THE Journal
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Osteopathic Medical Schools in Arkansas

Working to Lessen Future Shortages, Increase Access to Care

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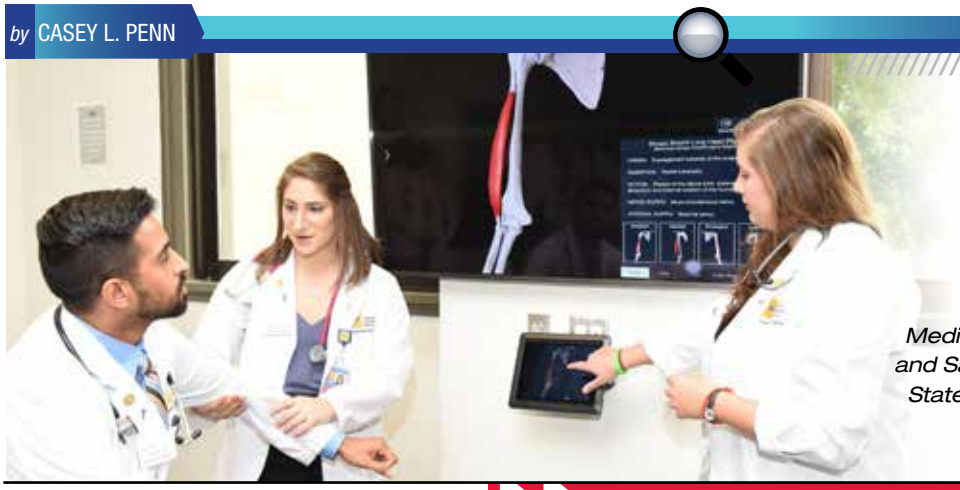
by CASEY L. PENN



ON THE COVER

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Medical students Sunbir Gill, Michelle Tedrowe, and Samantha Connor in NYITCOM at Arkansas State's Osteopathic Manipulative Medicine lab. Also pictured on cover: ARCOM building.

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COMMENTARY

Tim Paden, MD

STAND UP FOR MEDICINE

As physicians, we set our sights on the profession for a variety of reasons – interest in medicine, family tradition, a desire to comfort or heal others. In my case, I trace it back to fourth grade when my father, Robert W. Paden, a pharmacist in the small town of Yellville, influenced me the most with his compassion for others and willingness to help no matter the time of day or night. We can each identify a few influences in our past that directed us in some way into medicine. When reflecting on the driving nature and traditions in medicine that connect all of us in the profession across the globe no matter the location of your training now that we all practice in Arkansas, we have one thing in common – protecting the sanctity of our profession.

Long before health care became a hot topic in our nation based on expense, access, and health management, this profession was one of the healing arts. Men and women are drawn to the elements of protecting life, preserving health, or advancing treatment methods. Consider the sacrifices of our professional ancestors, going all the way back to Hippocrates. The focus on an individual in order to ascertain a diagnosis and subsequent treatment based on the current knowledge and treatment methods of the time to restore health or limit the damage, is still the underlying theme. Now, with the evolution of health care to this point – with the cost strategies, population management, and access and scope-of-care issues – what are we to do?

We are to stand up for health care. If you're in direct patient care with full office schedules and call, then take good care of your patients. Stand up for health care. If you're involved in administrative duties, organizational activities, or management positions, stand up for health care. If you're on the Arkansas Medical Society Board of Trustees and following legislation or in teaching positions of the university system, stand up for health care. Two years ago, I joined AMS after 28 years of practice in a small town. One reason for joining was because I felt that some of us need to stand up for health care. We must do this to keep the profession solid, honorable, and intact despite the direction of control or the demands of the "system." It is and always will be about the patient.

If it's a prescription the patient needs, then fight for it. If it's a position you hold on a hospital committee, fight for it. If you teach students, fight for it. On all ground and all places and all circumstances, we must fight for our profession.

Delegate others to help you. Inspire the youth to seek medicine and share why you went into medicine. Some say the Golden Age of Medicine is over. I say it is just beginning. Never before has our art form been needed more than it is today. So, stand up for health care and fight for it – not just for the income or for control, but for the sake of the profession itself. Our ancestors gave us a noble, honorable profession, so let's give the same to our offspring. AMS

> ***Stand up for health care and fight for it, not just for the income or for control but for the sake of the profession itself.***

THE Journal
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by CASEY L. PENN

Osteopathic Medical Schools in Arkansas

Working to Lessen Future Shortages, Increase Access to Care

Until 2016, Arkansas had only one medical school. Founded in 1879 and still the only traditional (allopathic) medical school in the state, the UAMS College of Medicine is a comprehensive academic medical center that plays a vital role in educating Arkansas physicians. Today, however, Arkansas is also home to two more medical schools, both osteopathic in nature. This month, we bring you an update on the state's osteopathic medical schools, New York Institute of Technology College of Osteopathic Medicine at Arkansas State University in Jonesboro and Arkansas College of Osteopathic Medicine in Fort Smith.

NYITCOM at Arkansas State medical students Matt Gorecki, Mirsha Stevens, Katherine Byrd, and Jay Patel.

Osteopathic and allopathic schools both offer a means to become a licensed physician in this nation.

They educate through many of the same courses – gross anatomy, biochemistry, pharmacology, pathophysiology, etc. In addition, they share similar degree paths consisting of two years in the classroom and two more in rotation, followed by three-plus years of residency. The osteopathic difference is indicated by the term itself, as NYITCOM Dean Shane Speights, DO, explained. The term *osteopathic* denotes an emphasis on the structure and function of the human body coupled with manipulative medicine. "On the osteopathic side, we embrace the whole body," he said. "In my opinion, this can also occur in allopathic schools; it's just that we put that at the forefront. We have an osteopathic manipulative medicine lab and a common belief that the body has the innate ability to heal itself if given the chance. That's not to say that DOs don't prescribe medications (antibiotics, chemotherapies, etc.) or perform surgery. They do."

Shane Speights, DO

In addition, osteopathic medical schools tend to produce more primary care physicians.* "DOs can – and do – enter any specialty from neurosurgery to radiation/oncology," said Dr. Speights. "However, about 60% of DOs, nationally, migrate to generalist specialties (family medicine, internal medicine, pediatrics, general surgery, OB/GYN, emergency medicine). When we talk about the needs of the state, shortages in those general areas really stand out."

A Medical School with a Heart for the Delta

NYITCOM at A-State operates through a public-private partnership between Arkansas State University and NYIT College of Osteopathic Medicine in Old Westbury, New York. The A-State campus is accredited for 115 students per class, and by the fall of 2019, will reach full capacity at 460 total students. The applicant pool is quite large, while the acceptance rate is tiny, just 6.1%. About 80% of students come from within the school's target market, which encompasses Arkansas and surrounding states. The student population is roughly 50% male and 50% female, with underrepresented minorities at about 14%.

NYITCOM's mission is to create and retain more physicians who stay and practice here in Arkansas, particularly in underserved areas around the state. "It isn't a job that one institution can solve," said Dr. Speights. "It takes a collaborative effort amongst many institutions, hospitals, medical schools, residency training programs, and communities. To truly see results, you must have enough physicians graduating from a medical school *in the state* that can then flow into residency programs *in the state* to try to increase the number that will stay *in the state*. We know that of medical students that graduate from a medical school in Arkansas and attend a residency program in Arkansas and graduate from that program, 80% of those graduates (based on current data), will remain in the state or region.** That's a statistic we need to capitalize on."

NYITCOM at A-State cares for all Arkansans, but is particularly committed to improving the quality of life in the Mississippi Delta region. "It's always been our focus to make a positive impact in this, one of the poorest, most underserved regions

in the nation," said Dr. Speights. "The challenges are great, and we're not naïve to think we can go in there with a couple of outreach programs and truly turn things around. But we have to start somewhere, and we have to start today."

Some of NYITCOM's work in the Delta happens through rotation and residency programs. Short of running residency programs of its own, the school supplies resources that support programs in its vicinity. "Through our partnership with Arkansas State University and our parent institution, we're able to provide resources like access to online medical libraries, a full simulation lab, faculty development, graduate programs, and the capacity to host speakers and events related to specific residency programs. We also support them by partnering with them on grants, scholarly activities, and research programs that align with our mission," said Dr. Speights. Indeed, through a USDA research grant, NYITCOM partners with St. Bernard's Internal Medicine Residency Program, Arkansas State University School of Health Professions, and UAMS Family Medicine Residency Program in northeast Arkansas to deliver health screenings and health education to rural areas through NYITCOM's Delta Care-a-van.***

The medical school feels a responsibility to provide vital health education and problem-solving support to K-12 and undergraduate programs and community and civic organizations. Toward this end, students are routinely sent into the community (classrooms, Lions Clubs, Rotary, etc.) to educate on topics like the importance of vaccines, hand washing, physical activity, and the spread of disease. "We believe this is just one way that our students can start changing health outcomes long before they graduate," said Dr. Speights.

Now that NYITCOM's inaugural class has entered rotations, students are experiencing firsthand the disparities of the Delta region and some are already committed to serving the region. Rotations are possible through relationships with roughly 150 hospitals, clinics, and individual physicians who provide training in the real world – a valuable step that helps students like Clayton Preston choose a path. "I did my undergrad in Jonesboro and established some roots there, so I had my heart set on staying there for my rotations," said the third-year student. However, things changed during Preston's rotation in his home town of Pine Bluff. At Jefferson Regional Medical Center, where he was born and had worked his first job in the hospital cafeteria, Preston felt a call to serve there as a pediatrician. "I've been exposed to so many cases that have provided unique learning opportunities, and I've had a great experience in Pine Bluff. Things work out the way they're supposed to."

During a recent Interview Day in Jonesboro, medical students Megan Patel and Colton Eubanks explain how NYITCOM at A-State uses fully-functioning mannequins in their training.

Nothing can replace training that comes from rotations, Dr. Speights indicated. "Physicians – particularly those in underserved areas – are truly on the front lines of health care – treating the sick, maintaining the well, and making a difference in the lives of patients and their families. Our students appreciate the education they receive by witnessing that care that's being provided. We make a concerted effort to rotate our students into areas like Arkadelphia, Gravette, Pocahontas, Mena, Monticello, Crossett, and many others."

A New and Fast-Growing Medical School

Affiliated with Arkansas Colleges of Health Education, **ARCOM** is housed on 228 acres at Chaffee Crossing in Fort Smith. Founded in 2014, the school welcomed its inaugural class in August 2017 and is currently educating its second class. Each class size is 150 students, from a large-and-growing applicant pool.

Students are excelling thus far, with average MCAT scores of over 500 and an average GPA of more than 3.5. The student population is roughly 50% male and 50% female, with 15% underrepresented minorities. Around 65% of enrolled students come from within the school's service area of Arkansas, Kansas, Kentucky, Louisiana, Mississippi, Missouri, Oklahoma, Tennessee, and Texas.

Frazier Edwards, MPA, is the executive director of ARCOM Clinical Resources and Continuing Medical Education. He is excited to share that ARCOM has the fastest growing applicant pool of any medical school in the country. As for reasons why, Edwards points to the school's "shiny and new" state-of-the-art facilities, faculty, and helical team-based curriculum.

ARCOM's mission, according to Edwards, is to "serve the underserved" and help solve public health issues facing Arkansas – specifically, physician shortages. Authors of a 2018 guest editorial published by the Arkansas Foundation for Medical Care touched on such shortages, particularly in rural areas of the state. "Several trends are driving this shortage," wrote authors Ray Hanley, AFMC president and CEO, and AFMC Board Chair Stacy C. Zimmerman, MD, FACP, FAAP. "An increased number of Arkansans have access to health care through the Medicaid-expansion program, Arkansas Works. Our population is aging, and the older we get the more medical services we use … another reason is more than a third of all active physicians will be age 65 or older during the next 10 years, and many will retire."

Working toward solutions, ARCOM focuses on producing primary care physicians. "There's a cliff coming," said Edwards. "That's why we're here. We must start now to plan for 10 to 15 years from now. A student will go through medical school followed by residency. That's a minimum of seven years and oftentimes more depending on the specialty. Doing this now will help lessen the cliff and ensure that we won't go through dips in access or quality of care. In our curriculum, we try to ensure that students are aware of the need in these areas."

ARCOM's third-and-fourth-year rotations allow students to discover and learn from systems already in place. "We'll send them to a large hos-

From left to right: ARCOM students Joseph Kordsmeier, Trent DeLong, Michael Page, Kelley Harris, and Dania Abu Jubara; Frazier Edwards, MPA.

pital for typical third-year core rotation training, but they're also required to do a community hospital rotation – usually a critical-access hospital in a rural area – and a rural family practice rotation," said Edwards. "Because these locations are short-staffed, students are right in there with the staff working … it's a 'roll-up-your-sleeve, let's get to work' approach."

Magnolia-native Michael Page is aiming toward just such a diverse, hard-at-work medical practice – in his home town, no less. Page is part of ARCOM's inaugural class and is among those currently gearing up for post-second-year exams. Upon passing, he will move on to rotations. Set to graduate in May 2021, Page plans to pursue residency in family medicine. He hopes to, eventually, be back in Magnolia to open his own family practice. "My interests in family medicine center around the broad training I can receive that will allow me to provide inpatient and outpatient services, perform procedures, deliver babies, and fulfill my desire to be useful to the rural population of patients I intend to serve," said Page. "Growing up, I had the opportunity to spend time at the local family doctor's office in Magnolia where my mother was the office manager. After seeing the family doctor serve many roles as a pillar in the community, I was strongly influenced."

Having more physicians is a win, particularly when those physicians remain in Arkansas to practice in underserved areas. ARCOM recently received accreditation to provide residency and fellowship education to its graduating students.**** In line with its goal of producing more Arkansas primary care physicians, the school is at work now to develop new residency programs in the areas where those students are needed. ARCOM has the capacity to assist area institutions in various roles. "We can be adaptive," said Edwards, who recently announced a residency partnership with Unity Health. "At Unity Health, we're going to be an academic partner. In other instances, we will be the sponsoring institution.

"We have several programs that are in the application process. CHI St. Vincent in Hot Springs is one example of a partnership that will benefit the community. They're a core rotation site for our third- and fourth-year students. Now, they're developing residency programs in internal medicine and family medicine to start with. So, the hope is to have those programs ready by the time those students graduate. Statistics show that students tend to stay where they train, and we want to develop as many programs as we can that work *with* that statistic. We want to start by recruiting them from our service area. If we can then train them through rotations in the area, and then if they can enter a residency program in the area, there's a good opportunity for a community to retain them in the area."

Support for All Medical Students and Physicians / AMS and AOMA

With more medical students in the state, there is much interest from professional societies to work together to provide support to future physicians. In addition to his role at ARCOM, Edwards is the executive director of the Arkansas Osteopathic Medicine Association. He advises students to take advantage of the support offered through medical specialty organizations. "There's an ongoing effort through the Winthrop Rockefeller Institute to find ways in which all medical schools and societies can come together to better serve the needs of the state. As for the AMS and AOMA, we have always worked closely together on difficult issues, whether it's at the capitol or in outreach efforts to try and get the profession engaged.

"We encourage students to join both the AMS and the AOMA. Students that graduate from an osteopathic medical school do have a uniqueness to their practice. They're able to perform osteopathic manipulative therapy, and some of that language is unique. So, having that unique voice that represents the profession is important. However, it's also important to make sure that voice is heard on multiple levels. The AOMA and the AMS have enjoyed a good working relationship already and continue to look forward to working together for the benefit of all medical students, physicians in the state, and ultimately, for the overall health of the state."

The AMS is pleased to shine a light on the state's osteopathic programs and their impact on the medical profession and the health of Arkansans. AMS Executive Vice President David Wroten encourages students to reap the benefits of society participation. "Medical students are the future leaders of their profession. We recognize that and want not only to be supportive but also to help students attain the skills and knowledge necessary to assume those leadership roles," said Wroten. "The first thing the new students will learn about AMS is that the organization makes a strong commitment for the entire length of their medical training. From the first year of medical school through their final year as a medical resident, membership in the AMS is available at no cost to the student.

"However, that's just the beginning of the Society's support. As part of our commitment to involving all students in our organization, AMS has amended its bylaws to pave the way for osteopathic students to create AMS student chapters."

To learn more about the state's osteopathic medical schools, visit nyit.edu/arkansas and acheedu.org/arcom.

***For more statistics on osteopathic students and practicing physicians (U.S.), download the latest Osteopathic Medical Profession Report** at https://osteopathic.org/about/aoa-statistics.

****The Association of American Medical Colleges provides Arkansas physician retention data and related statistics.** https://www.aamc.org/download/484516/data/arkansasprofile.pdf

*****Learn more about NYITCOM's Delta Car-a-van.** https://www.nyit.edu/box/Features/medicine_on_the_go

****** The following articles offer a more detailed look at ARCOM's work on the residency side.** https://www.swtimes.com/news/20180209/arkansas-college-of-osteopathic-medicine-enters-agreement-with-chi-st-vincent-at-hot-springs

https://talkbusiness.net/2019/01/arcom-gains-accreditation-for-residency-fellowship-programs/ AMS

Hydralazine-induced Rheumatologic Disease: Back to the Future

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ABSTRACT

We present a patient who developed both drug-induced lupus and vasculitis after taking hydralazine. Additionally, we review the literature about these disorders. An 81-year-old hypertensive female developed serositis, leukopenia, thrombocytopenia, positive ANA (Antinuclear antibody) and antihistone antibodies, hypocomplementemia, a pauci immune glomerulonephritis, and positive ANCA (Anti-Neutrophilic Cytoplasmic Autoantibody) after six months of hydralazine. Although lupus and vasculitis are known side effects of hydralazine, their frequency decreased significantly 25 years ago, as angiotensin-converting enzyme inhibitors replaced hydralazine. However, use of hydralazine increased recently after heart-failure patient survival improved with the combination of hydralazine and nitrates. It is important to recognize the autoimmune complications of hydralazine, especially in the setting of its increased clinical use.

INTRODUCTION

Hydralazine is an arterial vasodilator to treat hypertension and heart failure since 1953.[1] Although lupus and vasculitis are well described side effects of hydralazine,[2] their frequency has decreased significantly because angiotensin-converting enzyme inhibitors replaced hydralazine, resulting in several generations of physicians who are unfamiliar with its complications. In 2004, the recognition that heart-failure patients treated with hydralazine and nitrates survive longer has caused increased use of hydralazine and the possibility of a resurgence of its adverse effects.

We present a patient with hypertension who developed both lupus and ANCA positive pauci-immune glomerulonephritis after six months of hydralazine therapy.

CASE PRESENTATION

An 81-year-old female with renal insufficiency (baseline creatinine= 1.5 mg/dl), hypertension (treated with hydralazine for the prior six months), hypothyroidism, and hyperlipidemia was admitted to an outside hospital with four months of intermittent, subjective fever; malaise; fatigue; weakness; nausea; diarrhea; vomiting; 40 pounds of unintentional weight loss; and two weeks of decreased urination and leg swelling.

Her physical exam and diagnostic laboratory test results on admission to the outside hospital:

Temp: 98.1; BP: 137/71; HR: 75; RR: 20
Skin: morbilliform eruption of the neck and upper chest, arms and forearms bilaterally
Lung exam: rales at left lower base
Heart sounds: normal
Muscle strength: 4/5 in proximal upper and lower extremities

WBC: 1000/mm3 (nl= 3-12,000)
Hemoglobin: 9.1 g/dL (nl= 11.5-16)
Platelet: 76000/mm3 (nl= 150,000-500,000)
Potassium: 6.6 mmol/L (nl= 3.5-5.1)
Bun: 44 mg/dl (nl= 6-20)
Cr: 2.6 mg/dl (nl= 0.4-1.0)
UA: 40-50 RBCs/hpf (nl= 0-2/)
LDH: 986 IU/L (nl= 100-248)
Blood and urine cultures: sterile

She underwent dialysis to treat her hyperkalemia, received filgrastim for the leukopenia with improvement (5000/mm^3) but a worsened thrombocytopenia (35000/mm^3). Because of her acute kidney injury, thrombocytopenia, and elevated LDH, her doctors transferred her to our hospital to undergo plasmapheresis for atypical hemolytic uremic syndrome (HUS).

Her medications on transfer included: aspirin 81 mg daily, levothyroxine 75 mcg daily, hydralazine 25 mg TID, triamterene/hydrochlorothiazide 75/50 mg daily, megestrol acetate 400 mg daily, calcium/vitamin D 600mg/400 IU daily, simvastatin 40 mg nightly.

Her physical exam and diagnostic laboratory test results on arrival:

Vitals: Temp 98.2; RR 14; BP 135/75; P 75
General: patient appeared sick but in no acute distress
Lungs: clear to auscultation bilaterally
Skin: morbilliform eruption of the neck, upper chest and bilateral upper extremities, sparing the hands; Ecchymoses on her forearms
Cardiac: regular rate of S1 S2 without S3, S4, murmurs.
Abdomen: bowel sounds present, soft, nontender, without hepatosplenomegaly
Extremities: diffuse 4+ pitting edema
Neurologic: 3/5 proximal muscle strength; 4+/5 distal muscle strength

WBC 8840/mm^3 (nl= 3-12,000)
Hemoglobin 9.3 mg/dL (nl= 11.5-16 g)
Platelet count 37000/mm^3 (nl= 150,000-500,000)
Peripheral smear: rare schistocytes
Haptoglobin: 165 mg/dl (nl= 30-200)
Sodium 134 mmol/L (nl= 135-145)
Potassium 6.6 mmol/L (nl= 3.5- 5.1)

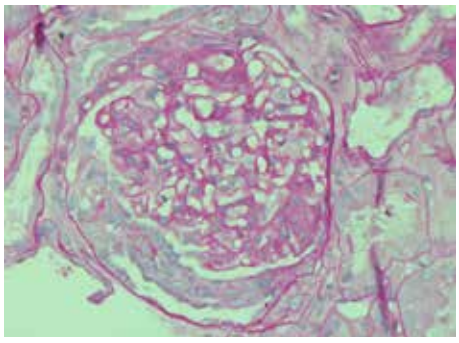

Figure 1. Partial-cellular crescent present in a normocellular glomerulus, PAS stain, 400X

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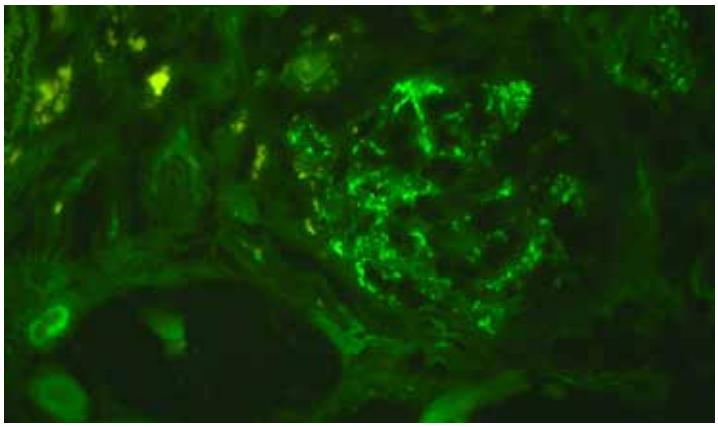

Figure 2. Mesangial C1q positivity (1+) by direct IF staining, FITC, 400X.

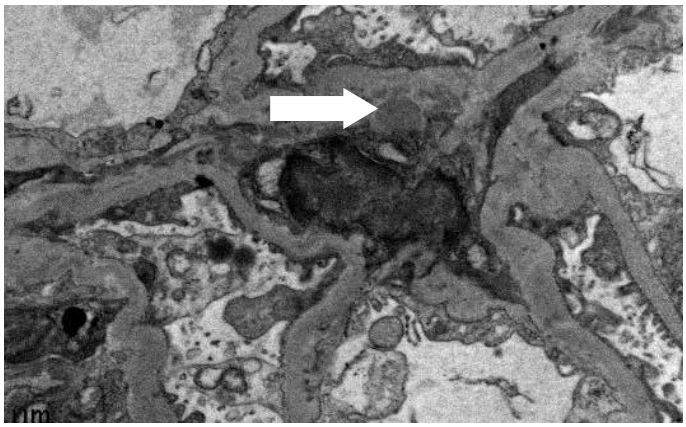

Figure 3. Electron microscopy showing small mesangial densities (Arrow).

Bicarbonate 12 mmol/L (nl= 22-32)
BUN 92 mg/dl (nl= 6-20)
Creatinine 6.2 mg/dl (nl= 0.4-1.0)
Calcium 7.8 mg/dl (nl= 8.6-10.2)
Phosphorus 6.3 mg/dl (nl= 2.5-4.5)
Magnesium 1.8 mg/dl (nl= 1.6-2.6)
AST 32 IU/L (nl= 15-41)
ALT 7 IU/L (nl= 5-45)
LDH 469 IU/L (nl= 100-248)
TSH: 2.07 IU (nl= 0.34-5.6)
CK 38 IU/L (nl= 38-234)
Aldolase: 18.8 U/L (nl= 1.5-8.1)
Myoglobin 402.3 ng/ml (nl= 3-70)
UA: Blood large; RBC >100 (nl= 0-2); WBC 0-2 (nl= 0-2); Dysmorphic RBCs present; Urine protein/creatinine: 1840 mg/24 hours

Immunology

ANA-positive (no titer was performed)
Anti histone antibody: >8.0 units (nl < 0.9)
Anti ds DNA antibody: 14 IU/ml (nl< 9),
Anti smith antibody: negative.
C3- 33.1 mg/dl (nl= 90-180)
C4- <10.0 mg/dl (nl= 15-45)
ANCA 1:5120 (nl < 1:20)
Anti MPO 137 AU/ml (nl< 19)
Anti PR3 40 AU/ml (nl< 19)
Cryoglobulin: negative

Infectious disease

HIV and hepatitis antibodies: negative

Diagnostic Radiology tests

Chest radiograph: large, left pleural effusion

Renal ultrasound: markedly echogenic kidneys suggesting medical renal disease without hydronephrosis

With a normal haptoglobin and rare schistocytes, HUS was less likely. Thus, she underwent a renal biopsy, revealing a crescentic glomerulonephritis (Figure 1) consistent with pauci-immune (ANCA related) glomerulonephritis; 80% global sclerosis; and cortical interstitial fibrosis with tubular atrophy. Additionally, her biopsy indicated a low-grade mesangiopathic glomerulonephritis with immunofluorescence showing full-house staining (Figure 2) and electron microscopy showing mesangial small, electron-dense deposits (Figure 3), favoring autoimmune etiology (such as lupus).

Because she began hydralazine six months prior to developing serositis, leukopenia, thrombocytopenia, positive ANA, positive antihistone antibody, hypocomplementemia (indicative of active lupus), and features of an ANCA-associated renal vasculitis (a strongly positive ANCA in a perinuclear staining pattern, anti MPO antibody and a pauci immune crescentic glomerulonephritis), we diagnosed this patient with simultaneous hydralazine-induced ANCA-positive glomerulonephritis and hydralazine-induced lupus.

DISCUSSION

Because neither denovo lupus nor denovo ANCA-associated pauci immune glomerulonephritis are likely in this 81-year-old patient and she took a drug known to cause these complications, we conclude that she had both hydralazine Drug-induced lupus (DIL) and hydralazine Drug-induced ANCA associated vasculitis (DIAV).

DIL more commonly affects older individuals (mean age > 50 years) without gender predominance. Most rheumatologists agree that patients with suspected DIL should develop lupus manifestations and a positive antinuclear antibody after beginning a suspected medication. Furthermore, these abnormalities should resolve after discontinuing the medication.[3] The following abbreviated drug list has been linked with DIL development and grouped into "Definite" and "Possible" categories (Table 1).

Patients with DIL tend to have milder disease and may experience fever, myalgias, rash, arthralgias, arthritis, serositis, cytopenias, hypocomplementemia, and anti-histone antibodies with rare renal, central nervous system involvement, or pulmonary hemorrhage. Up to 50% of patients on hydralazine can develop a positive ANA, but only 5-8% will develop DIL.[8]

DIAV has been reported for propylthiouracil, hydralazine, minocycline, and levamisole-cut cocaine, and is the most common forms of vasculitis. Contrasting with the idiopathic vasculitides, DIAV is usually milder, and the effects are often reversible once the offending agent is withdrawn. However, patients may develop more severe organ involvement with permanent damage if the drug is not withdrawn soon enough.

Patients with DIAV frequently present with subjective fever, nausea, vomiting, myalgias, arthralgias, rash (including palpable purpura), malaise, and weight loss or with hematuria, proteinuria, and an elevated serum creatinine representing acute kidney injury that rapidly progresses to renal failure.[9] Hemoptysis, indicating alveolar hemorrhage, is the

Table 1. Drug-Induced Lupus

Definite	Possible
Procainamide[4]	β interferon
hydralazine	γ interferon
penicillamine	anticonvulsants (esp phenytoin)
quinidine	rifampin
Isoniazid	nitrofurantoin
Minocycline[5]	lithium
diltiazem	captopril
(subacute cutaneous lupus rash)[6]	hydrochlorothiazide
anti-TNF-α agents[7]	sulfasalazine
α-methyldopa	terbinafine
chlorpromazine	amiodarone
	docetaxel
	HMG-CoA reductase inhibitors
	tetracycline
	griseofulvin
	gemfibrozil
	lamotrigine
	reserpine

most severe pulmonary manifestation of DIAV; it may initially manifest as only a cough and slight dyspnea. Patients with DIAV may also complain of chest pain, reflecting pericarditis. Neurologically, patients may experience nonspecific cognitive symptoms and sensorineural hearing loss. Finally, while uncommon, hypocomplementemia predicts a worse prognosis with more severe organ damage.[10]

When either DIL or DIAV are suspected, the diagnostic testing should include an ANA titer, antihistone antibody, C3, C4 for DIL, and an ANCA for DIAV. Furthermore, to assess the extent of the disorder, the practitioner should order a CBC with differential, CMP, and urinalysis with microscopy, with additional tests based on those initial test results. However, because these laboratory tests are not diagnostic for DIL or DIAV, an extensive differential diagnosis list should include infections, malignancies, endocrinopathies, and other autoimmune conditions.

The most important therapy/intervention in the management of DIL or DIAV is discontinuing the offending drug. Depending on the severity of the disease manifestations, nonsteroidal anti-inflammatory drugs can be used for arthralgias. Patients with serositis or other significant organ involvement may require systemic steroids or immunosuppressive agents after a tissue diagnosis.

In our patient, despite discontinuing the hydralazine and treatment with methylprednisolone- 1 gram intravenous/day x 3 days followed by oral prednisone-60 mg/day and rituximab-375 mg/m^2/week x 4 weeks, she remained dialysis dependent.

CONCLUSION

We conclude that it is important to recognize the autoimmune adverse effects of hydralazine, especially in the setting of its increased clinical use. When patients that have autoimmune disease as a complication develop new, unexplained symptoms after starting medications, prompt investigation is necessary to prevent irreversible end organ damage.

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A CLOSER LOOK AT QUALITY

New Guidelines on Pediatric Traumatic Brain Injury

LAURA J. HOBART-PORTER, DO, FAAPMR

Pediatric mild traumatic brain injury (mTBI) is complex and presents numerous challenges to physicians across multiple specialties. Children with mTBI made more than 2 million outpatient and nearly 3 million emergency department (ED) visits between 2005 to 2009.[1] Most recover in one to three months, but many patients have persistent and functionally impairing symptoms that require intervention.

In November 2018, the Centers for Disease Control and Prevention (CDC) presented a consensus guideline on the management of mTBI in children ages 18 and under, based on a systemic review of articles published between 1990–2015 and a period of public commentary in 2017.[2] This guideline recommended clinical use of mild traumatic brain injury in place of concussion.

Mild TBI is defined as "an acute brain injury from mechanical energy to the head from external physical forces including: (1) one or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, symptoms, or seizure; (2) Glasgow Coma Scale (GCS) score of 13-15 after 30 minutes post-injury or later upon presentation for healthcare."[3] This definition includes children with intracranial injury (ICI), which can be skull fracture or intracranial bleed. These children may recover more slowly than those with an uncomplicated mTBI.

CDC'S RECOMMENDATIONS

Forty-six recommendations were rated according to CDC committee level of confidence and strength of recommendation. Levels of confidence include High, Moderate, Low and Very Low. Strength of recommendations include Level A (should always be followed), Level B (usually should be followed), Level C (may sometimes be followed), Level U (insufficient evidence to make a recommendation) and Level R (should not be done outside of a research setting). A summary of committee consensus on diagnostics and TBI prognostic factors is presented here.

IMAGING RECOMMENDATIONS

Imaging is an oft-debated area of mTBI. Head computed tomography (CT) should not be used routinely for diagnostic purposes (Moderate level of confidence, Level B strength of recommendation). Rather, it is recommended that existing decision rules guide use of CT, such as the Pediatric Emergency Care Applied Research Network (PECARN).[4] Up to 8 percent of children seen in the ED will have ICI.[5] It is necessary to weigh risk factors that indicate possible need for CT imaging, including: age younger than 2 years, vomiting, loss of consciousness, severe mechanism of injury, severe or worsening headache, amnesia, nonfrontal scalp hematoma, GCS score of less than 15, and/or clinical suspicion of skull fracture.

Use of other cranial imaging options is appropriate only in specific circumstances. MRI should not be

used routinely in acute evaluation of mTBI, due to the need for sedation, study length and the exam's expense (Moderate, Level B). This is an evolving area, however, with successful use of rapid sequence MRI in non-sedated patients.[6]

Single-photon emission CT (SPECT) should not be used in the acute evaluation of mTBI, because of the need for sedation, contrast and higher expense (Moderate, Level B). Skull radiographs are not appropriate with mTBI, as some fractures and intracranial bleeds will not be visible with this modality (High, Level B).

OTHER ASSESSMENT TOOLS

Additional assessment tools are available, including symptom scales, computerized assessments and serum biomarkers. It is recommended that an age-appropriate, validated symptom rating scale be used as part of the diagnostic evaluation for pediatric acute mTBI (Moderate, Level B). There are several symptom scales available, but no single tool is strongly predictive of outcome. Use of a standardized tool to routinely track recovery is recommended (Moderate, Level B). Reaction time and balance testing may also be used to assess recovery (Moderate, Level C).

Age-appropriate computerized cognitive testing may be used in acute settings as part of diagnostic evaluation (Moderate, Level C). Several studies indicate that a computerized neurocognitive test battery can distinguish high school athletes with and without mTBI in the first four days after injury, although these studies only evaluated one product.[7]

Serum markers should not be used outside a research setting to diagnose children with mTBI (High, Level R).

FAMILIES NEED REASSURANCE

Education and counseling can provide reassurance and prevent complications. Patients and families should be advised that most (70-80%) of pediatric mTBI patients will not show significant related problems beyond one to three months from injury, and each child will follow his or her own path to recovery (Moderate, Level B). Currently, there is no identified single factor that can predict symptom resolution or outcome.[8] However, premorbid history should be obtained as this can guide providers in determining prognosis (Moderate, Level B). Specifically, children may have a delayed recovery if they have one or more of these comorbidities: premorbid TBI, lower cognitive ability, neurological or psychiatric disorder, learning disorder or problems, preinjury symptoms (headache) or family or social stressors. Certain risk factors can raise the likelihood of persistent post-mTBI symptoms (High, Level C), including: age (older children/adolescents), ethnicity/race (Hispanic), lower socioeconomic status or more severe initial presentation. Headaches tend to be more common in females with mTBI.[9]

Children who have not responded to standard treatment within four to six weeks should be referred for appropriate assessments and/or interventions (Moderate, Level B). ▲

Dr. Hobart-Porter is medical director, Spinal Cord Disorders Program and Concussion Clinic, UAMS and Arkansas Children's Hospital.

EDITOR'S NOTE: *Dr. Hobart-Porter will discuss mTBI management and treatment guidelines in the June "A Closer Look at Quality" column.*

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Relationship Between Visceral Fat and Health-related Quality of Life in Fifth and Sixth Graders in a Rural Public School in Arkansas

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Keywords: pediatric obesity, health-related quality of life, visceral fat, percent body fat, body mass index, body image

ABSTRACT

Obese children are more likely to suffer from body dysmorphia, depression, and decreased quality of life. Thirty-five fifth- and sixth-grade students (male, n=17; female, n=18) at a rural public school were asked to participate in this descriptive, correlational design to describe the relationship between visceral fat level (VFL), body image dissatisfaction (BID), and health-related quality of life (HRQoL). Body composition measures of body mass index (BMI) *z*-score and VFL had a significant, positive correlation with percent body fat (r=.851, *p*=.000; r=.937, *p*=.000 respectively) and BMI *z*-score and VFL had a positive correlation with one another (r=.745, *p*=.000, respectively). BID and HRQoL were significantly, negatively related (r=-.450, *p*=.011, respectively). When students were divided into three groups based on BMI *z*-score, obese participants were more likely than overweight or normal weight participants to report BID (*p*=.002 and *p*=.001, respectively). As BID increased, HRQoL decreased, and those who were obese had the highest levels of BID. Future interventions should aim at reducing BID while working to alleviate the incidence of obesity in this age group. Expanding this study to include urban and high minority schools will increase generalizability of findings.

INTRODUCTION

Overweight and obesity account for 33.9% of children aged 10-17 in Arkansas, ranking the state the ninth most overweight/obese in the nation for children of this age group.[1] Pre-adolescence is a crucial stage because of emotional and social changes that occur and influence body image. In females, this change takes place between 9 and 12 years of age, while in males, this occurs between 10 and 13 years of age.[2] Children who are overweight/obese are at risk for physical health problems as well as social, emotional, and psychological problems impacting health-related quality of life (HRQoL).[3] More than half of girls (55-59%) and about one-third of boys (33-35%) between the ages of 6 and 8 years state that the ideal body is thinner than their current body size. Body-image dissatisfaction (BID) may arise from discrepancies between actual and ideal weight.[4,5] Evidence suggests visceral fat level (VFL) is a more effective predictor of overall health and is linked more closely to metabolic syndrome. Metabolic syndrome is associated with a 70% increase in the risk of sudden cardiac death. Healthy VFL score is <10, and an excessive VFL score is ≥10.[6] Findings from the Bogalusa Heart Study[7] and from the American Academy of Child Adolescent Psychiatry[8] show that the obesity trend is rising among children and adolescents, and that parental obesity impacts pediatric obesity.

Financial Impact

Socioeconomic status (SES) is dependent not only on income but also educational achievement, financial security, and subjective perceptions of social status, social class, and health status.[9] In the 2002-2005 Medical Expenditure Panel Survey (MEPS), children who were obese had $194 higher outpatient visit expenditures, paid $114 more in prescription drug expenditures, and paid $12 more for emergency room visits than children of normal or underweight. Children who were overweight had $79 higher outpatient visit expenditures, paid $64 more in prescription drug expenditures, and paid $25 more for emergency room visits than normal or underweight children. Children who had an elevated body mass index (BMI) were associated with $14.1 billion in additional outpatient visit costs, prescription drug costs, and emergency room costs annually.[10]

METHODS

Study Design

This study used a descriptive and correlational design to describe the relationship between rural public-school students' VFL, BID, and HRQoL. Researchers received Institutional Review Board approval from the university before conducting the study.

Participant Recruitment

A sample of fifth- and sixth-grade students from a rural public school participated. Out of a possible 142 participants (grade 5 n=64, grade 6 n=78), 35 elected to participate. Of those, 49% were male (n=17) and 51% were female (n=18), ranging in age from 10 to 13 years (M=11.26, SD=.701).

Data Collection Procedures and Measures

A 23-question survey, including the PedsQL Core 4.0 for HRQoL, was used to collect data from the participants. BMI Figural Stimuli Silhouette (SIL) was used to determine self-perception of body mass and the desired body mass. A stadiometer was used to determine height. Body composition, including VFL, was analyzed using the InBody 570 Body Composition Analyzer. BMI *z*-score was calculated using CDC charts. BMI *z*-scores were then categorized as normal, overweight, or obese. The Stunkard Scale and the InBody 570 Body Composition Analyzer was used in this study to measure self-perceived body image and VFL of students (**Figures 1 and 2**).

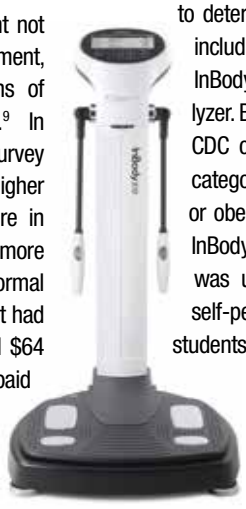

Figure 2. InBody 570 Body Composition Analyzer

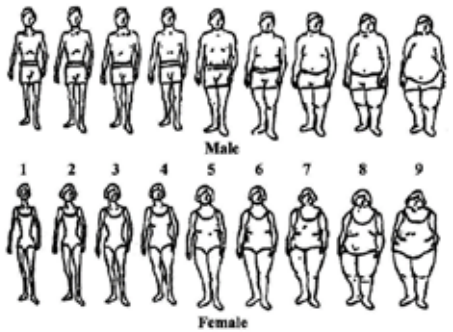

Figure 1. Stunkard's Visual Figures Scale

Statistical Analysis

Data was analyzed using descriptives and frequencies, bivariate correlations, one-way ANOVA, and independent samples *t*-test using the Statistical Package for the Social Sciences (SPSS).

RESULTS

Of the sample (n=35), the minimum VFL was a level 1 (n=4) and the maximum VFL was a level 20 (n=1). Majority (77%, n=27) of participants scored within healthy recommendations (VFL<10) and 22% (n=8) scored an excessive VFL (VFL≥10). All participants who classified as healthy weight and overweight also had a healthy VFL, while only three participants who were classified as obese had a healthy VFL.

The minimum BMI *z*-score was 19 (n=1) and the maximum was 99 (n=1). Approximately half (49%, n=17) of participants were within healthy BMI *z*-score, whereas 20% (n=7) were classified overweight, and 31% (n=11) were classified as obese. The minimum HRQoL was 32 and the maximum was 100 (M=80.9, SD=1508). Participants who scored less than 75% on the HRQoL were mostly of a healthy weight (n=11, 73.3%) see **Table 1**.

As predicted, positive correlations were exhibited between PBF and BMI z-score and VFL (r=.851, *p*<.000; r=.937, *p*<.000, respectively). A positive correlation was also seen between VFL and BMI *z*-score (r=.745, *p*<.000, respectively)—see **Table 2**. BID (M=.967, SD=.982) and HRQoL (M=80.90, SD=15.08) were significantly, negatively related (r=-.451, *p*=.012), and those who were obese had the highest levels of BID (M=1.8, SE=.29)—see **Figure 3**. Obese participants (n=11) were more likely than overweight (n=7) or healthy weight (n=17) participants to report body-image dissatisfaction (*p*=.002 and *p*=.001, respectively)—see **Figure 4**. Males had a greater BID (M=1.33) than females (M=.625), a greater BMI *z*-score (M=82.53) than females (M=67.5), and a higher VFL (M=7.59) than females (M=4.67)—see **Figure 5**. HRQoL's only correlation was to BID—see **Figure 6.**

Table 1. Participants HRQoL Score Range for Weight Classification

BMI z-Score Weight Classification 25-49%		HRQoL Score Range			
		50-74%	75-100%	Total	
Healthy Weight	Count	0	4	11	15
	% Within Weight Class	0%	26.7%	73.3%	100%
	% Within HRQoL Score Range	0%	44.4%	52.4%	48.4%
	% of Total	0%	12.9%	35.5%	48.4%
Overweight	Count	1	1	4	6
	% Within Weight Class	16.7%	16.7%	66.7%	100%
	% Within HRQoL Score Range	100%	11.1%	19%	19.4%
	% of Total	3.2%	3.2%	12.9%	19.4%
Obese	Count	0	4	6	10
	% Within Weight Class	0%	40%	60%	100%
	% Within HRQoL Score Range	0%	44.4%	28.6%	32.3%
	% of total	0%	12.9%	19.4%	32.3%
Total	Count	1	9	21	31
	% Within Weight Class	3.2%	29%	67.7%	100%
	% Within HRQoL Score Range	100%	100%	100%	100%
	% of total	3.2%	29%	67.7%	100%

DISCUSSION & FUTURE STUDIES

Although BMI *z*-score and VFL were closely related, the data for some participants presented anomalies. Many students who were classified as obese by BMI *z*-score were within acceptable VFL ranges. Elevated levels of BID were seen in every weight group. Some participants who were of healthy weight classification scored low HRQoL, while other participants of obese weight classification scored high HRQoL. In general, HRQoL was inversely related to BID, so higher levels of BID indicated lower levels of HRQoL.

Children of this age group may not yet be experiencing problems with teasing and bullying, or the children may not have mentally matured enough to identify adverse social conditions like many studies suggest. Another possibility is that due to the vast population of elevated BMI individuals in Arkansas, an elevated BMI *z*-score may appear to be considered "normal" to many of the children, so teasing may not occur.

Limitations include small sample size which may impact results, data collection from one school, and collecting data once in a school year. Further research will need to be conducted with the same participants as they continue into adolescence and until they graduate from secondary school. As students age, HRQoL will most likely change. Observing changes over time may provide more information about how to address BID, which often leads to other mental stressors. Establishing greater rapport with students and faculty may encourage greater participation in the next study. A major gap in literature pertaining to VFL cut-offs in adolescence made the present study of defining appropriate VFL challenging. Currently, there are not any VFL reference ranges for children or adolescents in the U.S. Due to this limitation, the adult threshold of 100 cm^2 was used.

Future studies to be carried out should work to resolve the following factors:

1) **Having a larger sample, adding additional schools or increasing participation within schools.** Having a larger sample will aid in

> Continued on page 256.

Table 2. Pearson's Product-Moment Correlation Results

	PBF	VFL	BMI z-score	BID	HRQoL
PBF	1	.937**	.851**	.577**	-.155
VFL		1	.745**	.531**	-.147
BMI z-score			1	.473**	-.185
BID				1	-.450*
HRQoL					1
*p<.05, **p<.01					

greater general knowledge of target population. Expanding the study to include urban and high minority schools will increase generalizability of findings.

2) **Define childhood and adolescent VFL reference ranges.** The BIA used (InBody 570) measures VFL between T1-T12 vertebrae. Threshold for adults is 100 cm^2. Other countries have done research to define VFL reference ranges. To better identify metabolic risk, a defined childhood/adolescent reference range is paramount.

3) **Record additional anthropometrics, e.g. blood pressure and waist circumference.** Having more information won't lengthen the data collection process by much, and the additional data will provide a better idea of where a participant is in reference to metabolic syndrome.

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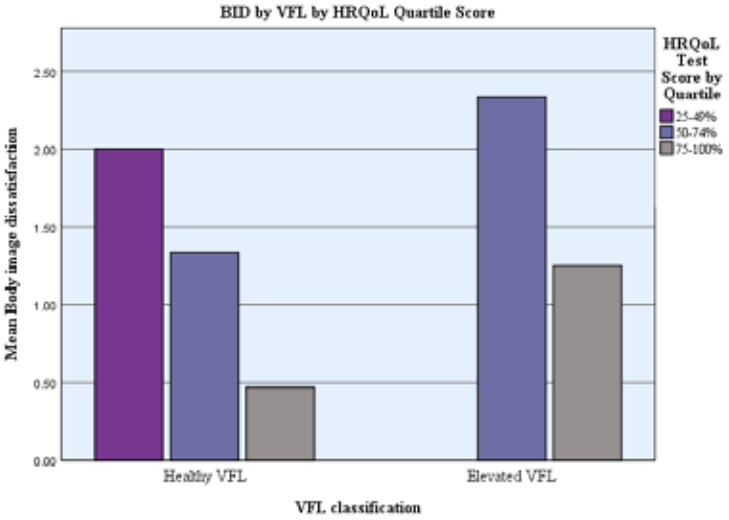

Figure 3. Mean Body Image Dissatisfaction, Visceral Fat Level, and Health Related Quality of Life Quartile Scores

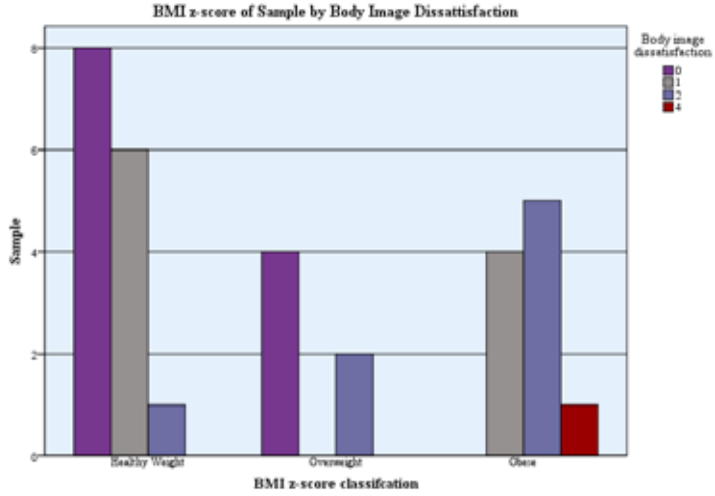

Figure 4. BMI z-score and body-image dissatisfaction BID of the sample population.

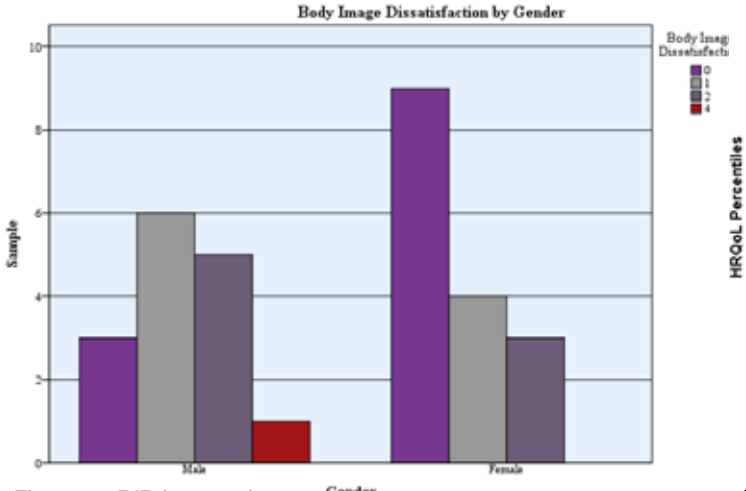

Figure 5. BID by gender.

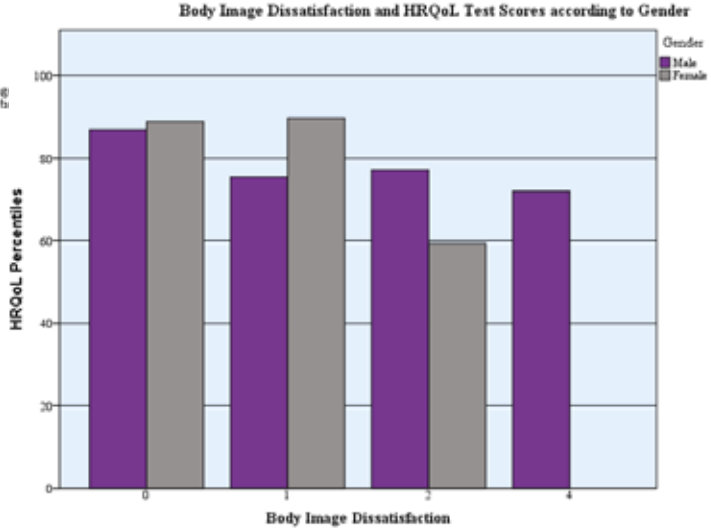

Figure 6. Percentile scores of HRQoL by dimensions, gender.

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Member Physicians Serve in the 92nd General Assembly as Doctor of the Day

Laura Haywood

During the legislative session, the Arkansas Medical Society commits to providing a physician member to serve as Doctor of the Day for the Arkansas State Legislature. This unique volunteer opportunity allows physicians to connect with legislators one-on-one, get a first-hand look at the legislative process and how it affects the practice of medicine.

As a part of this long-standing program, Doctor of the Day physicians are granted floor privileges to both chambers of the State Legislature and are introduced in the House and the Senate. They also have the opportunity to attend committee meetings, such as Public Health, Welfare, and Labor, where many of our front-line advocacy takes place.

Doctor of the Day is not only a distinguished title, but also an opportunity to provide health care to members of the Legislature, legislative employees, and other guests who are at the Capitol on that day. The Legislative Infirmary features its very own exam room equipped with basic exam equipment, and physician coverage is scheduled each day the Legislature is in session, typically January through April. It is also staffed with two experienced nurses to assist in any minor medical situation that may arise.

"There are some sample medications for use in the infirmary, but there are not any controlled substances," said Legislative Support Specialist Laura Hawkins, coordinator of the AMS Doctor of the Day program. "If a situation becomes serious, we will call MEMS and have the first responders take over."

Representative Lee Johnson, MD, an emergency medicine physician from Greenwood, said he's grateful for his colleagues volunteering their time to serve in this program. "The Doctor of the Day program provides a great opportunity for members of our medical community to interact with the legislative body. Our representatives and senators are very appreciative of the time our physicians give to be at the Capitol and enjoy the opportunity to visit with them during their participation in the program," he said. Dr. Johnson even got to experience the program from both sides. "One day this session our Doctor of the Day was unable to attend, so I stepped in. I saw five patients, four elected officials, and one government employee. I was surprised to learn Doctor of the Day was not just a figurehead, but actually has to work a little. My thanks to all that have participated and saved me from pulling double duty."

Doctors of the Day Dr. James E. Hunt (right) and Dr. Jeff Kirsch (left) with Gov. Asa Hutchinson on their day at the Capitol.

Doctor of the Day

Doctors of the Day represent a diverse audience of different specialties and organizations. "Many of our Doctors of the Day have served year after year," says Hawkins, "but we've added some new faces to the list this year. It's always exciting to share this experience with someone who hasn't seen firsthand the action of state government."

Kathyrn McCarthy, MD, OrthoArkansas spine surgeon, enjoyed her first experience as Doctor of the Day in March. "What a unique opportunity to see how the process comes to fruition! An insight into an entire other world bringing our skill set to the table. It was a pleasure to meet our lawmakers and be inthe Capitol for the day. I encourage people to do this ... you will not regret the time spent," said McCarthy.

Also serving for the first time was Johnathan Goree, MD, the Director of the UAMS Interventional Pain Management Services. "The nurses that run the clinic in the Capitol are OUTSTANDING. They are incredibly helpful with seeing patients and navigating the session. I look forward to serving again during the next session," he said.

Appathurai Balamurugan, MD, state chronic disease director for the Arkansas Department of Health, served as Doctor of the Day for five years. "Serving those who serve Arkansans gives me immense pleasure, and it also gave me a whole new understanding about governance by Arkansas Legislature," he said.

It's so important for our members to have a physical presence at the Capitol during legislative session in order to bring the voice of medicine to the Arkansas legislators. We appreciate all of our volunteers who have served our legislators, employees, and guests during this session. AMS

The Arkansas Medical Society and the Arkansas Department of Health would like to share our sincere gratitude to the Capitol Infirmary nurses, Sherry Barnard, RN, and Brenda Huett, RN, for their service during the 92nd General Assembly. Barnard and Huett have served in this capacity for five years.

1. Dr. Kathryn McCarthy and Sen. Will Bond
2. Dr. Johnathan Goree and Rep. Charles Blake
3. Dr. George Connor and Sen. Ronald Caldwell
4. Rep. Jim Sorvillo, Rep. Lee Johnson, MD, and Dr. Appathurai Balamurugan
5. Rep. Lanny Fite, Dr. Jeff Barber, Dr. Laurie Barber, and Rep. Monte Hodges
6. Rep. Steve Magie, MD, and Dr. Ralph Marrero
7. Rep. Joe Cloud, MD, Dr. Anil Kumar, and Dr E.J. Jones.

Thank you to all our Doctors of the Day!
Visit ARKMED.org for more photos.

CASE STUDY

Good's Syndrome: It's Good to Have a Diagnosis

Naga Saranya Addepally, MD

ABSTRACT

Good's syndrome is a rare condition with combined immunodeficiency and thymoma. We present a patient with severe, chronic diarrhea and history of thymoma. Workup showed markedly reduced levels of immunoglobulins. Treatment with intravenous immunoglobulins resulted in significant improvement in diarrhea and weight gain.

Keywords: Good's syndrome; Thymoma; Hypogammaglobulinemia

INTRODUCTION

Good's syndrome (GS) is a rare disorder characterized by combined humoral and cellular immunodeficiency associated with thymoma. It manifests a variety of recurrent infections. We present a case of chronic diarrhea in a patient with a history of resected thymoma many years prior to presentation. We briefly discuss the pathogenesis, presentation, and treatment of GS.

CASE PRESENTATION

A 50-year-old gentleman was evaluated for chronic diarrhea with duration of eight years. He reported having 8-15 loose stools every day along with unintentional weight loss of 100 pounds in the last year. He reported that stools were loose in consistency accompanied by abdominal cramps. There was no history of blood in stools. Diarrhea would wake him up from sleep, and he experienced diarrhea despite fasting. His past medical history was significant for incidental thymoma (status post thymectomy about 10 years ago). Extensive laboratory workup to rule out infectious etiology, fat malabsorption, celiac disease, and inflammatory bowel disease was negative. Colonoscopic exam was normal with random right- and left-sided biopsies showing mild focal active colitis; terminal ileum was normal. Trial of steroids and oral mesalamine failed to improve symptoms. After multidisciplinary evaluation considering history of thymoma and chronic diarrhea, we suspected GS. Serum quantitative immunoglobulins were found to be extremely low: IgG 55 mg/dL, IgA <25 mg/dL, IgM <17 (references values: 700-1600 mg/dL, 70-400 mg/dL, and 40-230 mg/dL respectively). Upon flow cytometry, B-cells were undetectable (<1% of total lymphocytes). These findings confirmed the diagnosis of GS. Patient was initiated on treatment with monthly Intravenous Immunoglobulin (IVIG). He experienced significant improvement of diarrhea over the following few weeks (1-2 formed stools/day) and had a 24-pound weight gain in two months.

DISCUSSION

Good's syndrome is a rare cause of combined immunodeficiency seen in adults and is characterized by a triad of thymoma, immunodeficiency, and hypogammaglobulinemia. This acquired immunodeficiency usually manifests in late adulthood and affects both cell-mediated and humoral immune system. Immunodeficiency in these patients puts them at risk of recurrent sino-pulmonary infections and many opportunistic viral, bacterial, and fungal infections. The first case was reported by Robert Good in 1954.[1] Around 3-6% of patients with thymoma have concomitant hypogammaglobulinemia.[2,3] GS usually manifests in the 40- to 50-year age group, with equal predominance in males and females. Although GS can present in children, it is very rare. According to the systematic review of more than 150 patients on Good syndrome, the incidence of GS in highest in the Europe.[4]

The pathogenesis of GS is heterogeneous. The primary immunologic abnormalities in this disease are hypogammaglobulinemia, reduced number of B cells, and CD4+ T lymphocytes.[4] Hypogammaglobulinemia was found in 100% of patients with GS across two reviews. A hypothesis suggests that certain cytokines arrest or impair B-cell maturation, leading to the above defects.[5] Abnormalities in CD4+:CD8+ T cell ratio are also commonly seen, and many of these patients have cutaneous anergy to two or more test antigens. Good's syndrome is also commonly associated with anemia, leukopenia, and thrombocytopenia. Some manifestations, like pure red-cell aplasia (PRCA) seen in GS suggest an autoimmune component in either etiology or pathogenesis of the disease.[6]

The initial presentation of GS can be varied. In many patients, the diagnosis of thymoma is usually preceded by recurrent infections with intervals of months to years. Thymoma is a slow-growing neoplasm presenting as a mediastinal mass. It can be a benign tumor or a malignant tumor that is capable of distant metastasis. Due to the location of tumor, it can present with respiratory symptoms including cough, dyspnea, hoarseness, chest pain, dysphagia, or compression symptoms including superior vena cava syndrome or Horner's syndrome. In some patients, it can be totally asymptomatic and found only incidentally. As these patients have defects in both cellular and humoral immunity, they are susceptible to a variety of recurrent infections. The most common bacterial infections reported in these patients is recurrent sino-pulmonary infections, especially with encapsulated organisms.[7] Hemophilus influenza (24%), pseudomonas (22%) and Klebsiella (13.2%) are the three most common organisms isolated.[4] Bacteremia, urinary tract infections, and bacterial diarrhea are the other common bacterial infections. Other infections reported include mycobacterial infections; viral infections with CMV, VZV, HSV, JC, HHV-8 and HPV; and fungal infections with Candida, Aspergillus, and Pneumocystis jiroveci.[4] Though uncommon, parasitic infections were also reported in these patients. It is important to note that chronic diarrhea is the presenting symptom in 50% of patients, as was the case in the patient we are reporting. While infectious etiology is the most common cause of diarrhea, malabsorption secondary to villous atrophy or immune-mediated colitis has also been reported. Salmonella, clostridium, Giardia, and CMV are a few organisms associated with diarrhea in these patients. However, in many patients, a definitive organism was not

» *Extensive laboratory workup to rule out infectious etiology, fat malabsorption, celiac disease, and inflammatory bowel disease was negative.*

isolated. Many autoimmune disorders like PRCA, Myasthenia gravis, Sweet's syndrome, Diabetes mellitus, primary sclerosing cholangitis (PSC), and ulcerative colitis (UC) have been described in association with GS.[6,8] Numerous hematologic abnormalities including aplastic anemia, hemolytic anemia, macrocytic anemia, and myelodysplastic syndromes are also reported in these patients.[2]

Diagnosis of GS requires a high clinical suspicion. All patients with thymoma or anterior mediastinal mass should be tested for underlying immunodeficiency. Presence of recurrent sinopulmonary infections, opportunistic infections, or reduced/absent B cells in these patients should prompt physicians for association with GS. Immunoglobulin values and flow-cytometric analysis of B and T cell subsets should be performed initially. Even if the initial levels are normal, the tests should be repeated every two years as they can develop immunodeficiency in the long run. Thymectomy should be considered in patients with thymoma. Depending on the extent of disease, concurrent chemo and or radiation should be offered. However, thymectomy is ineffective in reverting back immune deficiency or might even worsen hypogammaglobulinemia.[7,9] IVIG should be provided to all patients in doses necessary to maintain adequate level of serum immunoglobulins. Review of previous cases has shown beneficial effect of IVIG in decreasing hospitalizations and achieve better control of infections.[7] In our patient, the diarrhea responded promptly to administration of IVIG. Prognosis in Good's syndrome is thought to be worse than other immunodeficiencies. Reported survival rate is 70% at five years and 33% at 10 years.[10]

CONCLUSION

Good's syndrome can be an underlying etiology of chronic diarrhea, recurrent sino-pulmonary, or atypical infections. It affects both cell-mediated and humoral immunity. Diagnosis can be challenging and needs high clinical suspicion as thymoma and onset of immunodeficiency can occur at different time periods. Regular treatment with IVIG to target adequate serum levels has shown to be of benefit in reducing morbidity. Patients with thymoma should be regularly followed and physicians should have a low threshold for testing for immunodeficiencies in these patients.

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Morrilton
September 20-21, 2019

OBITUARY

FAYETTEVILLE - **John Warren Murry, MD**, 93, passed away on Feb. 8, 2019. Dr. Murry graduated from UAMS, Little Rock, in 1947. After completing an internship at Charity Hospital in New Orleans, he returned to UAMS and completed his general surgical residency. From 1953 to 1955, Dr. Murry served as a captain and surgeon in the U.S. Air Force. After completing his service in the military, he joined his father's medical practice in Texarkana. In 1957, he moved to Fayetteville and became the first board-certified general surgeon to practice in Northwest Arkansas. He practiced medicine for over 50 years. He was the founding member of Fayetteville Surgical Associates and former chief of the medical staff at the former Washington Regional Hospital. He was appointed by then Governor David Pryor to serve on the Arkansas State Board of Health. After retiring from practicing surgery, Dr. Murry served as an adjunct UAMS faculty member with AHEC-NW, where he taught family practice residents about surgical skills. During his long medical career, Dr. Murry was a member of the American College of Surgeons, American Medical Association, Southwestern Surgical Congress, and Arkansas Medical Society. He is survived by his three children: Susan Murry Jamerson, John Warren Murry Jr., and Dr. William Lee Murry. He leaves behind nine grandchildren and 10 great-grandchildren.

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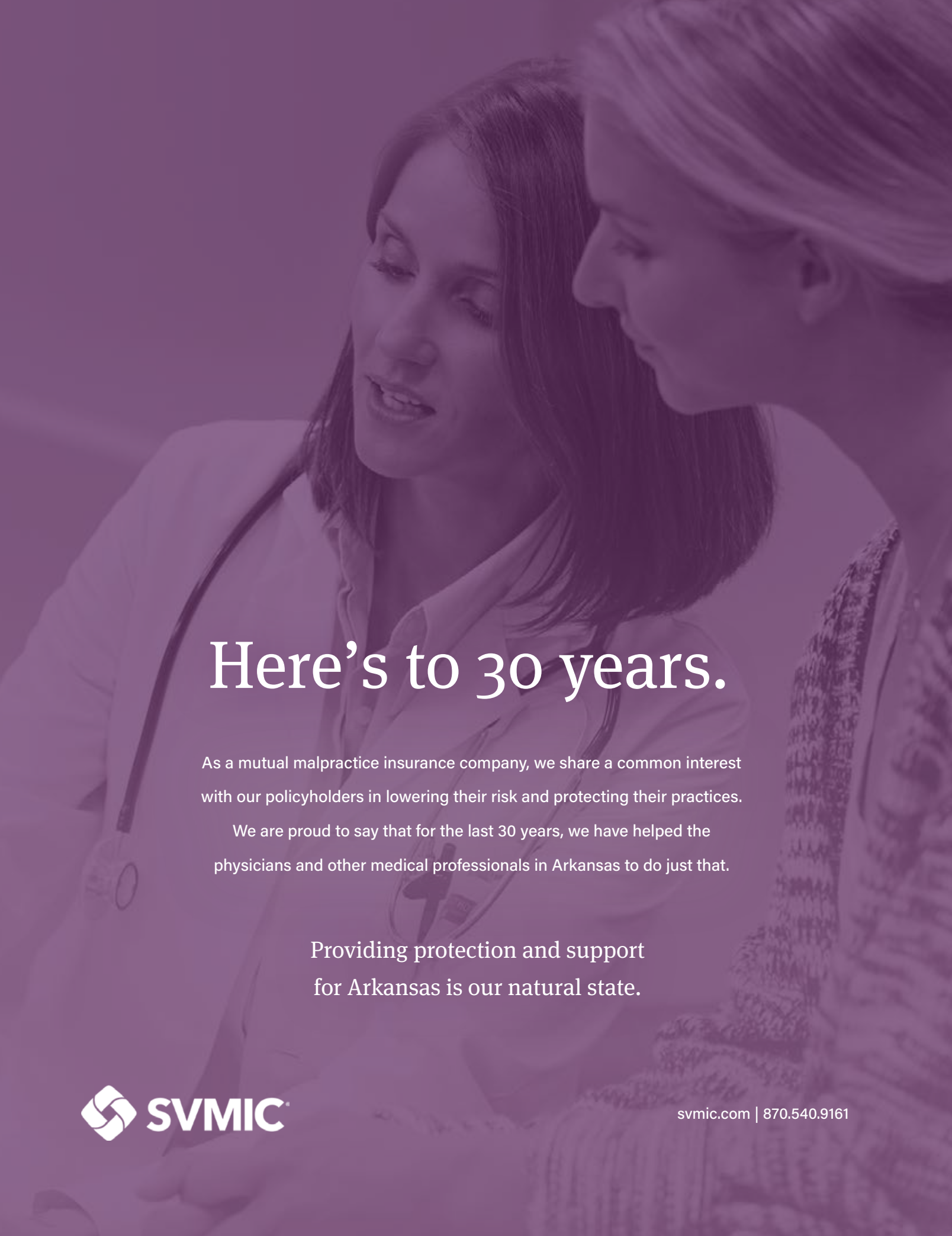

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