of gouty patients with normouricaemia at diagnosis. Ann Rheum Dis. Jan 2003;62(1):90-2.
39. Schlesinger N, Norquist JM, Watson DJ. Serum urate during acute gout. J Rheumatol. Jun 2009;36(6):1287-9.
40. Janssens HJ, Fransen J, van de Lisdonk EH, van Riel PL, van Weel C, Janssen M. A diagnostic rule for acute gouty arthritis in primary care without joint fluid analysis. Arch Intern Med. Jul 12 2010;170(13):1120-6.
41. Lee YH, Song GG. Diagnostic accuracy of ultrasound in patients with gout: A meta-analysis. Semin Arthritis Rheum. Apr 2018;47(5):703-709.
42. Lee YH, Song GG. Diagnostic accuracy of dual-energy computed tomography in patients with gout: A meta-analysis. Semin Arthritis Rheum. Aug 2017;47(1):95-101.
43. Mallinson PI, Coupal T, Reisinger C, et al. Artifacts in dual-energy CT gout protocol: a review of 50 suspected cases with an artifact identification guide. AJR Am J Roentgenol. Jul 2014;203(1):W103-9.
44. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. Jan 2017;76(1):29-42.
45. Roddy E, Clarkson K, Blagojevic-Bucknall M, et al. Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care. Ann Rheum Dis. Feb 2020;79(2):276-84.
46. Rainer TH, Cheng CH, Janssens HJ, et al. Oral Prednisolone in the Treatment of Acute Gout: A Pragmatic, Multicenter, Double-Blind, Randomized Trial. Ann Intern Med. Apr 5 2016;164(7):464-71.
47. Man CY, Cheung IT, Cameron PA, Rainer TH. Comparison of oral prednisolone/paracetamol and oral indomethacin/paracetamol combination therapy in the treatment of acute goutlike arthritis: a double-blind, randomized, controlled trial. Ann Emerg Med. May 2007;49(5):670-7.
48. Janssens HJ, Janssen M, van de Lisdonk EH, van Riel PL, van Weel C. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomised equivalence trial. Lancet. May 31 2008;371(9627):1854-60.
49. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care Res (Hoboken). Jun 2020;72(6):744-760.
50. Zhang YK, Yang H, Zhang JY, Song LJ, Fan YC. Comparison of intramuscular compound betamethasone and oral diclofenac sodium in the treatment of acute attacks of gout. Int J Clin Pract. May 2014;68(5):633-8.

Please note: Due to limited space, we are unable to list all references. You may contact South Dakota Medicine at ereiss@sdsma.org for a complete listing.

About the Authors:

Mashood Badshah, MD, Class of 2023 Internal Medicine Residency Program, University of South Dakota Sanford School of Medicine; Rheumatology Fellowship Program, University of Kansas, Lawrence.

Ifrah Nadeem, MD, Internal Medicine Residency Program, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Ibrahim Ahmed, MD, Internal Medicine Residency Program, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Touba Naim, MD, Avera Medical Group Hospitalists, Sioux Falls, South Dakota

Joseph Fanciullo, MD, Internal Medicine Residency Program, University of South Dakota Sanford School of Medicine; Avera Medical Group Rheumatology, Sioux Falls, South Dakota.

Acquired Risk Factors that Influence Risk for Dementia and Possibly Alzheimer Disease

Eric Novak, DO; Matthew Tochtrop, DO; David Schlagel, MD; and William Fuller, MD

Abstract

Various medicinal agents aimed at improving Alzheimer disease (AD) include cholinesterase inhibitors, memantine, aducanumab, and antioxidants. These medications are typically prescribed once AD is diagnosed in the clinical setting in order to slow progression. Though initiating treatment after being diagnosed with AD is important, significance should be placed on recognizing known acquired risk factors in order to potentially decrease the likelihood of developing dementia and perhaps specifically AD. This article summarizes the acquired factors that influence risk for dementia.

Introduction

Alzheimer disease (AD) burden is substantial worldwide with an estimated 47 million people being affected. It is estimated that this number will increase globally to greater than 130 million by 2050. In the U.S. in 2011 there were an estimated 4.5 million individuals over the age of 65 with clinical AD. Projections estimate a rise in the U.S. to 13.8 million by the year 2050.

Histologic examination is required for a definitive diagnosis of AD, but most studies rely on clinical criteria. Neuropathic changes that are essential to AD include: extracellular deposits of amyloid beta peptides; neuritic plaques associated with neuronal injury that are characterized by amyloid formed from amyloid beta; and neurofibrillary tangles. Documentation of presence and progression of dementia is usually aided by standardized mental status scales such as the Montreal Cognitive Assessment (MoCA) or Mini-Mental State Examination (MMSE).

Patients with a family history of dementia or specifically AD commonly appear in the clinical setting with concerns for their memory. Typically, if encountered early enough, these patients do not meet criteria for a major neurocognitive disorder. These patients can still be concerned with potential appearance and progression of a dementia process. It is important to inform the patients of acquired risk factors that influence the risk for dementia. Effectively watching for and treating acquired risk factors can help quell concerns from your patient by providing a framework on managing potential risk.

Clinical Diagnosis

Clinical diagnosis of Alzheimer disease per DSM-5

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains:
   a. Learning and memory
   b. Language
   c. Executive function
   d. Complex attention
   e. Perceptual-motor

B. Social cognition

   The cognitive deficits interfere with independence in everyday activities. At a minimum, assistance should be required with complex instrumental activities of daily living, such as paying bills or managing medications.

C. The cognitive deficits do not occur exclusively in the context of a delirium.

D. The cognitive deficits are not better explained by another mental disorder (eg, major depressive disorder, schizophrenia).

E. There is insidious onset and gradual progression of impairment in at least 2 cognitive domains.

F. Either of the following:
   a. Evidence of a causative Alzheimer disease genetic mutation from family history or genetic testing.
   b. All 3 of the following are present:

i. Clear evidence of decline in memory and learning and at least 1 other cognitive domain.

ii. Steadily progressive, gradual decline in cognition, without extended plateaus.

iii. No evidence of mixed etiology (ie, absence of other neurodegenerative disorders or cerebrovascular disease, or no other neurological, mental, or systematic disease or condition likely contributing to cognitive decline).

Summary of Acquired Risk Factors

1. **Hypertension**

Adjusting for cerebrovascular risk factors, midlife systolic blood pressure was the strongest blood pressure component predicting incident dementia. This finding was reiterated in an 8,845 person study consisting of 721 participants with dementia. Compared to participants with no risk factors, individuals with smoking history, hypertension, high cholesterol, and diabetes at midlife were each associated with a 20-40% increase in risk of dementia. The dementia risk increased by 1.27 for a single risk factor, including hypertension. In another study of 15,744 participants, 1,516 were identified with dementia. Among that subset of the total study population, the hazard ratio for hypertension and development of dementia was 1.39 signifying increased risk. Parameters to follow per the 2017 ACC/AHA signified normal blood pressure as systolic less than 120 mmHg and diastolic less than 80 mmHg. Stage 1 hypertension labeled as systolic 130-139 mmHg and diastolic 80-89 mmHg and stage 2 hypertension labeled as systolic at least 140 mmHg and diastolic at least 90 mmHg.

2. **Dyslipidemia**

The association between high LDL cholesterol and the development of AD is at times difficult to interpret. Aβ precursor protein's cleavage through α-secretase suggests that the lipid environment of the cleavage enzymes influences Aβ production and therefore AD pathogenesis. Though LDL does not cross the blood-brain barrier unless the barrier is damaged by other factors of vascular disease, observational data does generally support an association between risk of AD and elevated LDL. One study has shown that the apoE (involved in cholesterol metabolism) epsilon4 allele and elevated midlife total cholesterol levels are independent risk factors for AD. HDL cholesterol and triglyceride concentrations were not associated with rate of cognitive decline in 156 patients with incident AD. However, within the same study, each 10 unit increase in cholesterol and LDL-C was associated with a 0.10-SD decrease in cognitive score per year of follow-up. Further studies will need to be completed given evidence of oral statins not affecting the rate of decline in mild to moderate AD.

3. **Cerebrovascular disease**

It is important to note that about one third of patients diagnosed with vascular dementia (VaD) will have AD-type pathology at autopsy. Most patients with AD have Aβ amyloid angiopathy and degenerative conditions affecting capillaries. In a more recent study completed in 2007, persons without dementia, over 80%, had one or no diagnosis of chronic or acute brain abnormalities. Compared to persons with dementia, over 50% had multiple diagnoses including AD, Parkinson disease/ Lewy body disease, or infarcts. A larger analysis, the 2229 patient Framingham Offspring Study, showed white matter hyperintensities volume (WMHV), extensive WMHV, and MRI-defined brain infarcts were associated with an increased risk of dementia. These hazard ratios were 2.22, 3.97, and 6.12 respectively.

4. **Type 2 diabetes and obesity**

A 1.5-fold increased risk of AD has been associated with obesity and type 2 diabetes. The chronic inflammatory state of diabetes can deteriorate organ systems, of important risk is cerebral damage. The level of risk is less than that with the APOE4 allele. However, substantial increases in future incidence of AD could likely be seen due to the high prevalence of these disorders. In a larger meta-analysis completed by Biessels et al, 7/10 studies reported the incidence of any type of dementia was higher in individuals with diabetes than in those without diabetes. High risk was associated with both AD and VaD in 8/13 and 6/9 studies respectively. Various studies are being done currently to establish if a relationship exists between insulin and amyloid beta metabolism. A current hypothesis includes insulin-degrading enzyme leading to the accumulation of oligomeric beta amyloid.

5. **Lifestyle and activity**

As much of the previously mentioned research has shown, risk appears greatest when factors are present in midlife. This theme continues for exercise. One year of aerobic exercise in a large RCT of seniors was associated

Trustworthy. Dedicated. Caring.

Sanford Hospice is a trusted partner for quality, compassionate end-of-life care. Our team provides comfort through the next steps of life's journey.

We can ease the journey for your patients and their families with:

- 24-hour room service
- Bereavement counseling
- Pain management
- Spiritual and social support

Learn more about Sanford Hospice at sanfordhealth.org.

SANFORD HEALTH

488-685-386 1/24

with significantly larger hippocampal volumes and better spatial memory. A similar effect was also seen in healthy adults through a meta-analysis of 29 RCTs that documented significant cognitive benefits from sustained exercise in adults without dementia. Physical activity has been shown to be a protective factor in relation to neurodegeneration. A healthy diet and sustained physical and mental activity have wide-ranging positive effects for a multitude of disease processes. As such, informing patients to maintain these as much as possible could be one of the greatest risk reduction techniques available.

6. **Brain trauma**

Studies have inconsistently shown connections between brain trauma and AD. In a very small study consisting of 15 patients and 11 controls, beta-amyloid and beta-amyloid precursor protein were obtained in patients who died 3 hours to 56 days after a TBI. The positron emission tomography showed increased binding of beta-amyloid following TBI. Another study performed on Vietnam veterans did not show TBI increasing the risk for AD when measured by amyloid positron emission tomography. Another study showed that self-reported head injuries were associated with increased risk and earlier onset of cognitive impairment and dementia states. It is evident that more research needs to be done in order for a conclusive answer, especially larger scale studies.

7. **Medications**

When looking at medications administered to older adults, long-term exposure seems to have the most evidence for showing elevated risk of AD. Perhaps under the most scrutiny are benzodiazepines. A 2014 case-control study of 1796 participants with benzodiazepine use showed an increased risk of AD with an adjusted odds ratio of 1.51. The strength of association increased with drug half-life showing adjusted odds ratios of 1.43 and 1.70 for respective short acting and long acting formulations. Anticholinergics' irreversible effects on AD are reasonable considering cholinergic deficits in AD. Specific medications in question in a 2015 study included tricyclic antidepressants, first-generation antihistamines, and bladder antimuscarinics. This study showed a 10-year cumulative dose-response relationship for dementia with adjusted hazard ratios ranging from 0.92 to 1.54. Increased risk started with an adjusted hazard ratio of 1.19 for total standardized daily doses dispensed of 91-365. In the context of benzodiazepines and anticholinergics, short-term and low dose prescriptions are ideal when trying to mitigate risk of development of dementia and potentially AD.

Conclusion

A multitude of acquired risk factors, most relevant when presenting in midlife, influence risk for dementia and perhaps specifically the risk for AD. Individuals with 2 or more vascular risk factors in midlife had nearly a threefold higher odds of brain amyloid deposition in late life as measured by amyloid positron emission tomography. Effectively managing vascular risk factors during midlife represents a key strategy for reducing risk, progression, and severity of AD and other forms of dementia. Some estimates show that up to one third of AD cases worldwide could potentially be attributable to modifiable risk factors such as diabetes, midlife hypertension, and physical inactivity. Therefore, we should all be aware of and do our due diligence in identifying these individuals to minimize negative outcomes.

REFERENCES

1. World Alzheimer Report 2015: The Global Impact of Dementia. Retrieved from www.alz.co.uk/research/world-report-2015.
2. Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. Neurology. 2013 May 7;80(19):1778-83. Epub 2013 Feb 6.
3. Terry RD, Masliah E, Salmon DP, Butters N, DeTeresa R, Hill R, Hansen LA, Katzman R. Physical basis of cognitive alterations in Alzheimer's disease: synapse loss is the major correlate of cognitive impairment. Ann Neurol. 1991 Oct;30(4):572-80..
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington, VA 2013.
5. Freitag MH, Peila R, Masaki K, Petrovitch H, Ross GW, White LR, Launer LJ. Midlife pulse pressure and incidence of dementia: the Honolulu-Asia Aging Study. Stroke. 2006 Jan;37(1):33-7. Epub 2005 Dec 8.
6. Whitmer RA, Sidney S, Selby J, Johnston SC, Yaffe K. Midlife cardiovascular risk factors and risk of dementia in late life. Neurology. 2005 Jan 25;64(2):277-81.
7. Gottesman RF, Albert MS, Alonso A, Coker LH, Coresh J, Davis SM, Deal JA, et al. Associations Between Midlife Vascular Risk Factors and 25-Year Incident Dementia in the Atherosclerosis Risk in Communities (ARIC) Cohort. JAMA Neurol. 2017 Oct 1;74(10):1246-54.
8. Reitz C. Dyslipidemia and the risk of Alzheimer's disease. Curr Atheroscler Rep. 2013 Mar;15(3):307.
9. Kivipelto M, Helkala EL, Laakso MP, Hänninen T, Hallikainen M, Alhainen K, Iivonen S, et al. Apolipoprotein E epsilon4 allele, elevated midlife total cholesterol level, and high midlife systolic blood pressure are independent risk factors for late-life Alzheimer disease. Ann Intern Med. 2002 Aug 6;137(3):149-55.
10. Helzner EP, Luchsinger JA, Scarmeas N, Cosentino S, Brickman AM, Glymour MM, Stern Y. Contribution of vascular risk factors to the progression in Alzheimer disease. Arch Neurol. 2009 Mar;66(3):343-8.
11. Kalaria RN, Ballard C. Overlap between pathology of Alzheimer disease and vascular dementia. Alzheimer Dis Assoc Disord. 1999 Oct-Dec;13 Suppl 3:S115-23..
12. Love S, Miners JS. Cerebrovascular disease in ageing and Alzheimer's disease. Acta Neuropathol. 2016 May;131(5):645-58. Epub 2015 Dec 28.

Please note: Due to limited space, we are unable to list all references. You may contact South Dakota Medicine at ereiss@sdsma.org for a complete listing.

About the Authors:

Eric Novak, DO, Class of 2023 Psychiatry Residency Program, University of South Dakota Sanford School of Medicine; Clinical Instructor, Department of Psychiatry, University of South Dakota Sanford School of Medicine; VA Medical Center, Sioux Falls, South Dakota.

Matthew Tochtrop, DO, Class of 2023 Psychiatry Residency Program, University of South Dakota Sanford School of Medicine; Jefferson Barrack VA Hospital, St. Louis, Missouri.

David Schlagel, MD, Assistant Professor, Department of Psychiatry, University of South Dakota Sanford School of Medicine; Avera Medical Group Behavioral Health, Sioux Falls, South Dakota.

William Fuller, MD, Professor, Department of Psychiatry, University of South Dakota Sanford School of Medicine; Avera Behavioral Health, Sioux Falls, South Dakota.

In Memoriam 2023

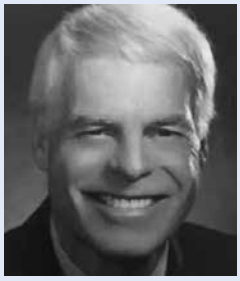
Honoring physician members of the SDSMA who passed away in 2023.

James E. Appelwick, MD
(passed away in Dec. 2022)

David W. Bean, Sr., MD

Richard G. Belatti, MD

John J. Billion, MD

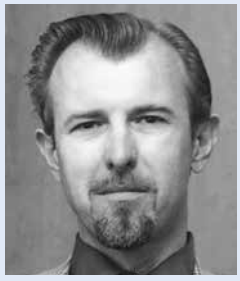


James F. Cole, MD

Mikel D. Holland, MD

O. Myron Jerde, MD

Matthew P. Owens, MD



Martin F. Petereit, MD

Morris L. Radack, MD

Elden R. Rand, MD

Hubert H. Theissen, MD

Wayne A. Wetzbarger, MD

Comprehensive Cardiac Care

Across Nebraska, the Region and Beyond

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

Scan the QR code to learn more about Children's Criss Heart Center and how to make a referral. For immediate consult or transport, call (855) 850-KIDS (5437).

Children's NEBRASKA

Member News

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

Legal Brief Highlight: Medical Malpractice

Physicians are held to certain standards of care in their treatment of patients, and when their treatment of a patient falls below this standard of care, they may be held responsible for damages for medical malpractice. A physician is not necessarily negligent if he or she makes an error in judgment or if treatment proves unsuccessful. Negligence only occurs if the error in judgment or lack of success is due to a failure to perform any of the duties associated with the care and skill ordinarily exercised under similar circumstances by similarly situated physicians.

South Dakota law imposes certain limitations on damages that may be awarded in a malpractice action. However, there is no limitation on the amount of special damages which may be awarded. "General damages" are damages for things like pain and suffering, loss of consortium, and loss of enjoyment of life. "Special damages" are more specifically-quantifiable items, such as past and future medical expenses, prostheses, and wheel chairs. The law also requires both physicians and their malpractice insurers to make reports on malpractice claims.

For more information, access the SDSMA legal brief *Medical Malpractice* at sdsma.org. The SDSMA provides legal briefs for member physicians on a variety of rules and regulations that apply to the medical profession. For nonmembers, legal briefs are available for purchase.

Call for Nominations — SDSMA Awards

Nominations for SDSMA Awards are open! The SDSMA Awards honor physicians for their contributions to health care, service to patients, dedication to improving medicine in South Dakota, or service to the SDSMA.

Nominations are being accepted at sdsma.org for the following awards:

- Distinguished Service Award
- Community Service Award
- COPIC Humanitarian Award - *the recipient of this award designates a $10,000 donation from COPIC to be provided to a healthcare related 501(c)(3) organization in South Dakota!*
- Outstanding Young Physician Award
- Richard P. Holm, MD, Media Award
- Young at Heart Award

Are there people that come to mind who deserve to be recognized? Nominate them today! Award recipients will be honored at the awards banquet in Rapid City during the SDSMA Annual Leadership Conference on May 31, 2024.

An individual may work right alongside of you, serve on a committee with you, volunteer in your organization or community, or have made a significant impact in the medical profession. Help your colleagues and supporters get the recognition they deserve!

For Your Benefit:

Fighting For You and Your Patients

The SDSMA serves as your vehicle for advocacy for your patients and the art and science of medicine through lobbying at the state and federal levels, grassroots activity, and legal initiatives.

SDSMA PAC is your grassroots avenue that works to impact public policy decisions through bipartisan political participation. SDSMA PAC supports and elects pro-medicine candidates on the state level. Members of the SDSMA and their spouses can join SDSMA PAC.

The SDSMA's motto is "Values, Ethics, Advocacy." We take our advocacy role to heart. With your help, SDSMA and SDSMA PAC have the opportunity to dramatically impact the political and legislative process to create meaningful changes in South Dakota's current health care system:

- Improving health and access to care in rural areas;
- Increasing Medicaid reimbursement;
- Promoting Medicare physician payment reform and stopping reimbursement cuts;
- Working to improve clinical quality and patient safety;
- Partnering with state agencies to tackle regulatory, socioeconomic, public health and scientific policy issues;
- Advocating for public health immunizations;
- Promoting adequate funding for medical education;
- Stopping inappropriate expansion of non-physician scope of practice;
- Defending the patient-physician relationship; and
- Reforming medical liability.

If you would like to become involved in any of our advocacy programs, call 605.336.1965 or visit sdsma.org.

"For Your Benefit" is the SDSMA's monthly update on programs and services available to physicians through their affiliation with the SDSMA.

The Issue Is...

2024 Legislative Session Began January 9

The South Dakota Legislature began the 2024 session on Tuesday, January 9 with Gov. Kristi Noem's State of the State address. The governor spoke on several issues and specifically mentioned a few related to the practice of medicine. She addressed the devastating issue of overdose deaths, particularly those attributed to fentanyl and now xylazine. To help combat the problem, the governor and attorney general brought a bill categorizing xylazine as a Schedule III controlled substance.

The governor spoke about the work that has been done over the past few years related to emergency medical services (EMS), including an analysis of the current state as well as more than 400 stakeholder meetings and declared the Department of Health will roll out a $7.5 million grant program to ambulance services later this year. She also praised the utilization of telemedicine in delivering high quality care, especially in our rural communities.

Governor Noem also emphasized the importance of early childhood development. She touted the Bright Start program to get one-on-one nursing services to first-time moms and their babies from pregnancy until the child's second birthday. The governor highlighted the Department of Social Services' Pregnancy Health Home that will offer care coordination to all pregnant mothers who are enrolled in Medicaid, who also have access to prenatal and postpartum coverage for up to a year after birth along with well-child and health maintenance exams.

To ensure that SDSMA members have access to the most current information throughout the legislative session, the newsletter InSession is emailed to members each week, covering what occurred in Pierre during the week, as well as a look ahead to important issues and legislation expected to be considered in committee and on the floor.

The SDSMA's 2024 Advocacy Agenda is available at sdsma.org in the Advocacy section.

Call For Abstracts: 2024 SDSMA Annual Leadership Conference Poster Session

The South Dakota State Medical Association announces the Call for Abstracts for presentation at the 2024 Annual Leadership Conference being held on May 31, 2024 at the Holiday Inn Rapid City Downtown.

The committee welcomes submissions of abstracts from USD SSOM medical students. Early submission of abstracts is appreciated. The abstract may be from basic science or clinical research.

SUBMISSION

Abstracts must be submitted to Keith.Hansen@sanfordhealth.org and ereiss@sdsma.org.

DEADLINE – Friday, March 8, 2024.

Please prepare your submission in accordance with the requirements listed below:

- Abstracts must be submitted in a Word document using Times New Roman Font with a font size of 12 and no more than 300 words (not including title and authors' names), single-spaced. Do not indent headings.
- Abstracts should be proofread prior to submission. Abstract data cannot be altered after the submission. Title and authors may not be changed.
- Abstracts must be original work and should not have been previously published.
- The initial aspect of the abstract should contain the title and the author(s) name and respective site(s) of the study. The author(s) MUST include a faculty member.
- The text should be structured to describe the objective of the study and results of your work. It should include the following headings:
  - **Introduction:** a brief statement about the purpose of the study and the current state of research in the field.
  - **Methods:** the method(s) of study or data collection used.
  - **Results:** a summary of the study results including sufficient details to support your conclusions.
  - **Conclusions:** a statement explaining the significance of your work and the implications for further research.
- In the title, please include type of study: case report, retrospective cohort study, etc.

Case reports should be structured as: Introduction, case report, and conclusion.

Notification will occur by March 30, 2024 for abstracts accepted for poster presentation at the SDSMA Annual Leadership Conference. One of the authors must attend the conference and present their poster.

The accepted abstracts will be published in the meeting program which will be a supplement of South Dakota Medicine. These abstracts will then be available in PubMed.

The accepted abstracts also will be submitted to a panel of judges for evaluation. One abstract will be selected for an oral presentation of their work at the SDSMA Annual Leadership Conference.

Nominations Being Accepted for SDSMA Leadership Positions

The SDSMA Nominating Committee will meet on March 13 to nominate officer candidates for 2024-25 to be voted on by the membership. Those positions include president-elect, vice president, and secretary-treasurer, and AMA delegate. This committee also nominates candidates for three at-large members of the Board of Directors and a Policy Council chairperson from among (or such persons must be) members of the SDSMA Policy Council.

All SDSMA members who have an interest in a leadership position as an officer, AMA delegate, at-large position, or Policy Council chair, must submit their name to one of the members of the Nominating Committee listed below by March 1. The Nominating Committee member will present your name at the committee meeting.

Those who have questions about the nominating or election process for SDSMA leadership positions may contact the SDSMA office at 605-336-1965.

Nominating Committee members:

- Jerome W. Bentz, MD – jerome.bentz@avera.org
- Rochelle S. Christensen, MD – jensrochelle@gmail.com
- Kara L. Dahl, MD – kara094@yahoo.com
- Laura J. Hoefert, MD – laura.hoefert@madisonhospital.com
- Lucio N. Margallo II, MD – drchichi1@mit.midco.net
- Mary Jo Olson, MD – maryjo.olson@sanfordhealth.org
- Tim M. Ridgway, MD – tim.ridgway@usd.edu
- Erica L. Schipper, MD – elschipper@gmail.com
- Stephan D. Schroeder, MD – steve.schroeder@sdfmc.org
- Robert E. Van Demark, Jr., MD – robert.vandemarkjr@sanfordhealth.org

Last Chance to Renew SDSMA Membership for 2024

Thank you for your membership in the SDSMA. Physician membership for those who have not yet renewed will expire this month. If you haven't renewed yet, please do so soon to ensure your benefits are not interrupted.

When you renew, you can choose to renew your AMA dues and sponsor a student's SDSMA membership dues for four years of medical school with one, easy transaction.

The SDSMA works hard to create value for your membership. As the association strives to improve health care in South Dakota, your involvement and advocacy strengthens physician voices, and provides a strong avenue for physicians to be advocates for patients.

Have you recently retired? Please let us know by contacting the SDSMA office at membership@sdsma.org or 605-336-1965.

Please note: if you are a life member, your membership is continuous. You do not need to take any steps to renew.

Follow us on Social Media!

Stay up to date with the latest from the South DakotaState Medical Association.
We are on Facebook, Twitter, and Instagram! Follow and connect with us.

SOUTH DAKOTA
BOARD OF MEDICAL & OSTEOPATHIC EXAMINERS

101 N. Main Ave., Suite 301 Sioux Falls, SD 57104
Phone 605-367-7781 Fax 605-367-7786
www.sdbmoe.gov sdbmoe@state.sd.us

Shutterstock

The medical team representing the Board's regulated professions

South Dakota Board of Medical and Osteopathic Examiners

President

Aaron Shives, MD

Vice President

Gary Timmerman, MD

Secretary

Chris Dietrich, MD

Jennifer L. Tegethoff, MD

Philip Meyer, DO

Suzanne Veenis

Jeffrey A. Murray, MD

Richard G. Hainje

Laurie B. Landeen, MD

- Protects the health and welfare of the state's citizens by ensuring that qualified medical health care professionals are licensed to practice in South Dakota
- Licenses and regulates over 11,500 licenses within fourteen different medical categories
- Establishes regulations by proposing legislation and adopting administrative rules
- Provides Safe Haven, supports, and promotes confidential monitoring of its healthcare providers

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

BEYOND COVERAGE

COPIC's premier medical liability insurance offers comprehensive support built on unparalleled expertise and decades of experience. We share our knowledge through meaningful CME/CNE education, an extensive library of resources, in-depth site visits, and more. All of which help you avoid risks, improve practice protocols, and solve urgent issues quickly. **That's Value Beyond Coverage.**

COPIC is proud to be the endorsed carrier of the South Dakota State Medical Association. SDSMA members may be eligible for a 10% premium discount.

COPIC®
Better Medicine • Better Lives

CALLCOPIC.COM | 800.421.1834

DOC TALK

WITH

MONUMENT HEALTH

Tune into your health with Monument Health.

A weekly podcast featuring Monument Health physicians discussing the latest topics in health care.

Listen wherever you get your podcasts or at monument.health/podcast.