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OF THE ARKANSAS MEDICAL SOCIETY
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The Good with the Bad

Looking Back on a Difficult Legislative Session

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by CASEY L. PENN

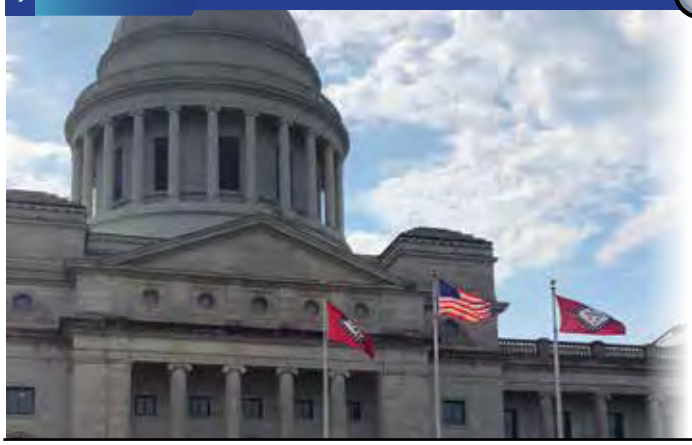

PHOTO BY JEREMY HENDERSON.

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COMMENTARY

Appathurai Balamurugan, MD, DrPH, MPH

Be Well Arkansas

In Arkansas, our leading causes of death include heart disease, stroke, cancer, and diabetes. These diseases negatively impact the health of our fellow Arkansans beyond just death alone. They result in significant disability and reduced quality of life due to complications. More than 86% of the nation's health care costs are associated with these chronic diseases, and most of the costs are preventable. Behaviors such as tobacco use, physical inactivity and poor diet contribute to these conditions that directly impact the health of our state.

While tobacco use decreased in Arkansas over the past few decades, Arkansas still ranks third in the nation with a high prevalence of cigarette smoking. Additionally, the increasing use by Arkansans of newer tobacco products, such as vapes and e-cigarettes is posing a challenge to our tobacco prevention and control efforts. In addition to tobacco-use cessation, engaging in healthy eating and increasing physical activity can pave the way for decreasing the burden due to heart disease, stroke, and diabetes in the state. Making these healthy choices and refraining from risky behaviors can be a challenge at every stage of life in today's culture.

The good news is that many of these diseases and behaviors can be managed, or even prevented, with access to the right resources. The Arkansas Department of Health recently launched Be Well Arkansas, a new campaign to enhance tobacco cessation services and provide Arkansans with resources to improve their health and well-being. With Be Well Arkansas, the Department has staff serving as wellness counselors, answering calls from Arkansans who are interested in improving their health. These counselors are MD Anderson-trained tobacco treatment specialists (TTS) that are able to provide over-the-phone tobacco and nicotine cessation services. In addition, they provide wellness counseling for diabetes management and blood pressure control.

Wellness counselors are also able to connect people to in-person counseling if available in their community. They also direct callers to online and text resources and services that may be available to them through their insurance plans, if they have insurance.

In brief:

- Through Be Well Arkansas, Arkansans can receive tobacco and nicotine cessation services to help them quit using tobacco and vape products. Eligible callers may receive nicotine replacement therapy.
- Be Well Arkansas offers more than cessation services; it links people to diabetes management and hypertension control resources.
- The toll-free phone number that patients can call is 1-833-283-WELL. Also, if people call the 1-800-QUIT-NOW, the national tobacco quit line number, they will now be routed to Be Well Arkansas. Call is answered during normal business hours from 8 a.m. to 4:30 p.m. Calls received after hours will receive a call back within one business day.
- There is a new website, www.bewellarkansas.org, that has updated resources for patients and providers, and an online chat component for cessation services.
- Be Well Arkansas offers local, in-person cessation counseling as an option for patients.
- ADH Local Health Unit staff across the state has received TTS training to provide these cessation services.
- Be Well Arkansas has a cessation texting service with advice and tips and an app for 24/7 support.

The ADH is excited to link our services together to provide enhanced wellness resources for our fellow Arkansans! AMS

THE Journal
OF THE ARKANSAS MEDICAL SOCIETY

Jhablall Balmakund, MD

Professor, Pediatric Neurology
UAMS/Arkansas Children's Hospital

Communicated expectations may enhance the ability to gauge performance on all levels of an organization. A definition of goals, and their connection to the process, may help employees understand their role in the success of the organization. Grading employees against known standards provides a more objective review. A performance-monitoring system helps with the retention of quality employees and can be used to reward employees and compare departments, teams, projects, and budgets. This system can help increase team efficiency and decrease expenses. It creates a broader base of knowledge and data to be used in planning and budgeting.

Greater than 50% of physicians own their practices and actively participate in the administration of the practice.[3] The rest are in practice settings run by administrators who may dictate the rules of the practice and possibly influence patient care. Physicians' performances are gauged by RVUs, provider scorecards completed by patients, and other methods. These performance rules may be used to determine continuity of employment, eligibility for raises, staff privileges, etc., while administrators, it seems, are not held to similar benchmarks. With expectations outlined and communicated, employees better understand their roles in the success of the department or program. Using standards for every job position, and grading the employee against standards of performance measures, may create a sense of fairness.

Evaluations may offer several benefits, including information about an employee's performance, insights into the way employees interact with each other, a glimpse into the strengths and weaknesses of employees, and reinforcement of a team environment.

Administrators, like other employees, should be evaluated by surveying those who work under and with them. Grading administrators can sometimes be difficult. Evaluations may offer several benefits, including information about an employee's performance, insights into the way employees interact with each other, a glimpse into the strengths and weaknesses of employees, and reinforcement of a team environment.

Evaluations do have drawbacks. A yearly survey may not capture projects that span years. The definition of success on the job can take a variety of forms. Sometimes, measures used to gauge success are tangible and linked to specific metrics such as industry benchmarks or a dollar figure. Other times, the mark of a job well done is more nuanced, defined by successful working relationships or a simple sense of satisfaction about employees' roles in making their institution the best it can be.[1] Sometimes administrators know they have been successful when they have been able to garner support from staff on an important issue.[1] Evaluations are subjective, as overworked employees may feel overwhelmed when they have to complete evaluations for their peers. Evaluations can lead to confusion and irrelevant assessments if evaluators are not familiar with the job description of the person being evaluated.

In the bid for philanthropic dollars, having visible evaluations – especially if the results are good – may be a boon to the company. There are many issues and decisions where evaluations at all administrative levels may provide some improvement. To show unity, it may be helpful to have all employees surveyed. Administrators, like non-administrators, should be held accountable to the group they are working with and should be subject to similar benchmarks.

Plans should be developed to assess an administrator's work. The purpose of such periodic reviews should be the improvement of the performance of the administrator during his or her term of office. This review should be conducted on behalf of the governing board for the president, or on behalf of the appointing administrator for other academic administrators. Fellow administrators, faculty, students, and others should participate in the review according to their legitimate interest in the result, with faculty of the unit accorded the primary voice in the case of academic administrators. Once the review is completed, a summary should be released with a list of steps to resolve any issues.[4]

In summary, an evaluation of all employees may bring out the best in employees while determining individual expertise and the opportunity to assign specific jobs to the employees whose evaluations show an inclination to that job.

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by CASEY L. PENN

The Good with the Bad

Looking Back on a Difficult Legislative Session

"This was probably the most challenging legislative session faced by the Arkansas Medical Society, at least in my 35-year career," began AMS Executive Director David Wroten, from the conference room of the Society's Little Rock office. Having come from months of daily work at the Capitol, Wroten and AMS Governmental Affairs Director Scott Smith sat down to reflect on the high and low points of the 92nd Arkansas General Assembly.

CP: Before we get into the bills themselves, talk to me about what made this such a difficult session.

DW: As for the *why*, I think there were several factors. Some of it had to do with a shakeup in committees – particularly in the House, where legislators didn't know what committees they would be on until the first day of the session. In the Senate, six members of the Senate Public Health Committee were replaced.

SS: In addition, due to a new rule, you didn't have to worry about a bill-filing deadline, so you had bills coming in at the last minute. Also, the sheer volume of scope-of-practice bills was higher than normal. We started off with five APRN bills, two CRNA bills, three pharmacy bills, telemedicine bills, and more.

CP: Despite notable wins – AMS-initiated legislation being passed into law – there were some disappointing losses – particularly in the realm of scope-of-practice. Could you provide a summary of what took place on that front?

DW: Let's start with the bad news first. The optometry bill (HB 1251/Act 579/Jon Banks-R, David Wallace-R) was a hard-fought battle that we lost. Highly publicized, this legislation will allow optometrists to perform certain surgical procedures.

SS: The opposition presented the bill as if it would only allow optometrists to perform a few basic procedures. In fact, the way it was written, it could allow over 100 procedures including the one most publicized, laser eye surgery.

DW: It's worth noting that the optometrists had been working on the bill for more than a year. They made massive campaign contributions leading up to the session. This was part of a nationwide effort by the American Optometric Association to push this legislation into states. Arkansas was a target because Louisiana, Oklahoma, and Kentucky all allow similar procedures to what was passed in Arkansas.

CP: Does the public understand the difference in training between an optometrist and an ophthalmologist?

SS: I'm not sure, but we certainly point out that difference to legislators. After college, ophthalmologists have four years of medical school, one year of internship, and a minimum of three years of in-depth ophthalmology residency.

DW: There's no comparison in the training. Also, during the battle, we commissioned a public opinion survey and found that an overwhelming majority of the public thought this bill was a bad idea.

CP: One of the arguments for the bill had to do with access. Could you speak to that?

DW: It's a common argument. The proponents of this type of legislation argue that this will increase access, yet legislation has never required proof. There is no evidence that other states that have adopted these types of scope-of-practice laws have seen an increase in access. In reality, in states that have done some of these things, the evidence is that they do *not* increase access.

CP: What about some of the other scope-of-practice bills?

DW: We lost the optometry battle, but we had some wins on the APRN side. This APRN bill (HB 1267/Act 593/Justin Gonzales-R, Kim Hammer-R) will prove helpful to our members who utilize APRNs in their practices. First, this will allow APRNs to provide continuity of care once it has been initiated by a physician for up to six months. For example, a physician has a patient with ADHD and starts him on medication. The APRN working for the physician would be authorized to write follow-up prescriptions for up to six months before the patient would need to be seen by the physician again.

SS: This allows APRNs also to write a one-time, up-to-a-five-day prescription for opioids. This was a compromise that we offered, and as a result, we were able to pass that bill.

CP: What happened on the pharmaceutical front?

DW: An oral contraceptive bill (HB 1290/Aaron Pilkington-R, Barton Hester-R) would have allowed pharmacists to dispense oral contraceptives without a prescription. AMS opposed the bill because it did not have enough safeguards. That bill failed.

SS: The nicotine replacement bill (HB 1263/Act 651/Les Eaves-R) would have allowed some pharmacists to dispense Chantix® and other smoking-cessation prescription drugs. AMS was successful in amending that bill to limit it to smoking-replacement products such as nicotine gum.

DW: An immunization bill (HB 1278/Act 652/Jimmy Gazaway-R) allows pharmacists to give immunizations to 7-to-18-year-olds under a statewide protocol. Currently, they can give immunizations to this age group under a physician-patient-specific prescription. This only applies to three types of immunizations. AMS opposition to this bill was minimal, due in part to the fact that many physicians' offices have discontinued providing these immunizations.

CP: CRNA bills?

SS: There was an AMS-opposed CRNA bill (SB184/Gary Stubblefield-R, Justin Gonzales-R) that had plenty of support from the other side. This would have removed physician supervision from CRNAs. It failed on its first attempt to pass the House Public Health Committee. On second attempt, it passed by one vote. It then failed on two occasions on the House floor due to overwhelming lobbying efforts by the AMS and the Arkansas Society of Anesthesiologists. This was a close call, but thankfully, a win.

CP: Were there any other AMS-opposed bills defeated?

SS: There were several. One that comes to mind was an attempt to gut the Clean Indoor Air Act. The bill (HB 1696/Justin Gonzales-R, Mark Johnson-R) was an effort to poke a hole in the law by exempting all private businesses. The exemption would have engulfed the rule, basically. AMS was prepared to help fight this bill, but it failed to get out of committee.

CP: Telemedicine has been a big fight in recent years. What happened this year with telemedicine that stood out?

SS: The telephone-only bill (HB 1220/Dan Sullivan-R) was a telemedicine bill supported by a single telemedicine vendor, Teladoc. This was strongly opposed by AMS. The bill would have removed safeguards that AMS fought hard (for two sessions in a row) to achieve and would have allowed the doctor-patient relationship to be established without the physician ever having to see the patient in person or through audio-visual equipment – in other words, by telephone only.

Teladoc amended its bill a couple of times to try to get it out of committee. It failed in House Public Health Committee, was amended and passed the second time by one vote, and then failed on two occasions to pass the House.

DW: Representatives of Teladoc continue to try to make the case that Arkansas is the only state in the country that doesn't allow "audio only" to establish a doctor-patient relationship. This is contrary to evidence from other states that this is not the case. An interesting note on the telemedicine discussion: Teledoc's representatives, with a straight face, tried to make the case that states that prohibit "audio only" meant simply that you could not use voice mail (a one-way communication).

SS: That shows the ridiculous nature of their argument. Even Teladoc agrees that leaving voice mail is no way to establish a relationship, and yet they want a simple phone call to suffice.

CP: Could you describe more AMS-supported legislation that successfully passed into law?

DW/SS: Despite massive resources that went into defeating bad bills from the opposition, AMS worked with legislators to draft and pass the majority of its own good legislation. These wins included the following:

- The fetal alcohol syndrome bill (HB 1861*/ Deborah Ferguson-D) requires establishments that have a permit to serve alcohol to post a sign warning of the dangers of pregnant women consuming alcohol.
- Health care contracting (SB 480/ Act 734/ Missy Irvin-R, Mark Lowry-R) and assignment of benefits (SB 512/Act 736) are two new laws that give physicians and other health care providers more leverage in contracting with insurance carriers. Act 734, among other things, prohibits so-called "all-products clauses." Act 736 requires insurance carriers to recognize and accept assignment of benefits for services provided by out-of-network providers.
- The identification disclosure act (SB 527/Act 706/Cecile Bledsoe-R, Deborah Ferguson-D) requires insurance companies to clearly indicate on ID cards whether a plan is "insured" or "self-funded." This will make it easier for clinics to determine whether a patient's insurance is governed by state or federal rules.
- An amendment to the Patient Protection Act prohibits an insurance company from terminating a physician's network membership over peer-review actions that do not involve standard of care or potential harm to patients. Essentially, this makes it clear to insurance carriers that if there's a disciplinary action taken, that action must pertain to a patient-care issue.
- A prior authorization bill (HB 1656*/Deborah Ferguson-D, Cecile Bledsoe-R) will prohibit prior authorizations for medication-assisted treatment for opioid abuse.

> Continued on page 272.

Licensure Issues

- The osteopathic license bill (HB 1658/Act 607/ Justin Boyd-R, Jimmy Hickey-R) addresses a provision in the Medical Licensure Act requiring osteopathic physicians to be citizens of the U.S. to obtain their Arkansas license. (The provision does not exist in licensing requirements for allopathic licensing.) This allows for osteopathic physicians that are legal residents of the U.S. to practice anywhere in Arkansas.
- A bill sponsored by Sen. Missy Irvin-R (SB 456/ Act 701) changes/renames an educational license as "academic" license and allows physicians who have an academic license to apply for a regular license after two years.
- Maintenance of Certification (SB 339/Act 804/ Missy Irvin-R) prohibits insurance companies and hospitals from using MOC as sole criteria for credentialing. Certain exclusions for academic centers would allow MOC to be used if adopted by the medical staff of an organization.
- A bill regarding asthma inhalers (HB 1745*/ Lee Johnson, MD-R, Missy Irvin-R) allows for schools to have a supply of inhalers on hand, just as they would epinephrine injectors.
- The biologic similar substitution bill (HB 1269/ Act 637/Austin McCollum-R), jointly initiated by the AMS and the Arkansas Pharmacy Association (ARPA), allows for and sets rules for pharmacists' substitution of interchangeable biologic products. The bill is designed to create a framework for substitution once the FDA begins approving biosimilar drugs as interchangeable (none currently exist).

CP: Any other bills AMS physicians should be aware of?

DW/SS: Other bills that should be of interest to physicians (some didn't pass) include two healthcare council bills, a mandatory E-prescribing bill, and a genetic counseling bill.

HB 1568 and SB 192 by Missy Irvin-R and Lee Johnson, MD-R (Health-Care Council bills): they failed, illustrate the contention that exists regarding scope-of-practice legislation. They would have created an independent review body through the Arkansas Health Department to provide unbiased, accurate information regarding education, training, and potential for increasing access to care for scope-of-practice legislation. While we recognize the potential two-edged sword, we strongly believe it's better than what we're having to do now (for examples, refer to the scope fights listed in this article).

SB 174/Act 447 (mandatory E-prescribing): Beginning 1/1/21, Arkansas will require that all scheduled drugs must be prescribed using electronic prescribing software. This piggybacks on the Medicare requirement that also takes effect 1/1/21. This eliminates prescription pads and thereby will reduce forging. Many states have already done this, and there are some waivers/exclusions in the bill.

SB 190/Act 686 (licensure for genetic counselors): This has to do with licensure for genetic counselors and will create a provision for them to be regulated by the Arkansas State Medical Board. AMS was neutral on this, but we worked with sponsor Sen. Leding to ensure that the wording on this did not allow genetic counselors to order genetic tests without a physician.

CP: If AMS and AMS-friendly legislators weren't present daily, to watch for and put out fire after fire, many of these opposing groups would get their way without much of a fight. They seem prepared to keep coming back. Are you feeling worn down from relentless, repeat pursuits from groups who want more and more independence from physicians? What kept you going?

DW: We *are* worn down, truth be told. We do it for our members and their patients – simple as that. It's an overarching theme, and it's true of so many bills. It's fair to say to our members: 'Stop for just a minute, doctor, and think about how many bad bills would now be law, if you didn't have the Society looking out for your interests.'

SS: Most of these opposing groups come forth to advance *one* issue. We deal with *all* of these in addition to our own issues that we're also putting a lot of work into for the benefit of our members.

For more information about the Society's work as a legislative advocate, contact Scott Smith or David Wroten.

*Bill passed; no Act number established as of press time. AMS

AMS Efforts Praised by Physician Constituents

During any given session of the Arkansas Legislature, Wroten and Smith – along with additional AMS staff members, AMS-friendly legislators, and advocacy groups – are working at the Capitol on legislative issues facing medicine now. Despite the disappointments of this year's session and the relentless nature of the opposition, the Society's efforts were considered a grand success to the advocacy groups they fought alongside.

"It was a tough session. I appreciate greatly the support AMS offers, not only to Arkansas physicians and medical specialties, but also to patients across the state. They do a fantastic job supporting good legislation and defeating legislation that adversely affects patient safety."

– Joshua Chance, MD
President, Arkansas Society of Anesthesiologists

"Of the bills the AR AFP testified against, David and Scott were excellent at stating, in just a few words, why the bills we were so passionately against should not become law. There would not be many who could wrap up testimony the way David so eloquently stated the facts."

– Carla Coleman, Executive Vice President
Arkansas Chapter, American Academy of Family Physicians AMS

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Clostridium Difficile Infection Can Mask Diagnosis of Other GI Infections In Immunocompromised Patients: A Tale of Co-Existing Bacteria and Fungus

Naga S. Addepally, MBBS[2]; Jagpal S. Klair, MBBS[1]; Mohit Girotra, MD[2]; Daniel K. Brown MD[2]

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[2]Central Arkansas Veterans Health Services (CAVHS), Little Rock, Arkansas

INTRODUCTION

Clostridium difficile infection (CDI) can occur commonly in immunocompromised patients. However, lack of response to treatment should alert physicians to actively re-investigate for the presence of other co-existing GI infections, which our interesting case alludes to.

CASE PRESENTATION

A 55-year-old man with HIV (CD_4 43/mm^3, non-compliant with medications) and hepatitis-C presented with RLQ pain with fever, night sweats, and intermittent bloody diarrhea lasting two weeks. An outside hospital work-up (abdominal CT and stool studies) was unremarkable, except for (+) Clostridium difficile antigen. Patient was started on PO Vancomycin, to which he initially responded, but was later re-admitted with worsening pain and persistent bloody stools. Repeat CT revealed concentric bowel wall thickening/edema in cecum/ascending colon along with lymphadenopathy. Antibiotics were restarted for assumed recalcitrant CDI, but after 21 days of unsuccessful therapy, patient was transferred to us. Colonoscopy divulged inflamed, edematous and friable-appearing cecum/ascending colon, with multiple discrete, punched-out ulcers throughout the colon. Biopsies were consistent with histoplasmosis. Patient had no co-existent pulmonary lesions or other sites of dissemination. He responded well to liposomal amphotericin B.

DISCUSSION

Diarrhea is common in patients with HIV/AIDS; however, bloody diarrhea is not very common. When present, it should be seriously investigated. Hematochezia could be from both infectious and non-infectious causes. Non-infectious causes include hemorrhoids, IBD, anal fissures, idiopathic ulcers, and colon cancer. Though bacterial gastroenteritis like – salmonella, shigella, and Clostridium difficile – can present with bloody diarrhea; opportunistic infections like CMV, HSV, histoplasma, and Mycobacterium tuberculosis contribute to most of the infectious

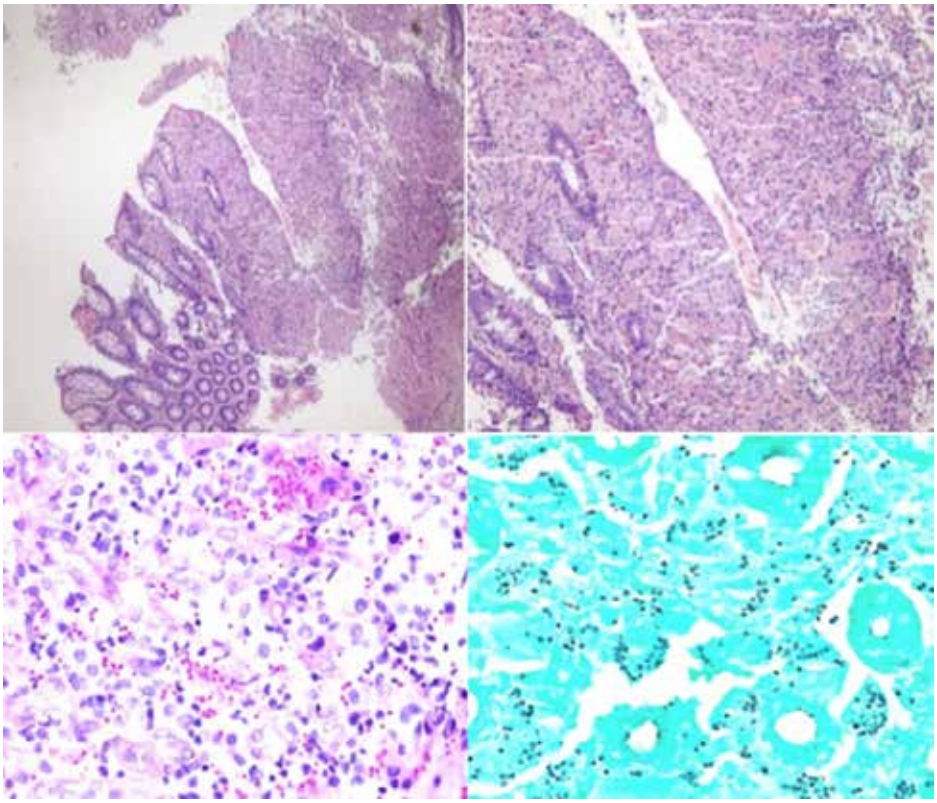

Figure 1: Colonoscopy divulged inflamed, edematous and friable-appearing cecum/ascending colon, with multiple discrete, punched-out ulcers throughout the colon.

causes of bloody diarrhea in these patients.[1] Sometimes, coinfection with two different organisms can cause severe diarrhea, as in our patient. Hence, we need to be very cautious.

Histoplasma is a common, opportunistic infection in HIV/AIDS patients living in endemic areas. Histoplasmosis is caused by an invasive fungus called Histoplasma capsulatum, which is endemic to certain parts of U.S. including Mississippi, Ohio, and the St. Lawrence River Valley. The fungus is found abundant as spores in the soil that is contaminated by bird feces. The disease is transmitted upon inhalation of the spores, which convert into yeast form. They are engulfed by macrophages, where they multiply and spread throughout the body via reticulonodular system. In immunocompetent patients, infection is usually self-limited and most often time goes unnoticed. However, patients who are immunocompromised can have serious illness. It can present either with isolated pulmonary infection or disseminated disease with multiorgan involvement (skin, GI tract, liver, spleen, meninges, kidneys, adrenal glands, etc.).

Histoplasma can be identified in the GI tract of 70-90% patients with disseminated disease, but only 3-12% of those are symptomatic.[2,3] It usually presents with non-specific symptoms like fever, night sweats, nausea, vomiting, diarrhea, abdominal pain, hematochezia, melena,[4] and oropharyngeal ulcerations. Sometimes it can present as a mass leading to intestinal obstruction. Lesions occur anywhere in the GI tract from mouth to anus but are more common in the terminal ileum due to abundance of lymphoid tissue.[5,6] Typical endoscopic lesions are patchy or continuous superficial-deep ulcerations, accompanied by diffuse mucosal erythema, and rarely as polypoid masses causing obstruction or annular constricting ulcers leading to strictures.[6] These findings can often be misdiagnosed for malignancy or IBD; hence, a careful evaluation and high index of suspicion is warranted. Mouth ulcers are usually very painful and can mimic malignancy by their appearance.

Antigen detection in tissues samples (blood, urine, BAL) is useful for diagnosis of disseminated histoplasmosis. It is positive in >90% patients with disseminated disease. However, it may be falsely negative in patients with localized GI involvement. Hence, biopsy is warranted for appropriate and accurate diagnosis. Pathology suggests abundant inflammatory infiltrate and multiple intracellular, ovoid-spherical, narrow-based budding yeast cells, visualized better with methenamine silver stain. Treatment is not indicated for mild pulmonary illness or self-limiting illness (symptoms lasting for <1 month). However, all disseminated histoplasmosis, acute pulmonary histoplasmosis with symptoms lasting for > one month, or those who have hypoxia, need to be treated. Treatment is divided into two different phases: induction treatment and lifelong suppressive therapy. Patients with less severe disease may be treated with itraconazole, but amphotericin-B is merited in moderate-severe disease.[4] Length of induction therapy varies depending on the severity of illness and is usually in weeks. As patients have a high chance of relapse, lifelong suppressive therapy with either itraconazole or fluconazole is warranted. Trials have shown better remission with itraconazole compared to fluconazole. Some people use serum antigen levels to monitor response to therapy. Disseminated histoplasmosis carries high mortality (~80%), hence early identification and treatment is necessary.

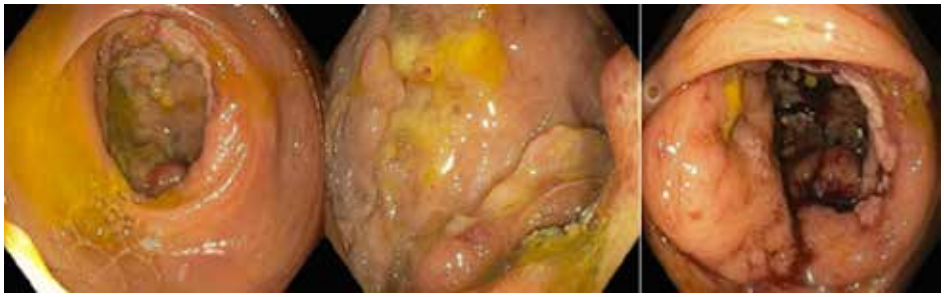

Image 2a: Photomicrograph showing active colitis with ulcerated colonic mucosa; 2b: Extensive accumulation of macrophages within lamina propria; 2c: Image showing positive PAS stain; 2d: GMS stain highlights accumulation of numerous intracellular 2-4 um fungal spores consistent with Histoplasma capsulatum.

CONCLUSION

Coinfection with common nosocomial bugs like Clostridium difficile may masquerade the underlying histoplasmosis, hence a high index of suspicion is essential, especially in immunocompromised patients. Due to a lack of specific signs and symptoms for GI histoplasmosis, this entity may be missed many times. Any patient with unexplained GI symptoms in HIV/AIDS patients should be evaluated for histoplasmosis.[7] Disseminated histoplasmosis carries high mortality up to 80%, hence early identification and treatment is necessary. Treatment decreases mortality to less than 25%.

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A CLOSER LOOK AT QUALITY

Management and Treatment Options for Pediatric Traumatic Brain Injury

LAURA J. HOBART-PORTER, DO, FAAPMR

EDITOR'S NOTE: *In the May issue, Dr. Hobart-Porter discussed the diagnosis and prognosis for pediatric mild traumatic brain injury. She continues this month with its management and treatment.*

Pediatric mild traumatic brain injury (mTBI) is a common but complex and potentially serious condition, which affects millions of children each year.[1] Most recover in one to three months, but some patients have persistent and functionally impairing symptoms that require additional management.

The Centers for Disease Control and Prevention (CDC) presented a consensus guideline in November 2018 on the management of childhood mTBI, based on a systemic review of articles published between 1990-2015.[2] Use of the term mild traumatic brain injury in place of concussion is now recommended.

Mild TBI is "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]

Recommendations regarding prognosis, diagnostics, management and treatment options were rated according to the CDC committee's level of confidence as well as strength of recommendation. Level of confidence included High, Moderate, Low and Very Low. Strength of recommendation included Level A (should always be followed), Level B (usually should be followed), Level C (may sometimes be followed), Level U (insufficient evidence to make recommendation), and Level R (should not be done outside research setting). The following is a summary of committee consensus on management and treatment of mTBI.

EDUCATE FAMILY ABOUT TREATMENT

In addition to providing reassurance and education, health care professionals should provide families with counseling on warning signs of more serious injury, instructions on when to return to play and school, injury prevention, and clear follow-up instructions. In the past, absolute rest was often prescribed for those recovering from mTBI. Inactivity beyond a few days may worsen self-reported symptoms and has the potential to prolong recovery.[4,5] It is now recommended that after the first several days, children gradually resume both physical and cognitive activities that do not exacerbate their symptoms (Moderate level of confidence, Level B strength of recommendation). After a gradual return to activity is successful, providers should offer an active rehabilitation program of progressive reintroduction of noncontact aerobic activity (High, Level B).

As with any return-to-activity recommendation in mTBI, it is vital that providers closely monitor symptom expression and that mTBI patients stop activity that exacerbates symptoms. Children should return to full activity when they return to premorbid performance and are symptom free at rest and with increased levels of exertion (Moderate, Level B). For instance, a child who has symptoms with jogging should be returned to the prior level of symptom-free activity — light activity or walking. Activity level may be

advanced again after at least 24 hours of symptom-free activity.

RETURN-TO-SCHOOL PROTOCOLS

Returning to school should be a collaborative effort between health care and school-based professionals, gradually increasing the duration and intensity of academic activities as tolerated (Moderate, Level B). The goal is to increase participation without worsening symptoms. This may require abbreviated class schedules, lessened homework loads or a temporary hold on testing, depending on the child. Return-to-school protocols should be customized for each child, based on severity of symptoms (Moderate, Level B) with the recognition that each child has a different recovery trajectory. Some children may require additional educational supports, such as an Individualized Education Plan (IEP) or 504 plan. If a child has prolonged symptoms that interfere with classwork performance, need for an IEP should be assessed by the school (High, Level B).

Ongoing monitoring of academic performance to collaboratively determine needs for additional or ongoing educational supports is crucial (High, Level B). There is a balance between prompt return to school and the necessary cognitive recovery that must take place. Cognitive impairment can occur in the setting of mTBI, and treatments should be directed to its presumed etiology (High, Level B). A formal neuropsychological assessment can help determine etiologies and recommend specific helpful interventions (High, Level C). These assessments, particularly as they relate to academics, should be shared with the child's school, with a parental release of information.

TREATING PAIN

Acute headache is an extremely common symptom after mTBI. Emergency department professionals should consider head computed tomography (CT) in children with severe or worsening headache, particularly when associated with other risk factors, including age younger than 2 years, vomiting, loss of consciousness, severe mechanism of injury, amnesia, nonfrontal scalp hematoma, GCS score of less than 15 and/or clinical suspicion of skull fracture[6] (High, Level B). Children with headache and acutely worsening neurologic symptoms should have emergent neuroimaging (High, Level B). Hypertonic 3 percent saline should not be administered for treatment of acute headache in mTBI outside of research settings (Moderate, Level R). Caregivers and health care providers should offer non-opioid analgesics (acetaminophen or non-steroidal anti-inflammatories) for acute mTBI-associated headache (Moderate, Level B). Counsel the family on the risk of analgesic overuse and rebound headaches.

Chronic headaches after mTBI tend to be multifactorial, requiring multidisciplinary approach (High, Level B). This may include psychology, physical therapy, and additional physician specialists such as physical medicine and rehabilitation, neurology, sports medicine, and pain or sleep medicine. Analgesic overuse is often a significant contributory factor. Additional factors may include vestibulo-oculomotor dysfunction, which may respond to rehabilitation (Moderate, Level C). Sleep disorders can also contribute to headaches and to overall recovery. Education on proper sleep hygiene should be provided to families (Moderate, Level B).

Pediatric mTBI is a challenging and dynamic diagnosis to manage and treat. Careful progression to play and academics is vital for recovery but can be complicated by post-traumatic symptoms. If a child is not recovering as expected, referral to a specialist who manages mTBI is recommended. Arkansas Children's Hospital offers a weekly concussion clinic. For appointments call 501-803-2599.

More detailed guideline and family education materials at: **www.cdc.gov/HEADSUP**. ▲

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CASE REPORT

Cannabinoids in Pediatric Epilepsy

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Abstract

Many states (including Arkansas) have passed medical marijuana legislation to allow for the sale and use of cannabis-derived products (CBD) for medical therapy of epilepsy and many other medical and psychiatric disorders. A class 1 evidence of CBD as an add-on therapy is now available in Dravet syndrome and Lennox-Gastaut syndrome. However, controlled studies are required to determine the effectiveness of CBD in other types of epilepsy. Moreover, CBD is far from a miracle cure and it is of paramount importance to have a reasonable expectation of its usefulness as an antiepileptic medication. It is also a misconception that CBD is free of adverse effects attributed to its derivation from a natural source. Rather than spontaneous treatment without medical supervision, adequate medical oversight is indicated to monitor and manage adequate dosage, side effects, the validity of the product, and drug-to-drug interaction.

Key Words: cannabinoids; CBD; epilepsy; Dravet syndrome; Lennox-Gastaut syndrome

Much attention has been given to the use of cannabidiol for the treatment of children and adults with severe forms of epilepsy. Many states (including Arkansas) have passed medical marijuana legislation to allow the sale and use of cannabis-derived products for medical therapy of epilepsy and many other medical and psychiatric disorders. Regardless of state law, all cannabinoid components and products derived from cannabis or, specifically, *Cannabis Sativa,* are considered controlled substances classified as Schedule I agents by the U.S. Drug Enforcement Agency.

Marijuana consists of a dried mixture of cannabis leaves and flowers and is commonly used for recreational or medical use. *Hemp* specifically refers to the hearty fibers in the stalk and stems of the plant. Delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the major cannabinoids, and different marijuana strains have varying amounts of THC and CBD. Scientific cultivation has led to the development of strains that are extremely high in THC, while other strains have high CBD and low THC contents. THC is a psychoactive agent, a drug of abuse, and equivocal in seizure control. In some circumstances, THC has been felt to increase seizure activity. CBD is a non-psychoactive agent, and both anecdotal and scientific evidence indicate it can be effective as an antiepileptic medication, especially for some specific epilepsy syndromes.

Dating back as far as 2700 BC, cannabis has been used for a number of various medicinal purposes.[1] Before its removal as a medicinal compound in 1941, cannabis preparations were included in the U.S. Pharmacopeia (USP) since 1851.[2] The federal Controlled Substances Act labeled cannabis as a schedule 1 substance (no accepted medical use and a high potential for abuse) in 1970, as it was increasingly associated with recreational use. The use of cannabis for the treatment of epilepsy declined in the 20th century due to the progressive introduction of antiepileptic medicines and the change in legal status. However, sporadic observations suggesting the effectiveness of cannabis continued to be reported. In comparison to FDA-approved antiepileptic drugs, cannabidiol is structurally unique and has potentially novel multimodal

mechanisms of action. Preclinical data have shown cannabidiol to have activity against seizures in in-vitro and in-vivo models.

A Cochrane review in 2012 assessed the safety and efficacy of cannabinoid use in patients with epilepsy.[3] A total of four studies (blinded and unblinded randomized clinical trials) were included in the review; however, all these trials were of low quality with small sample sizes and variations in product, dose, frequency, and duration of treatment. It was determined that the efficacy of CBD in the treatment of epilepsy could not be confirmed, but a dose of 200-300 mg daily can be administered safely over a short period. Two of these studies were subsequently included in a systematic review by the American Academy of Neurology in 2014 to assess the role of medical marijuana in various neurologic diseases such as multiple sclerosis, epilepsy, and movement disorders.[4] It was concluded that the data were insufficient to support or refute the efficacy of cannabinoids for reducing seizure frequency. However, the use of cannabinoids, specifically CBD, has increased in response to several anecdotal reports of remarkable response in epilepsy, and the perception that a substance or medicine derived from a natural source would be safer. One such report was broadcasted on a CNN special documentary, "Weed." This special presented a girl named Charlotte Figi, who has Dravet syndrome, a rare and intractable genetic epileptic encephalopathy syndrome associated most commonly with *SCN1A* mutation. At five years of age, her mother started giving her an oral liquid, high-CBD, low-THC extract (later called Charlotte's Web) made by the Stanley brothers in Colorado. Charlotte had suffered from very frequent seizures and experienced significant developmental delays and cognitive compromise. She had been treated with several antiepileptic drugs, with little or no improvement. In response to treatment with CBD oil, she experienced a >90% reduction in seizure frequency within three months and a remarkable improvement in cognition.[5] This and other similar reports prompted many parents to move their families across the country to gain access to CBD products.

Up to 85% reduction in the seizure frequency and increased alertness, better mood, and improved sleep were reported in several papers derived from online surveys and retrospective chart reviews. However, several confounders were present in these open-label retrospective studies; there were high expectations and motivations leading to reporting bias and acting as obstacles to determine the actual efficacy of oral cannabis extracts. Subsequently, the recent interest in research in this sphere has led to the completion of several well-controlled studies in epilepsy, using a liquid proprietary oral formulation of CBD. Devinski et al. conducted a double-blind, placebo-controlled trial at 23 centers in the U.S. and Europe, with random assignment of 120 children and young adults with the Dravet syndrome and drug-resistant seizures to receive placebo vs. 20 mg/kg/day of CBD.[6] The median frequency of convulsive seizures per month decreased from 12.4 to 5.9 in response to CBD, compared to a decrease from 14.9 to 14.1 with placebo. A $\geq$ 50% reduction in convulsive seizure frequency was achieved in 43% of the CBD

> ***CBD is far from a miracle cure, and it is of paramount importance to have a reasonable expectation of its usefulness as an antiepileptic medication.***

treated group vs. 27% in the placebo group. The patient's overall condition improved by at least one category on the seven-category Caregiver Global Impression of Change scale in 62% of the CBD-treated subjects compared to 34% in the placebo group. The frequency of total seizures of all types was significantly reduced in response to CBD (P=0.03), but there was no significant reduction in nonconvulsive seizures. CBD therapy rendered seizure freedom in 5% compared to 0% in the placebo group (P=0.08). A major weakness of the trial was the failure to report changes in the plasma concentration of clobazam and N-desmethylclobazam (level can in-

> Continued on page 280.

crease five fold when CBD is added). It is notable that 66% of patients in the CBD group were on clobazam; it was uncertain if improvement in seizure frequency was due to a direct action of CBD or increased plasma level of the active metabolite of clobazam. A multicenter, randomized, double-blind, placebo-controlled trial (GWPCARE4) investigated the efficacy of CBD as add-on therapy for drop seizures in patients (aged 2-55 years) with treatment-resistant Lennox-Gastaut syndrome.[7] The median percentage reduction in monthly drop seizure frequency from baseline was 43.9% (IQR −69.6 to −1.9) in the CBD group and 21.8% (IQR −45.7 to 1.7) in the placebo group. Adverse events were common in patients treated with CBD occurring in 86% (74/86), and 14% withdrew from the study due to adverse effects with the most common being diarrhea, somnolence, pyrexia, decreased appetite, and vomiting. Twenty (16 with concurrent use of valproate) patients experienced serum transaminase elevation without concomitant bilirubin elevation. Potential drug-drug interaction, long-term safety, and efficacy were not examined in this study.

Smaller, uncontrolled studies and case reports have suggested that CBD may be effective in the treatment of other forms of drug-resistant epilepsy and seizures such as tuberous sclerosis, febrile infection-related epilepsy syndrome (FIRES), and Sturge-Weber syndrome.

In summary, a class 1 evidence of CBD as an add-on therapy is now available in Dravet syndrome and Lennox-Gastaut syndrome. However, clarification of the independent effects of CBD and clobazam comedication effect needs to be addressed. Controlled studies are required to determine the effectiveness of CBD in new-onset seizures, other epilepsy syndromes, and refractory focal seizures. Controlled, randomized trials have revealed that the actual reduction in seizure frequency in response to CBD is comparable to that achieved in response to other antiepileptic drugs, and have failed to achieve the 80-85% responder rates in unblended, web-based surveys based on parental reports. CBD is far from a miracle cure, and it is of paramount importance to have a reasonable expectation of its usefulness as an antiepileptic medication. It is also a misconception that CBD is free of adverse effects, a claim attributed to its derivation from a natural source. Rather than spontaneous treatment without medical supervision, adequate medical oversight is indicated to monitor and manage adequate dose, side effects, the validity of the product, and drug-drug interaction.

Many parents continue to purchase CBD products from local growers or online. Many of these products are without quality validation and may have contents significantly different from that stated on the label. Furthermore, many parents do not pay attention to the CBD concentration of the purchased product or comprehend that a very dilute solution is unlikely to provide a therapeutic effect. One report described two children with symptoms concerning for THC intoxication and seizure exacerbation with a resolution of symptoms after switching from a "CBD-enriched cannabis extract" to a purified CBD formulation.[8] Well-standardized formulations with fixed high-CBD and low-THC concentrations should be preferred for treatment of epilepsy. It is essential that formulations have a very low THC content, as the antiseizure activity of THC is equivocal and can potentially aggravate seizures; moreover, it can be associated with addiction liability, psychiatric disorders, cognitive and motor impairments, and cardiovascular toxicity. The adverse effects of THC can be more problematic in the immature brain with impairment of structural and functional connectivity. Adequate safety data for young children exposed to CBD, and safety of use during pregnancy, are needed in the future. Evolving legislation and the increased use of cannabinoid products with little or no regulation and medical oversight may increase the risk of accidental ingestion, increased emergency room visits, and increased call volumes at Poison Control Centers. Strict regulation in manufacturing, packaging, and labeling should be absolutely warranted in order to ensure safe administration. Yet, in many cases, unregulated products may be marketed and sold in a number of venues, including online orders via the internet. The American Academy of Pediatrics has recommended robust health surveillance; strict enforcement of rules and regulations that limit access, marketing, and advertising to youth; and use of child-proof packaging to prevent accidental ingestion and discourage adults from using marijuana in the presence of children.[9]

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Pseudocellulitis From Pemetrexed (Alimta) In a Patient With Non-Small Cell Lung Cancer

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A 40-year-old male with no history of skin cancer presents with a dark "mole" on his left posterior shoulder. It is asymptomatic and has never bled, but his spouse has noticed enlargement over the past nine months. Clinical and dermoscopic photographs are below:

INTRODUCTION

Pemetrexed (Alimta) is a multitargeted antifolate drug used in combination with cisplatin or carboplatin for treatment of non-small cell lung cancer and mesothelioma. Cutaneous adverse reactions frequently observed have been reduced with preventive administration of B12 and folate supplementation and high dose dexamethasone administered one day before and after Alimta administration.[1] Pseudocellulitis, a nonnecrotizing inflammation of the dermis and subcutis from a noninfectious etiology is a rare complication of Alimta therapy. This is easily confused for cellulitis leading to hospitalization and antibiotic therapy.[2, 3]

CASE PRESENTATION

An 82-year-old, white male with stage 4 non-small cell lung cancer received four cycles of carboplatin and Alimta (pemetrexed) and two cycles of maintenance Alimta. He was admitted to the hospital with worsening erythema, swelling, and pain of right lower extremity. He had been started on Bactrim after a negative Doppler evaluation of his right leg by his primary care physician. He had noticed swelling of his right leg for two months, after wearing a brace for foot drop. On examination, he was afebrile, non-toxic, and generally doing well. He had confluent rash involving right foot and extending into the right

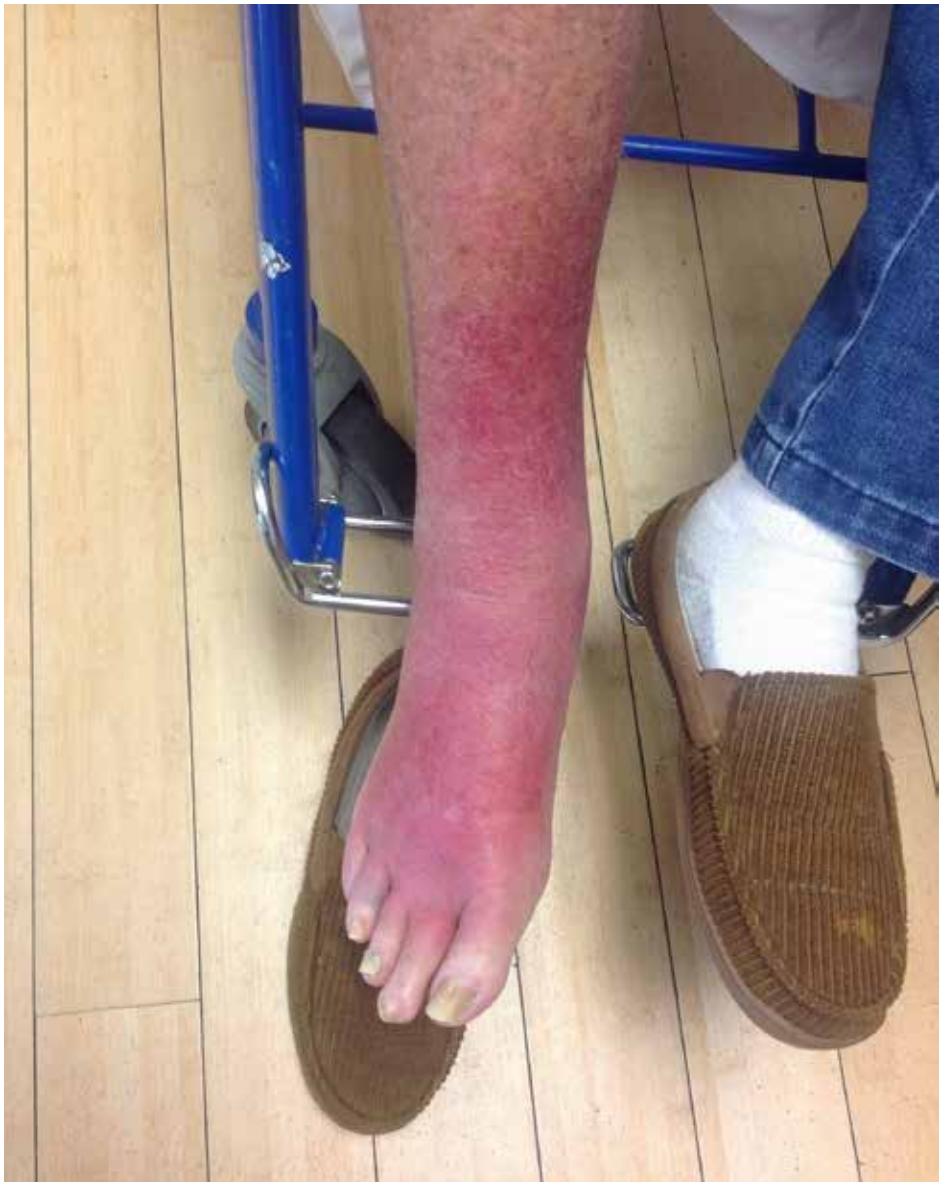

Figure 1: Confluent erythema, edema, and warmth mimicking cellulitis.

Pseudocellulitis is a rare complication of chemotherapy administration reported after administration of gemcitabine and more recently pemetrexed.

shin; warmth and tenderness were noted. (fig1). White cell count was low at 2.7 x 10^3/µL, neutrophil count was 1.97 x 10^3 /µL. He was initiated on Vancomycin IV; he continued to be afebrile, however he had worsening erythema and tenderness on account of which he was started on imipenem. He continued to do well without any fever. Blood culture on admission grew Staph. Epidermidis, which was sensitive to vancomycin and resistant to Bactrim. Blood culture repeated two days later was negative. Absence of fever, neutrophilia, and systemic symptoms prompted discontinuation of parenteral antibiotics. Skin biopsy revealed focal interface dermatitis with underlying acute interstitial dermatitis. Since pathology did not completely rule out cellulitis; fungal and bacterial cultures obtained from a repeat skin biopsy were negative. Skin lesion significantly improved on topical clobetasol (0.05%) twice daily.

DISCUSSION

Pseudocellulitis is a rare complication of chemotherapy administration reported after administration of gemcitabine and more recently pemetrexed. Both these agents are associated with several forms of cutaneous toxicities. Inhibition of DNA synthesis by gemcitabine, a pyrimidine antimetabolite and pemetrexed an antifolate drug is thought to be responsible for increased incidence of cutaneous toxicities.[1,4] B12 and folic acid supplementation by improving the functional folate status has been shown to reduce myelotoxicity, mucositis, and diarrhea associated with pemetrexed. Dexamethasone in addition to supplementation of B12 and folic acid has significantly reduced cutaneous toxicities.[1] Our patient received supplements of folic acid and B12; he did not receive dexamethasone on account of diabetes, despite which he received multiple cycles of alimta without cutaneous toxicity. Increasing edema of right foot noticed by the patient may have a causative role in development of pseudocellulitis.[4] Differing histologic findings have been reported in pseudocellulitis[2]. Pseudocellulits is mainly treated with systemic and topical steroids. Our patient recovered well on topical steroid alone. Increased awareness of this condition may avoid hospitalization and antibiotic therapy, Procalcitonin level, which is low in pseudocellulitis, may be used to differentiate from cellulitis.[3]

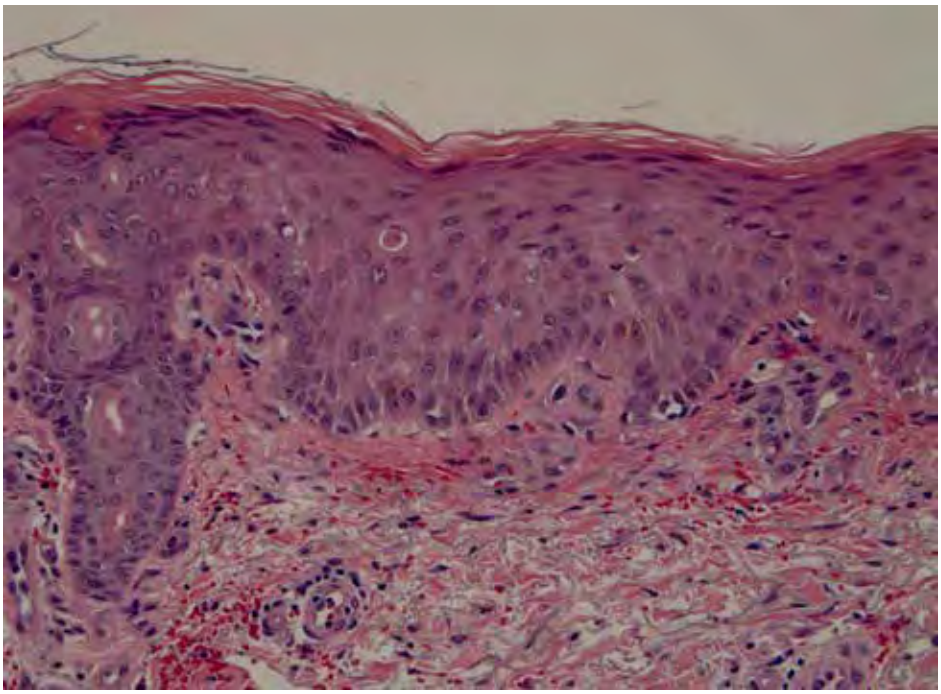

Figure 2: Focal interface change and an apoptotic keratinocyte.

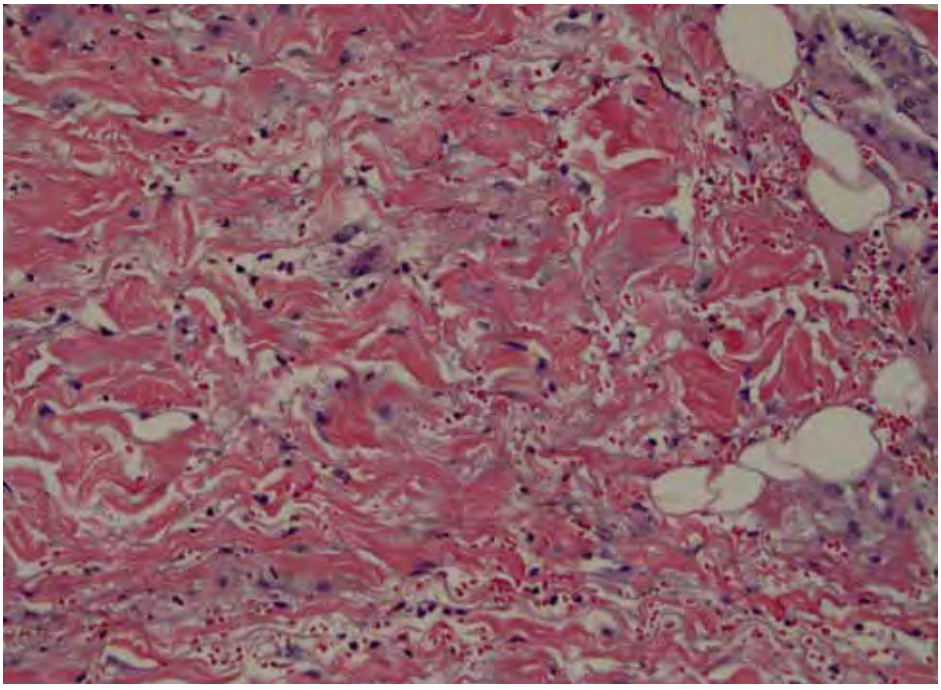

Figure 3: Interstitial infiltrate of neutrophils in the superficial and deep dermis.

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iCASE STUDY

Blueberry Muffin Rash in a Neonate

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A 36-week newborn, followed prenatally for an enlarged liver, microcephaly, and Dandy-Walker malformation, was delivered by caesarean section due to non-reassuring fetal heart tones to a 25-year-old G1 mother without significant past medical history. The mother had appropriate prenatal care, and the pregnancy had been complicated only by the abnormal ultrasound findings and an afebrile exanthema, which occurred during the first trimester. The infant was noted to have jaundice, a purpuric rash with petechiae (Panels A and B), and hepatosplenomegaly.

Cranial sonography revealed punctate foci in the periventricular white matter. Echocardiogram revealed a moderate pericardial effusion. She had hepatitis with a direct bilirubin of 19, disseminated intravascular coagulopathy with severe thrombocytopenia (platelet count was 21,000), and respiratory failure. She had elevated serum IgG and IgM titers as well as a positive urine polymerase chain reaction for cytomegalovirus.

Magnetic resonance imaging of the brain revealed microcephaly with diffuse cerebral volume loss, periventricular calcifications, and neuronal migration abnormalities. Hearing screens were failed bilaterally. Thrombocytopenia responded to multiple platelet transfusions. Neutropenia developed during antiviral treatment and required multiple doses of granulocyte-monocyte colony stimulating factor.

» *Magnetic resonance imaging of the brain revealed microcephaly with diffuse cerebral volume loss, periventricular calcifications, and neuronal migration abnormalities.*

The infant completed a six-week course of intravenous ganciclovir before transitioning to oral valganciclovir. She was discharged from the neonatal intensive care unit on room air, taking full oral feedings at seven weeks of life. She is enrolling in developmental therapies and will require close follow-up of her growth and development.

While usually asymptomatic, 10% of newborns with congenital cytomegalovirus infection will have manifestations at birth. Among symptomatic patients, multi-organ involvement is common and a small subset present with life-threatening disease. The preferred diagnostic tests are viral culture or polymerase chain reaction in urine. Treatment with ganciclovir (IV) is recommended. Once stable, treatment can be provided orally (valganciclovir). Mortality remains high at 3-10% for newborns with symptomatic disease. Sequelae are common, specifically sensorineural hearing loss and neurodevelopmental disability.[1]

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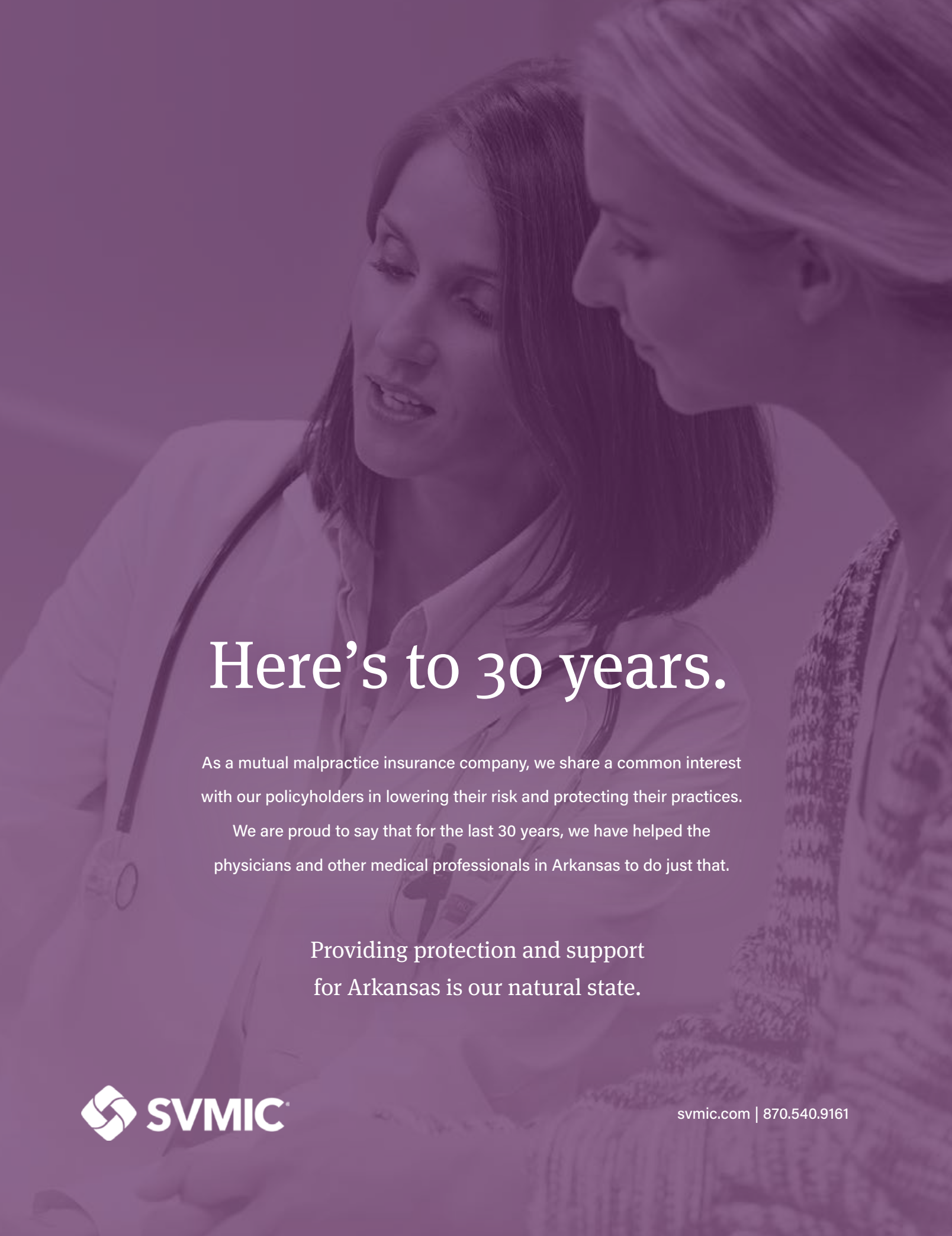

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