THE Journal
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A New Battle in an Old War:
Tobacco Smoking Gives Way to Vaping

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by CASEY L. PENN

ON THE COVER

A New Battle in an Old War:

Tobacco Smoking Gives Way to Vaping

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Feature Articles

ENDING THE HIV EPIDEMIC

Naveen Patil, MD, MHSA, MA, FACP, FIDSA; Charles Bedell, MD, MPH; Nick Butler, BS

254 That's the number of persons reported as newly-infected with Human Immunodeficiency Virus (HIV) in Arkansas in 2017. In that same year, an additional 152 persons were reported as new cases of Acquired Immuno-Deficiency Syndrome (AIDS). Across the U.S., for the same year, there were 1.1 million people with a diagnosis of HIV, of which 38,739 were new infections. Also important, 15% currently infected (one out of every seven persons) are not even aware of their infection.

Despite advances in HIV treatment and care, there has not been a decline in the number of new infections, which remains at about 39,000 per year over the past five years. The apparent levelling off of reported new cases was explained as being due to (i) effective HIV prevention measures and (ii) effective available HIV treatment not adequately reaching those who could most benefit from it. It must be noted that the reported new infections of HIV are neither equally distributed across the U.S. nor across the 75 counties in Arkansas. Nationwide, HIV surveillance depicts a striking geographic distribution pattern for new cases of HIV. Data from 2016-2017 show that 50% of new HIV diagnoses occurred in only 48 counties, Washington D.C., and San Juan, Puerto Rico. These "hot spots" further define intervention gaps, particularly in rural areas in the U.S. South, where seven states are shown to bear a substantial rural burden of new HIV transmissions (Alabama, Arkansas, Kentucky, Oklahoma, Mississippi, Missouri, and South Carolina). In these states, this shows up among affected populations that include African Americans and Latinos, especially in men who have sex with men.

During his 2019 State of the Union address before the Congress on Feb. 5, 2019, President Trump challenged the country to work towards the elimination of the HIV epidemic in the U.S. by 2030. To this end, the President made it a cardinal pillar of his administration to undertake significant, simultaneous, and sustained activities backed by established HIV scientific research and development and allocation of additional federal funding through the Centers for Disease Control and Prevention and Health and Human Services to "end the epidemic." The President's goal, simply stated, is to ensure a 75% reduction in new HIV infections in five years, and at least a 90% reduction in new HIV infections in 10 years.

Four primary areas of emphasis have been defined to achieve this goal:

- ***D**iagnose all people with HIV as early as possible after infection.*
- ***T**reat new infections rapidly and effectively in order to achieve sustained viral suppression.*
- ***P**rotect people at risk for HIV using proven and potent interventions, including PrEP.*
- ***R**espond rapidly to detect growing HIV clusters and prevent new infections.*

To bring all this together, state HIV workforces, coordinating with federal partners at Health Resources Services Administration (HRSA) and CDC, must set up elimination teams dedicated to the success of these initiatives within each jurisdiction. The Arkansas Department of Health has an Infectious Disease Branch that has administrative responsibilities for HIV prevention and HIV care and treatment. Both program areas collaborate with federal agencies via specific funding arrangements to implement activities for HIV prevention, care, and treatment with the goal of diagnosing all HIV infections within the jurisdiction and linking persons diagnosed to care and treatment services for the attainment of HIV virologic suppression or control. In Arkansas, as of December 31, 2017, 6087 persons were diagnosed and living with HIV disease (HIV: 3,452; AIDS: 2635).

One significant driver of the HIV epidemic, particularly new infections, is individuals infected but not diagnosed. Per the CDC, it is estimated that 1,122,900 adults and adolescents in the 50 states and the District of Columbia were living with HIV at the end of 2015. Of those, 162,500 (15%) had not received a diagnosis, but had contributed to the majority of new infections. Living infected and undiagnosed forms the basis of one of the major focuses of ongoing HIV prevention efforts by both the CDC and HRSA. At the moment, ADH efforts are to integrate with and support ongoing HIV prevention initiatives to target this cohort.

Another aspect of the initiative is to equip high-risk individuals who may develop HIV with Pre Exposure Prophylaxis (PrEP). ADH is exploring options to identify these high-risk individuals who may benefit from PrEP and at the same time are encouraging community providers to offer PrEP to high-risk groups. ADH has the expertise to train community providers who may be interested in offering PrEP services in their practices.

ADH currently has an Integrated HIV Prevention & Care Plan for the state of Arkansas as well as an Ending the Epidemic plan under development. All these prevention, care, and treatment efforts in Arkansas are being enhanced with the President's expressed drive to end this epidemic by 2030. The ADH Infectious Disease Branch is working closely with several community partners and health care providers in our state to implement these HIV prevention, care, and treatment programs. **AMS**

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Arkansas Hospice

by CASEY L. PENN

A New Battle in an Old War:

Tobacco Smoking Gives Way to Vaping

New delivery system. Same old tobacco stain. Those of us who lived through Big Tobacco's undoing in the 90s may not want to believe it. As physicians, you especially may be growing weary to see another tobacco-related health crisis reemerging as alternative forms of nicotine delivery have become increasingly, and shockingly popular.

Most people understand that cigarette smoking is harmful to their health. However, when it comes to *other* forms of nicotine inhalation – namely, vaping and e-cigarettes – knowledge of the potential harm appears to be lacking, particularly among young people.

According to the U.S. Centers for Disease Control and Prevention, more than 28% of high school students now use e-cigarettes on most days. And that's the ones we know about. Even as the number of smokers has decreased, the number of nicotine addicts is steadily rising due to the invention and popularization of e-cigarettes, vaping devices, and other electronic nicotine delivery systems, or ENDs.

Vaping is defined "to draw in and exhale the vapor from (an e-cigarette or similar device for marijuana)" (dictionary.com). Unlike traditional cigarettes, e-cigarettes do not produce tobacco smoke. They produce an aerosol that is often mistaken for simple water vapor. Jeffrey Roth, MD, president of Clark County Medical Society in Nevada authored a concise article* explaining what's really in the vapor of most e-cigarettes – and it certainly isn't just water. "Many of these particles contain varying amounts of toxic chemicals, which have been linked to cancer as well as respiratory and heart disease," wrote Dr. Roth. "Vaping devices include not just e-cigarettes, but also vape pens and advanced personal vaporizers (also known as 'MODS'). E-cigarettes, which resemble smoked cigarettes, and vape pens, which resemble large fountain pens, are typically simpler in design and less expensive than devices that have been customized by the user."

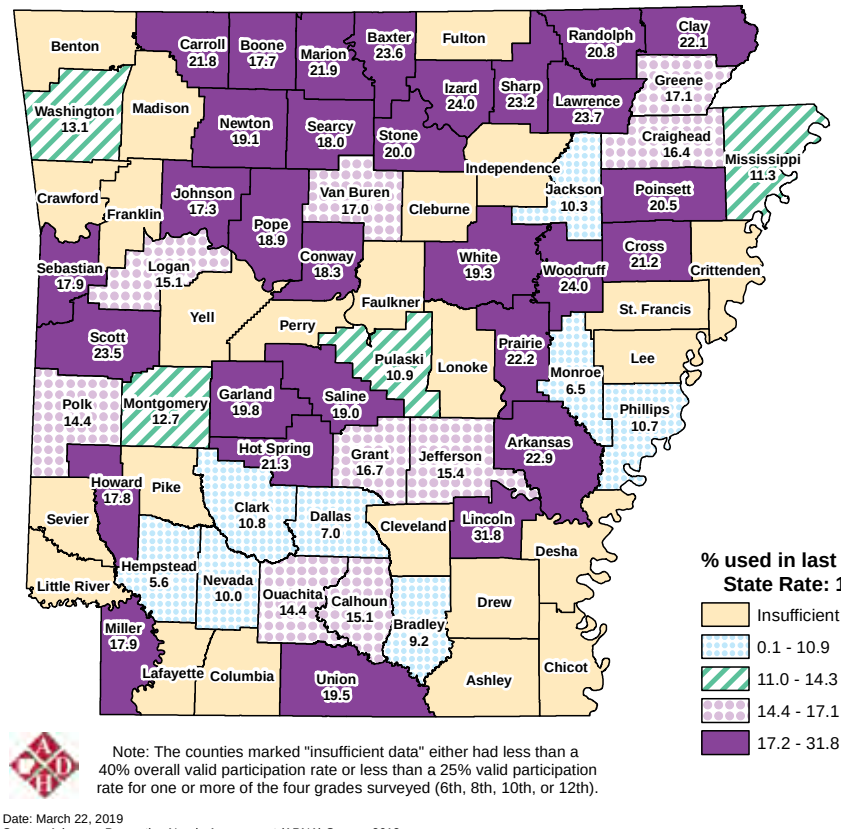
In 2016, U.S. Surgeon General Vivek Murthy, MD, MBA, declared vaping an epidemic among teens.*

The current U.S. Surgeon General Jerome Adams* picked up the anti-vaping fight by also declaring the problem an epidemic and issuing a PSA featuring his own voice asking questions like "Did you know the nicotine in e-cigarettes can harm brain development?" and "Did you know the nicotine in e-cigarettes can prime the brain for addiction – especially while it is still growing?" His answer? "It's a fact."

And the numbers are still rising. A 2018 study published in the *Journal of Adolescent Health* found that compared to just under 10% of students surveyed (grades 6-12) who perceived cigarettes as harmful, 37.5% perceived "no" or "little" harm from intermittent use of *e-cigarettes.* Further, the study found that "youth with lower harm perceptions were more likely to report current use."

Current use trends by the National Youth Tobacco Survey* (released by the CDC and the Food and Drug Administration) reported that e-cigarettes or similar devices, have become *more* commonly used by our youth than cigarettes. CDC tobacco data shows also that recent increases in the use of e-cigarettes is driving increases in tobacco product use among youth. The stats are alarming and show an increase of roughly 1.5 million youth in just one year: "The number of middle and high school

Current E-cigarette Use among Youth
Arkansas 2018



Note: The counties marked "insufficient data" either had less than a 40% overall valid participation rate or less than a 25% valid participation rate for one or more of the four grades surveyed (6th, 8th, 10th, or 12th).

Date: March 22, 2019
Source: Arkansas Prevention Needs Assessment (APNA) Survey, 2018
Map created by: Donald McCormick, MSHI

students using e-cigarettes rose from 2.1 million in 2017 to 3.6 million in 2018."

That doesn't mean that young (or older) vapors won't work their way around to traditional cigarettes, too. A John Hopkins Medicine's article, "5 Truths You Need to Know About Smoking," shared a study that found that "most people who intended to use e-cigarettes to kick the nicotine habit ended up continuing to smoke both traditional and e-cigarettes."

Perhaps the saddest thing the article reports: "A new generation is getting hooked on nicotine," states author Michael Joseph Blaha, MD, MPH. "What I find most concerning about the rise of vaping is that people who would've never smoked otherwise, especially youth, are taking up the habit. It's one thing if you convert from cigarette smoking to vaping. It's quite another thing to start up nicotine use with vaping."

Source: https://www.cdc.gov/vitalsigns/youth-tobacco-use/index.html

The problem is fast-growing nationwide and in Arkansas. Last fall, The Arkansas Department of Health reported that e-cigarette use here had increased 80% since the previous year.

As information spreads, it's hard to know what is or isn't reaching our adolescent population. For this reason, it's important to talk to your teen patients about e-cigarettes and other ENDS and to make sure you and your staff fully understand the products' dangers and effects.


Chad Rodgers, MD

"Most teenagers don't think vaping is harmful," warned Pediatrician and AMS President-Elect Chad Rodgers, citing conversations he has had with his young patients. "They don't see the dangers. Many of these products get marketed with flavors and names that appeal to youth, and they are told that it is not harmful."

Dr. Rodgers is clearly alarmed by the misperceptions among his patients and of their parents. "It is now one more issue I have to address. I have even had a couple of parents who were vaping in the exam room. It is a real public health issue that needs to be addressed. I tell patients that it is not safer than smoking and I have counseled many patients to stop the habit."

National and Local Attempts to Curb the Trend

Last year, the American Medical Association made a strong attempt to publicly address this issue when they called on the FDA to also strengthen its policies related to e-cigarettes and e-cigarette marketing practices. "The AMA is committed to keeping harmful tobacco products out of the hands of young people, and we will continue to urge the FDA to ban flavors, as well as marketing practices, that enhance the appeal of these products to youth," said Albert J. Osbahr, III, MD, a member of the AMA Board of Trustees. "We believe more stringent policies will help protect our nation's youth from the harmful effects of tobacco use." Last November, the FDA did propose a ban on flavorings like gummy bear, peach, and cotton candy used to entice young buyers of tobacco products sold in stores and online.*


Gary Wheeler, MD

Arkansas is among 15 states that have strengthened its policies against e-cigarettes. A recent edition of "Arkansas Week" focused on preventable ailments and their cost to the state. In that edition, President and CEO of Arkansas Center for Health Improvement Joe Thompson, MD, discussed the newer enticement of e-cigarettes and the recent legislation enacted to combat the problem. "It's the upstream risks that ultimately cause downstream conditions: almost one in four Arkansans continue to use tobacco products," noted Dr. Thompson, who praised recent positive steps by the state's policymakers to address the problem. "This past session, the state raised the purchasing age for tobacco products to 21. We know that nicotine is as addictive as cocaine. Nationwide, if we can keep people from starting to smoke in their teen years and [thereby] becoming addicted to nicotine, that will have the single largest policy effect on the number one cause of conditions still in this state: tobacco."


Joe Thompson, MD

Act 580,* passed into law during the 92nd Arkansas General Assembly, increases the minimum age from 18 to 21 to buy, use, or possess tobacco products, including vapor and alternative nicotine products. The law exempts members of the Armed Forces as well as those individuals turning 19 by Dec. 31, 2019. Notably, the new law authorizes certified law enforcement officers and school officials to confiscate tobacco and nicotine products from minors and puts in place penalties for offenders that include community service and tobacco education. To Dr. Thompson's point, a 2015 Institute of Medicine report found that raising the minimum age for tobacco sales, etc., leads to fewer young people starting to smoke and thereby reduces smoking-related deaths.

Gary Wheeler, MD, is the president of Arkansas Chapter of the American Academy of Pediatrics and a long-time AMS member. While he is encouraged by recent legislation, he wants to see even stronger measures put in place. "Arkansas has lagged behind on evidence-proven methods to reduce the incidence of tobacco and nicotine use," said Dr. Wheeler, who would like to see the state increase prices on tobacco products, impose taxes, ban coupons, and prohibit the use of tobacco products in all public spaces. "This also includes e-cigarettes, which have no tobacco taxes in Arkansas and are allowed in public spaces under current law (although private businesses can prohibit them.) Most puzzling to me is why Arkansas, which has no tobacco production activity and has huge costs from our high use of tobacco as recently documented by ACHI and

> Continued on page 56.

others, fails to pass these regulations which have been regularly introduced … The saddest thing about these choices is that we allow the ongoing predatory practices of these businesses to addict children and sentence them to poor health and less economic options going forward for their futures."

"Arkansas Week" also featured Appathurai Balamurugan, MD, the deputy chief medical officer and director of Chronic Diseases for ADH. "Our fight against tobacco use has been a long, drawn-out one, and it's been challenged now with the new tobacco products – like e-cigarettes and vaping," he said. "E-cigarettes and vaping products have made our continued public health efforts in tobacco prevention and cessation more essential. To that end, physicians need to ask their patients about e-cigarette or other vaping product use at every office visit and offer counseling similar to smoking cessation."

Appathurai Balamurugan, MD

Dr. Balamurugan also spoke about ADH's new "Be Well Arkansas" program. Be Well Arkansas is a holistic approach to addressing tobacco cessation (including vaping and ENDs), high blood pressure, and diabetes and includes positive messages about living well. The state's Be Well call center is available to assist Arkansans trying to quit tobacco use – including e-cigarette and vaping product use. Physicians are encouraged to refer patients to the call center for help as they talk to patients regularly about the hazards of all forms of nicotine ingestion. "The toll-free phone number that patients can call is 1-833-283-WELL," explained Dr. Balamurugan. "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. You may also text 501-588-8445 Monday-Friday between 8 a.m. and 4 p.m. There is a new website, www.bewellarkansas.org, with updated resources for patients and providers, and an online chat component for cessation services."

Greg Bledsoe, MD

The 2016 U.S. Surgeon General's report about youth and electronic cigarettes (e-cigarettes) contained useful information. To help pediatric clinicians interpret its findings, The American Academy of Pediatricians Julius B. Richmond Center of Excellence created a fact sheet. The following suggestions may help clinicians as they broach the subject with patients:

"When counseling, choose messages that resonate with adolescents … consider talking about the expense of e-cigarettes or the loss of freedom that occurs when you're addicted to nicotine. Talk with them about the tobacco industry's efforts to target them with misinformation and advertising."

"For both users and non-users, mention the dangers of secondhand e-cigarette exposure, and advise teens to avoid secondhand e-cigarette aerosol, and to discourage others from using e-cigarettes around them. For teens who babysit or have young siblings, explain that e-liquid is poisonous and can be fatal if ingested. Ensure that e-liquid is kept in childproof containers, and out of the reach of children."

The AAP's fact sheet also suggested evidence-based tobacco interventions that can be adapted for use with e-cigarrettes. The U.S. Public Health Service's "5As" Tobacco Cessation Intervention can be used to guide your e-cigarette conversation with parents and with youth:

- *ASK about e-cigarette use.*
- *ADVISE against e-cigarette use and about avoiding secondhand vapor exposure.*
- *ASSESS whether teen is ready to quit using e-cigarettes .*
- *ASSIST them in quitting by setting a quit date and giving them practical advice for a successful quit attempt and for prevention of secondhand exposure by non-users.*
- *ARRANGE follow-up to check on the teen's progress with quitting.*

Here at home, Arkansas Surgeon General Greg Bledsoe, MD, worries not only about the dangers of vaping, but also the dangers of using vaping devices with other drugs. He offered the following key points to Arkansas physicians to use in their discussions with patients.

1. Vaping is unsafe.

"In advising your young patients about the dangers of vaping and ENDS, it's important to understand that many young (and some older) patients still assume that vaping is safe. We're finding out that it's as unsafe [as cigarettes], just in different ways. You don't have the same chemicals as you have with a cigarette, but you have other chemicals that are super-heated and inhaled deeply into the lungs. That's a problem for anyone but particularly in young people whose bodies are still developing. When you couple that with the nicotine addiction, it's a major issue."

2. In combination with cannabis, vaping in young people carries developmental risks.

"The other troubling aspect is that there are young people who are using vaping technology to consume cannabis and various marijuana products. This is very concerning because the evidence is very clear that people under the age of 25 who are using marijuana once per week never regain their full cognitive function. They're permanently altered, so even if they stop later in life, their IQ is already stunted."

The evidence is clear. Once again, our country's citizens, especially our youth, are at grave health risks from nicotine, but unlike 40-50 years ago, we know this time around the severity of the risks involved. As physicians on the front line of public health, you can do something about it. Talk to your patients. Their future depends on it..

*Sources for Further Study

- https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Richmond-Center/Pages/Understanding-the-2016-SGR-Fact-Sheet.aspx
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Neuroendocrine Tumor: Presenting as a Case of Intractable Nausea

Naga S. Addepally, MD; Mohit Girotra; Benjamin Tharian, MD

Division of Gastroenterology and Hepatology, UAMS Department of Medicine

Keywords

Neuroendocrine tumor, nausea

Introduction

The term *neuroendocrine* tumor is referring to a group of cells that secrete hormones in response to neural or chemical stimuli. These cells are widely distributed throughout the mucosa of the GI tract and secrete a variety of hormones that lead to varied clinical presentation and symptoms. Initially, it was thought that these cells are derived from neural crest cells, but they are now believed to be derived from local multipotent stem cells[2]. There are at least 13 different types of neuroendocrine cells known to be present, which secrete a variety of hormones in response to various stimuli. They contain secretory granules in the cytoplasm, which stain positive for Chromogranin A (CgA), synaptophysin, neuron-specific enolase, and CD-56.[2] Typical symptoms are related to the hormones secreted. Back in 1907, when little was known about neuroendocrine tumors, these tumors were thought to be benign, and the word *carcinoid* was coined by Oberndorf.[3] However, with more knowledge about these tumors and their malignant potential, the word *carcinoid* is obsolete and WHO has changed the nomenclature. The word GEP NET (gastroenteropancreatic) is now being used to address NETs originating from the GI tract (GNET) and Pancreatic NET (PNET) for the NETs arising from pancreas. The incidence of GEP NET is increasing: 2.5 to 5 cases per 100,000, with incidences as high as 8.4/100000 in autopsies.[4,15,16] However, the number might just be a low estimate of the actual incidence as majority of tumors are asymptomatic and are missed.[15,16] Incidence of GNET is much higher than PNET. While most of the cases are sporadic, NETs are associated with familial endocrine cancers such as MEN, NF, VHL syndrome.[17] A population-based study conducted in 2004 showed the distribution of these tumors to be highest in the small intestine (44%), followed by the rectum (19.6%), appendix (16.7%), colon, and stomach. The study also showed that GNET are more common in females and African American.[17]

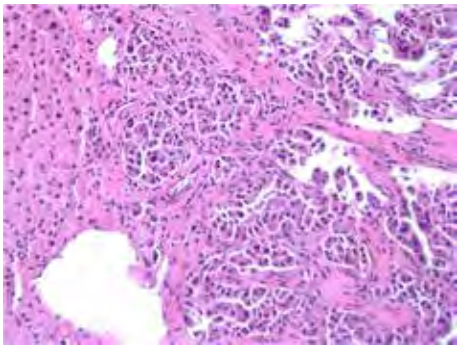

Image 1: Liver involved by metastatic neuroendocrine tumor composed of small cords and nodules.

Case presentation

A 33-year-old Caucasian woman with a history of learning difficulty and seizure disorder was referred for workup of a possible pancreatic mass seen on CT scan. She had a 10-month history of nausea and RUQ pain with fatty meals. No other associated symptoms including fever, chills, vomiting, altered bowel habits, hematemesis, melena, weight loss, or rash. PSH is significant for appendectomy in her childhood. Physical exam was unremarkable including abdominal exam, which showed non-tender abdomen, without any signs of acute abdomen and good bowel sounds were present in all quadrants. Lab work was negative including liver function tests, lipase, and amylase. Ultrasound and CT scan of the abdomen showed cholelithiasis and a multilobulated mass in the right paramedian aspect of the abdomen, adjacent to duodenum and closely associated with pancreas. It was unclear whether the mass was arising from pancreas vs. duodenum vs. adrenal vs. retroperitoneal from the cross sectional imaging. Tumor markers including AFP, CA-19, CEA and adrenal markers including ACTH, cortisol, aldosterone, and metanephrines were normal. Endoscopic Ultrasound (EUS) evaluation showed 8 x 8 cm heterogenous-appearing mass arising from duodenal wall distinct from pancreas and right kidney. Fine needle aspiration showed grade I well-differentiated neuroendocrine tumor positive for pan-CK, synaptophysin, and chromogranin. CDX2 staining was positive, confirming the gastrointestinal origin. Laparotomy showed a large mass arising from second portion of the duodenum and densely adhered to duodenum, head of pancreas, and a second mass adhered to the root of mesentery. There was also a metastatic lesion to segment VI of the liver and antrum. Whipple procedure (pancreaticoduodenectomy) with wedge resection of the liver segment was performed. Biopsy of the mass and the liver lesion was consistent with well-differentiated grade 2 neuroendocrine tumor.

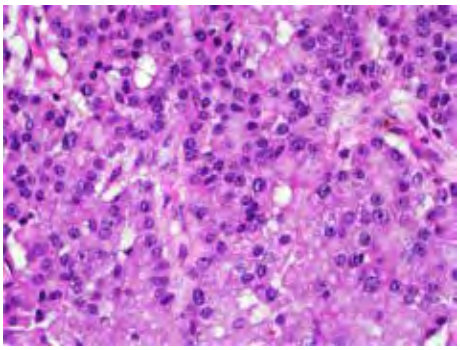

Image 2: 40x image of well-differentiated neuroendocrine tumor, involving the duodenum, showing focal nucleoli along with typical "salt and pepper" nuclei spread throughout.

Discussion

The term *carcinoid* is now obsolete, and is replaced by the more descriptive terminology, neuroendocrine *tumors (NET)*. The gastroenteropancreatic NET (GEP-NET), incidence of which is increasing (2.5 to 5 cases per

100,000),[1,2,3] includes tumors arising from the GI tract (GNET) and Pancreas (PNET). Within the GI tract, these are found commonly in small bowel and appendix, followed by rectum and stomach[4]. Duodenal occurrence of NETs is very rare and represents only 2-3% of all NETs.[4,5] Most of these tumors are small, submucosal masses[5,6] and are divided into five types: duodenal gastrinomas, duodenal somatostatinomas, nonfunctioning NETs, ganglioytic paragangliomas, and poorly differentiated NE carcinomas. They may occur sporadically or in association with Multiple Endocrine Neoplasia (MEN-1) and Zollinger-Ellison Syndrome (ZES). The tumor seen in our patient was a nonfunctioning NET.

Although the old term *carcinoid* sounds benign, these tumors are capable of local and distant metastasis. The most common presentation is abdominal pain, but presentation may vary from nonspecific dyspepsia to GI bleeding.[5,6] Given the indolent and slow-growing nature of these tumors, NETs may remain asymptomatic until they grow large or may be incidentally discovered on imaging or endoscopy. In our case, patient had intractable nausea, likely due to intermittent, low-grade outlet obstruction from the tumor growing in duodenal wall.

Routine imaging, including CT and MRI, can detect large-sized NETs and also metastases but fails to reliably detect smaller submucosal lesions.[7] In such scenarios, EUS is the most useful diagnostic modality to detect accurately the tissue of origin, as in our patient, which may be difficult at times with conventional imaging. EUS serves well in defining the size of tumor, level of invasion, histology by FNA, and regional lymph-node metastasis.[4,7,8] Additionally, serum chromogranin levels are seen elevated in 80% of the tumors.[9] In addition to cross-sectional imaging and EUS, somatostatin

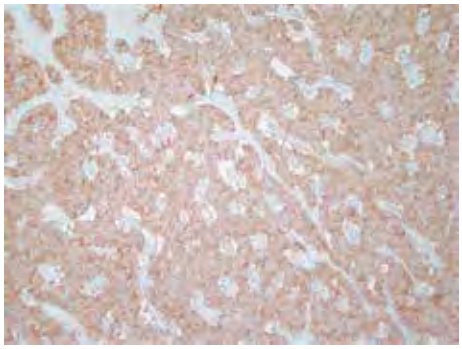

Image 3: Synaptophysin immunohistochemical stain showing diffuse positive cytoplasmic and membranous staining of tumor cells.

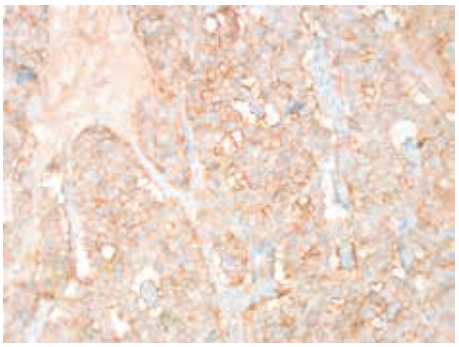

Image 4: CD56 immunohistochemical stain showing diffuse membranous positivity of tumor cells.

scintigraphy (SRS) is valuable in identifying small, metastatic lesions, owing to the increased expression of somatostatin receptors by these tumors.[10,11] Histologically, NETs stain positive for pan-sensitive neuroendocrine markers, including Chromogranin A, synaptophysin, and neuron-specific enolase.[10] Moreover, Ki-67 level, which measures the proliferative capacity of the tumor cells, is measured to grade the tumors according to the WHO classification, which determines the overall prognosis.[12] If the Ki-67 index is <2%, tumors are graded into G1, 2-20% into grade 2, and >20% into G3.

Management of NETs depends on size and grade of tumor and extent of metastasis. Small, submucosal tumors of < 1cm without any regional lymph node involvement can be safely removed by endoscopic resection. For larger tumors, full thickness excision is needed either by laparoscopy or laparotomy. Alternative therapy (medical) is considered for non-resectable, metastatic tumors or high-risk surgical candidates, which may include somatostatin analogues, interferon, and chemotherapy,[13,14] (all evolving fields). Radiation therapy (external beam radiotherapy; EBRT) may be considered for palliative purposes and is suitable for patients with increased uptake of specific radionucleotide agents (like I-MIBG). Additional modalities, including radiofrequency ablation or hepatic artery embolization, may be needed for management of non-resectable hepatic metastatic lesions and for symptomatic control of functional NETs.

Learning points

» Duodenal NETs are rare, slow growing, and may have insidious presentation, like our patient with nausea, which was likely due to intermittent, low-grade-outlet obstruction.

» This is a very uncommon presentation, but teaches endoscopists to investigate thoughtfully such purportedly trivial complaints to unravel unexpected findings, like NETs.

» EUS is an irreplaceable asset in investigation of submucosal masses and can help differentiate the tissue of origin even in cases where cross-sectional imaging fails.

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A CLOSER LOOK AT QUALITY

Impact of Caregiver's ACEs on Their Child's Diabetes Outcomes

RACHEL EKDAHL, MD; HEATHER CANTRELL, APN; ANNIE WANG, MD; and EMIR TAS, MD

Type 1 Diabetes (T1DM) is a complex chronic disease that requires adherence with a rigorous and regimented care plan to achieve optimal control. Non-adherence leads to poor control and an increased risk for complications. Pediatric diabetes is unique in that caregivers are intimately involved in disease management. The ideal caregiver involvement should be inversely proportional to the child's developmental stage, focusing on providing support as needed and supervision of treatment adherence.

The Hemoglobin A1C (HbA1c) test is used to monitor adherence to diabetes treatment. An HbA1c of 7.5 percent or lower indicates good diabetes control; 9 percent or higher indicates poor control. During the first year of diagnosis, good diabetes control is often attained easily due to production of endogenous insulin; known as a *honeymoon period.* The American Diabetes Association recommends follow-up for diabetes every three months, starting at diagnosis.

Adverse Childhood Experiences (ACEs) — stressful, traumatic events occurring before age 18 — have become a popular topic in pediatric care. The hallmark Kaiser ACE Study found a strong dose-response association between the number of ACEs and negative health outcomes in later life. Further studies suggest the intergenerational transmission of trauma, including the role of epigenetics and the influence of maltreatment experiences on later parenting practices. Given the importance of caregiver involvement in pediatric diabetes care, caregiver ACE scores could reflect caregiver challenges that might affect diabetes control in young patients. Data on the impact of the caregiver's ACE score on children's chronic disease management is limited.

Arkansas has the highest prevalence of children in the United States who have experienced ACEs. A devastating 56 percent of Arkansas' children have experienced at least one ACE; one in seven have experienced three or more ACEs.

We conducted a study to determine the impact of caregiver ACEs on management of their child's diabetes at Arkansas Children's Hospital's diabetes clinic. We used the standardized ACE Questionnaire to calculate caregivers' scores. This self-report measure identifies childhood experiences of abuse and neglect, including psychological, physical or sexual abuse; emotional or physical neglect; loss of a parent; mother treated violently; substance abuse; mental illness or criminal behavior in the household. The questionnaire was distributed to caregivers of patients up to age 13 during regular diabetes clinic visits. Patients with a T1DM diagnosis within the last year were excluded to avoid data skewed by a potential honeymoon period. The primary caregiver was asked to notate the number of questions that applied to them, but no specific answers were collected. Other data collected and results are summarized in Table 1. The student t-test was used to compare the means, and chi-square was used to compare categorical variables.

Sixty-one families completed the questionnaire between December 2018 and March 2019. Study participants' average HbA1c was 8.1 percent, indicating marginal diabetes control. Only 13 percent of children in this cohort were seen in clinic four times per year, as recommended and this subgroup had a better average HbA1c (7.5%). The caregiver ACE scores were not low in this subgroup.

We compared the mean data of children of caregivers with ACE scores

TABLE 1. Characteristics of children distributed by primary caregiver ACE score

Caregiver ACE Score	0	1-3	4 or more
Number (percent) of caregivers	19 (31%)	25 (40%)	18 (29%)
Average age	9.5 years old	9.4 years old	9.8 years old
Gender distribution	57% female, 43% male	72% female, 28% male	52% female, 48% male
Ethnicity/race	79% White, 21% African American	80% White, 20% African American	95% White, 5% African American
Average diabetes duration	3.9 years	3.9 years	4.1 years
Average HbA1c (last 4 visits)	8.3%	8.3%	8.2%
Percentage of patients in diabetic ketoacidosis at diagnosis	42%	48%	52%
Average number of diabetes clinic visits per year since diagnosis	3.1	3.0	3.1

of zero, one to three, or four or more. We found no significant difference in the average HbA1c, the average number of diabetes clinic visits, or the frequency of diabetic ketoacidosis (DKA) at diagnosis.

Families of children with T1DM have an exceptional burden of care. Peer relations and family dynamics play a critical part in adherence to care and diabetes control. Psychosocial factors and family stressors need to be evaluated on a routine basis, as they are linked to poorer glycemic control. It is vital that the diabetes team be aware of needs for mental health or resource referrals. Social workers and certified diabetes educators play a crucial role in screening patients and connecting them to appropriate resources during clinic visits. ACEs scores are not part of the current screening process.

This study did not show a significant link between primary caregiver's ACE scores and child's T1DM control. However, a surprising number of caregivers were found to have high ACE scores, compared to the average number of ACEs experienced in Arkansas: 69 percent of caregivers reported at least one ACE; 29 percent reported four or more ACEs. Considering the well-established relationship between higher ACE scores and adverse health outcomes at the individual and generational levels, it is imperative to analyze the long-term consequences of these findings in longitudinal studies. Almost a third of caregivers, with an ACE score of four or more, are themselves at higher risk of adverse health effects and may benefit from additional resources.

Another study finding is that the percent of patients who presented in DKA was higher (but not statistically significant) with higher primary caregiver ACE scores. We cannot conclude if the caregiver's ACE score was a contributing factor to the severity of DKA; however, the effect of ACEs on the caregiver's ability to recognize signs and symptoms of diabetes may be examined. Following diagnosis, there was no notable difference between groups in diabetes-related ED visits or hospital admissions for DKA. Conclusions based on the results of this study cannot be made given the study's small sample size, but additional exploration is warranted.

A fine balance needs to be met regarding the level of caregiver involvement in their child's diabetes management. Over-involvement can lead to stress, burnout and potentially poor control. Under-involvement can lead to increased acute or chronic diabetes-related complications. Protocols are in place for screening patients and families for depression, understanding family dynamics, stressors, and roles in responsibility of care, disordered eating and poor social adjustment. However, the focus of these tools is the child, not the caregiver. The ACE screening questionnaire may serve as an adjunct tool to alert the health care team to a family's need for increased social support. ▲

The authors work in the Division of Diabetes and Endocrinology, Arkansas Children's Hospital.

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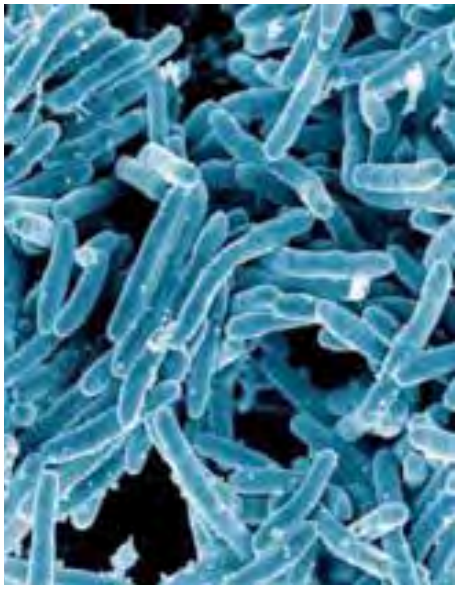
Visit **afmc.org/ACEs** for more information about the 2019 Arkansas Adverse Childhood Experiences and Resilience Summit.

Tuberculosis in Arkansas: An Interview With Dr. Joseph Bates

Teresa Bau, MD
UAMS (South Central) Family Medicine Residency

Arkansas has a monumental figure of our state's medical history tucked away on the third floor above the UAMS Library, and his name is Joseph Bates, MD. Dr. Bates is a pulmonologist who has truly lived a life of service and unrelenting commitment towards his research. He is one of the founding fathers of modern tuberculosis epidemiology and treatment. More importantly, while working together with Paul Reagan, MD, and William Stead, MD, he changed the paradigm of how tuberculosis now can be treated in an outpatient setting.

I had the pleasure of interviewing Dr. Bates for my family medicine residency senior research project. I did not realize that my interview with Dr. Bates would be a history lesson, but I should have known better. Tuberculosis, in much of the present-day western world, has largely become an uncommon disease; however, this was not the case merely 60 years ago when the incidence of TB in 1953 was 52.6 per 1,000,000 as compared to the present value of 2.9. In the 1940s and before, being diagnosed with tuberculosis was a serious death threat. Those with active disease had a 50% mortality rate! In the present-day developing world, tuberculosis continues to be one of the most widespread and deadliest diseases, including one of the leading killers of those with HIV. My conversation with Dr. Bates started with some basic statistics followed by some epidemiological facts to put it all in perspective of Arkansas history. In 1882, the bacillus that causes TB, *Mycobacterium tuberculosis,* was discovered by Robert Koch. In the same decade, Louis Pasteur was working on the pasteurization of milk to prevent the spread of "germs." The work by Koch and Pasteur reported in the 1880s led to the understanding that microbes could infect humans and cause disease—thus the Germ Theory was established. Of note, Waksman and Schatz discovered streptomycin in 1944; Damage and Fox co-discovered isoniazid in 1947. These two antimicrobials are still part of the large number of available drugs for the treatment of tuberculosis today.



Mycobacterium tuberculosis

Dr. Paul Regan (left), Dr. Joseph Bates (center), and Dr. William (Bill) Stead (right) at the Arkansas Department of Health in 1975.

Dr. Bates's passion for his research was quickly evident as he became quite emotional talking about visiting his uncle at one of the earliest TB sanatoriums in Booneville, Ark. In the late 1800s, sanatoria were developed where patients with tuberculosis were "prescribed sunshine and fresh air" to treat their disease. These sanatoria were typically self-sufficient medical complexes where patients could live and be removed from the rest of society. However, these patients also were subjected to experimental treatments by physicians trying to find a cure for this illness. TB was thought by many to result from a failure of will or from "over-intensity." Many modes of treatment were tried including collapse of the infected lung via surgical removal of up to eight ribs on the involved side or inducing lung collapse by inducing a pneumothorax repeatedly over

» A most-unexpected opportunity presented itself when Dr. Bates was asked to help control a tuberculosis outbreak at juvenile correctional facility at Wrightsville, Ark. At the time of this outbreak, it was thought that the disease spread via close contact with a person who had active disease.

many months or years. None of these measures were ever subjected to a proper clinical trial to measure their effectiveness.

Dr. Bates was determined to find a better treatment, but before a new approach to treatment could be developed, more basic information was needed concerning how the disease was transmitted from person to person. Dr. Bates knew of important work done by Dr. Richard Riley, who worked with guinea pigs and showed that the infectious unit responsible for disease transmission in the guinea pig was a very tiny droplet containing only one or two bacilli. Of key importance about this observation was that these tiny units did not settle to the floor, but remained airborne in any occupied room. Until this time, it was thought that large clumps of bacilli as are found in sputum from TB patients were the ones that transmitted the bacilli to the next susceptible human. Riley's findings could change the basic idea of how TB is transmitted in people, but how could this be tested in man?

A most-unexpected opportunity presented itself when Dr. Bates was asked to help control a tuberculosis outbreak at juvenile correctional facility at Wrightsville, Ark. At the time of this outbreak, it was thought that the disease spread via close contact with a person who had active disease. However, when Dr. Bates discovered that the boys in the facility were: assigned bunk beds located in a single, large room; separated by age into two groups by iron bars that essentially divided the room in half; and exposed to a disease transmitted at random throughout all parts of both sides of the room (instead of the new infections only clustering around the bunk where the newly diagnosed infectious case was assigned), he knew that transmissions did not require close contact but had to have spread by small airborne droplets as observed by Riley in the guinea pig experiment.

Results from this outbreak were published in the *New England Journal of Medicine*. From this study, additional work was done evaluating the effect of chemotherapy on eliminating the infectiousness of a newly treated patient with TB. Sentinel work on this was done at Jefferson Regional Hospital in Pine Bluff.

Dr. Bates, working closely with Dr. Reagan and other members of the hospital clinical staff, formed a clinical unit at Jefferson Regional Hospital exclusively for treating TB patients. It was perhaps the first such unit located in a private, general hospital in the U.S. After about three years of the unit's operation, a careful analysis of the therapeutic outcome for the patients and their household contacts showed that a very short period of hospitalization, followed by continuing treatment on an ambulatory basis, gave highly satisfactory outcomes. Also of great importance, it was observed that the patients discharged on chemotherapy while still sputum-culture positive were no more infectious for their household contacts than were the patients who were culture negative at time of discharge. This work led to acceptance that TB patients can be treated effectively in general hospitals and that ambulatory treatment rather than prolonged hospitalization and bed rest are required for tuberculosis control.

Thereafter, Dr. Bates saw the closure of tuberculosis sanatoria across the U.S. with the McRae Sanatorium at Alexander, Ark., closing

Patients on a ward at a tuberculosis sanitorium.

» ***This work led to acceptance that TB patients can be treated effectively in general hospitals and that ambulatory treatment rather than prolonged hospitalization and bed rest are required for tuberculosis control.***

in 1965 and the state sanatorium at Booneville closing in 1972. Within 10 years of these reports, over 600 TB sanatoria across the U.S. were closed. Dr. Bates' story is one of lifelong dedication that has had an enduring impact on the epidemiology and infectious disease. My conversation with Dr. Bates concluded with a moment of silence as he reflected on these memories, and he returned my gaze with the contented smile of someone who has lived a most-fulfilled life. "Thank you for letting me relive those memories," he said to me.

Recommended Literature

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Gunnels JJ. Bates JH and Swindoll H. Infectiousness of culture-positive tuberculosis patients on Chemotherapy. *Am Rev Resp Disease*; 1974:109:323. [This work was done at Jefferson Hospital while Dr. Gunnels was a pulmonary fellow under Dr Bates' direction and Ms. Swindoll was a public health nurse assigned to Arkansas from the CDC. It was this paper that provided the basic science that showed how quickly the infectiousness could be controlled by proper chemotherapy. This paper got lots of attention and Dr Gunnels was invited to London, England, to read the paper at a major medical meeting.]

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CASE STUDY

Determination of Spread of Injectate After Ultrasound-Guided Pecto-Intercostal Fascial Plane Block: A Cadaveric Study

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ABSTRACT

Objectives: The goal of this observational study was to establish the expected spread of local anesthetic throughout the pecto-intercostal fascial (PIF) plane using ultrasound-guided injection of methylene blue dye. Five lightly embalmed cadavers were injected bilaterally within the PIF plane under ultrasound guidance, and the chest walls were then dissected to determine injectate spread.

Results: Ultrasound-guided injection of the PIF plane achieved a spread throughout the plane entirely.

Conclusion: Ultrasound-guided injection of the PIF plane reliably involves the anterior cutaneous branch of the intercostal nerves that innervate the sternum.

INTRODUCTION

Most pain-management techniques for anterior-chest-wall pain following chest-wall trauma, sternotomy, thoracic drainage tube placement, and mastectomy have involved the judicious use of opiate medications in the belief that they are associated with optimal hemodynamic stability and pain control. However, large amounts of intravenous opioids can delay extubation and have multiple side effects including respiratory depression, sedation, urinary retention, constipation, and puritus.[1] The pecto-intercostal fascial plane block (PIFB) is an innovative, local technique that presents an alternative method of providing analgesia for rib-cage and sternal pain.[2]

Patients in pain will have prolonged immobilization, insufficient respiratory function, difficulty coughing and a subsequent longer period of mechanical ventilation, longer ICU stays, and longer overall hospital stays.[2] Inadequate analgesia and uninhibited perioperative surgical-stress responses also have the potential to initiate pathophysiologic changes in all major organ systems leading to hemodynamic instability, cardiac overload, increased oxygen consumption, and increased risk of myocardial ischemia.[3]

Different techniques, including blind parasternal injection and large-volume local anesthetic infiltration of the sternotomy wound, have previously been described as a way to decrease opioid requirements, provide early postoperative analgesia, and facilitate early extubation.[4,5] In one study, the use of ultrasound to guide local anesthetic placement in the PIF plane was described as a way to assist in the extubation of critically ill patients who were difficult to wean from ventilators.[6,7]

It is believed that the utilization of the PIFB to anesthetize the anterior cutaneous and lateral branches of intercostal nerves will ultimately reduce opiate consumption and the complications associated with their use. There is no anatomical description of local anesthetic spread for the PIFB in the literature. The goal of this study is to establish the expected spread of local anesthetic throughout the PIF plane and the nerve involvement using an ultrasound-guided injection of dye into the hemi-chest walls of lightly embalmed cadavers.

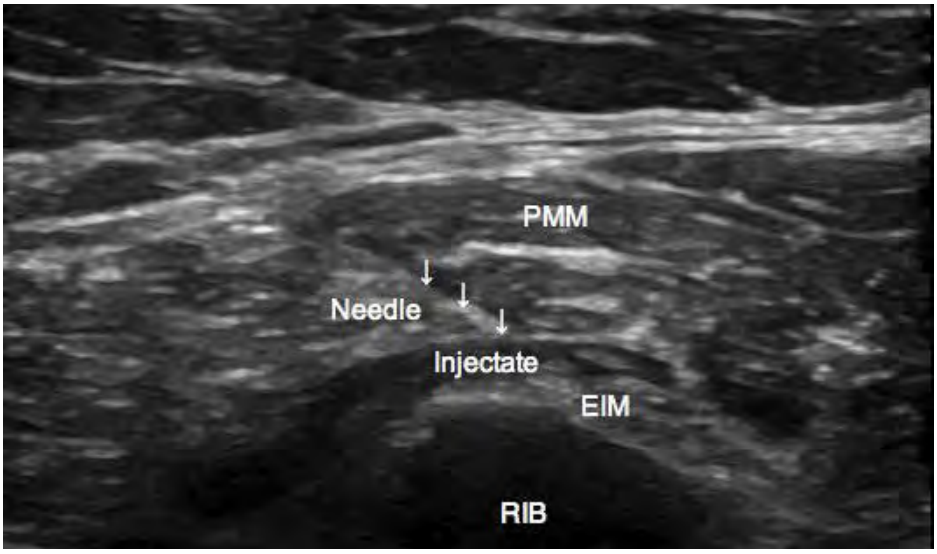

Figure 1: Spread of injectate within the PIFB plane between the pectoralis major muscle (PMM) and the external intercostal muscle (EIM). The needle is indicated by arrows.

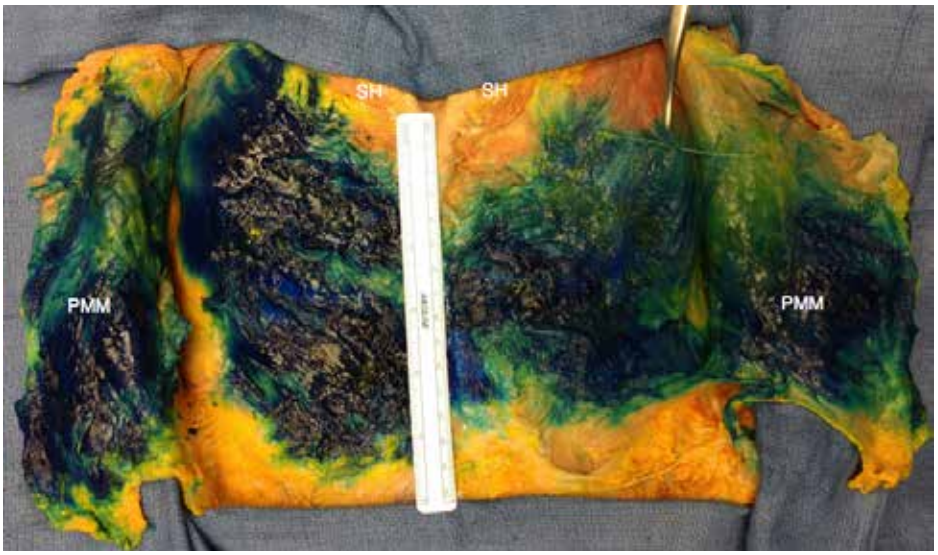

Figure 2: Dissection down to the PIF plane shows that the injectate spread throughout the PIF plane entirely, proving involvement of the anterior cutaneous branches of the intercostal nerve. Lateral spread of injectate is likely to involve the lateral cutaneous branch of the intercostal nerve as well. In this figure the pectoralis major muscle (PMM) is reflected bilaterally. A 12 cm ruler is placed in the midline over the sternum at the base of the sternal notch. The sternal head of the sternocleidomastoid muscles (SH) are indicated bilaterally.

METHODS

With the approval of the UAMS Institutional Review Board, five lightly embalmed cadavers were obtained from the Department of Anatomy. The cadavers were embalmed in house using the methods described by Anderson, stored at 4 degrees Celsius until the day of use, taken out the morning of the procedure and allowed to warm to room temperature for six-to-eight-8 hours.[8] Under ultrasound guidance, methylene blue dye was injected into the PIF plane of each hemi-chest wall of each cadaver for a total of 10 hemi-chest walls.

For each left-side hemi-chest wall, a single injection was performed at the level of the fourth rib, into which 20mL of dye was injected. For each right-side hemi-chest wall, two separate injections at the third and fifth ribs were performed; 10mL of dye was injected at each site. In total, each hemi-chest wall was injected with 20mL of dye.

A draped, linear-array NextGen LOGIQ e ultrasound transducer (GE Healthcare UK, Ltd., Chalfont, Buckinghamshire, UK) was used. The ultrasound probe was placed 2 cm laterally from the sternal border in the parasagittal plane, and the indicated rib was identified. A two-inch echogenic 20-gauge block needle (B. Braun Medical Inc., Bethlehem, PA, USA) was then advanced using an in-plane technique from cephalad to caudad starting at the superior border of the probe until the needle tip was seen between the pectoralis major muscle (PMM) and the external intercostal membrane (EIM). After a test dose of 1-2 mL of normal saline to confirm correct needle placement by hydrodissection, the indicated volume of blue dye (equal parts 0.25% methylene blue dye with normal saline) was injected through the needle. (Fig. 1) After the injection was complete, the injectate was allowed to settle for 20 minutes. An experienced anatomist then dissected the chest wall down to the PIF plane.

RESULTS

Dissection of the cadavers confirmed successful injection in nine of the 10 hemi-chest walls and showed that the dye spread entirely throughout the PIF plane (Fig. 2). One injection of a left hemi-chest wall failed due to incorrect needle-tip placement within the PMM. The mean single-injection (left side) maximal superior-inferior spread was 13.75 cm (standard deviation 2.10 cm). The mean double-injection (right side) maximal superior inferior spread was 16.63 cm (standard deviation 3.67 cm). The mean single-injection maximal lateral spread was 12 cm (standard deviation 2.16 cm). The mean double-injection maximal lateral spread was 12.25 cm (standard deviation 1.70 cm). The single-injection achieved a mean intercostal-space spread of 4.75 spaces (standard deviation 0.5 spaces). The double-injection achieved a mean intercostal-space spread of 5.75 spaces (standard deviation 1.22 spaces).

> Continued on page 66.

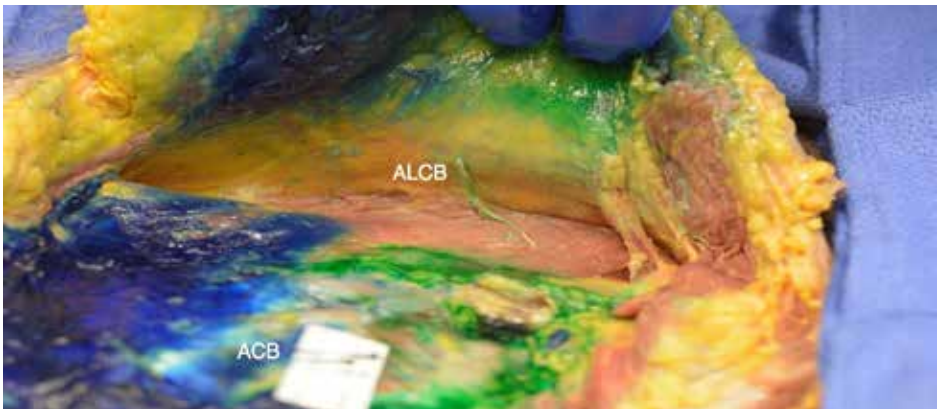

Figure 3: Dissection showing the anterior cutaneous branch of the intercostal nerve in the PIF plane. Lateral spread of the injectate has stained the anterior cutaneous nerve a green color.

DISCUSSION

This is the first anatomical study of the PIFB. There are two main findings of the study: first, the PIFB injectate spread effectively involves the anterior cutaneous branches of the intercostal nerves; and secondly, the PIFB spread approached the anterior border of the serratus anterior muscle to involve the lateral branches of the intercostal nerves as they emerge from the external intercostal muscles (Fig. 3). The hemi-chests that received the injections over the third and fifth ribs showed a larger injectate spread compared to the single injection at the fourth rib.

The layers of the thoracic chest wall from superficial to deep include skin, subcutaneous fat, pectoralis major muscle, anterior intercostal membrane, external intercostal muscle, internal intercostal muscle, and the innermost intercostal muscle. The intercostal nerves lie in the intercostal space deep to the internal intercostal muscle and superficial to the innermost intercostal muscle. As the trunk of the main intercostal nerve passes laterally around the thoracic wall, it divides into three branches. The main branch is the anterior cutaneous nerve, which runs inferior to the specified rib in the subcostal groove. The anterior cutaneous branch terminates after piercing the intercostal and pectoralis major muscles parasternally to supply the skin and sternum.

The collateral branch of the intercostal nerve runs in the inferior border of the intercostal space at the superior edge of the rib below. The collateral branch may rejoin the main nerve or end independently as an additional anterior cutaneous nerve. The last branch of the intercostal nerve is the lateral cutaneous branch. It begins roughly between the angle of the rib and the mid-axillary line and terminates after piercing the intercostal muscles and lateral thoracic wall obliquely to innervate the overlying skin.[9, 10] It is important to note that utilization of the PIFB will require diffusion of local anesthetic across an anterior, intercostal membrane and the external intercostal muscle before reaching the intercostal nerves.

> Continued on page 68.

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Limitations of this study included the use of lightly embalmed cadavers rather than fresh-frozen unembalmed cadavers, as post mortem changes may limit the spread of dye. Light embalming differs from standard embalming in that the embalming solution is weaker, a smaller volume of embalming fluid is used, and the fluid is not allowed to accumulate in the body under pressure. [11] This process has allowed lightly embalmed cadavers to consistently achieve satisfactory conditions for soft-tissue work. Research studies utilizing lightly embalmed cadavers range from routine regional dissection to the studies of nerves and blood vessels and even the ultrasound diagnosis of pneumothorax. The condition of tissue is close to that found in the living body, both in color and texture and is suitable for clinical procedural training. [11, 12]

Ultimately, injection of dye into the PIF plane of the lightly embalmed cadavers had a similar sonographic appearance to the injection of local anesthetic in vivo.

In conclusion, the dissection of the chest walls of lightly embalmed cadavers following the ultrasound-guided injection of the PIF plane has proven that injectate reliably spreads throughout the entire plane. The involvement of the anterior cutaneous branch of the intercostal nerve was consistent suggesting that reliable analgesia should be achieved for sternotomy pain.

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Tuesday, October 29, 2019, North Little Rock
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OBITUARIES

Siloam Springs - **Charles Harvey Stinnett, MD**, passed away June 14, 2019. Dr. Stinnett first attended the University of Arkansas in 1952 for agriculture, but with encouragement from Dr. Dickinson, his hometown doctor, and Fred Sharp, the pharmacist he worked for in high school, he switched to pre-med. He was admitted to the University of Arkansas College of Medicine in February 1955 during his junior year. He completed residency in 1961 and joined Drs. Huskins and Puckett in Siloam Springs, where he practiced medicine in for 44 years. Dr. Stinnett was a member of the National Guard from 1960 to 1968. He is survived by his wife, Barbara; his sons, Scott (Kelley) & Steve (Cindy); and his grandchildren.

Little Rock - **John Robert Stotts, MD**, passed away June 1, 2019. Dr. Stotts attended Hendrix College and went to pharmacy school in St. Louis. He joined the Army and was stationed at Dougway Proving Ground and later at the Pine Bluff Arsenal. Upon leaving the Army, he used the GI Bill to attend medical school at UAMS and worked as a pharmacist while earning his medical degree. Dr. Stotts built a family practice in the Heights area of Little Rock for 38 years. He also worked with Arkansas Teacher Retirement and the Arkansas Highway Department, reviewing medical charts. He was a football enthusiast who loved the Dallas Cowboys and the Razorbacks and was the team doctor for Pulaski Academy, Joe T. Robinson, and other Little Rock schools. He is survived by his daughter, Leslie Layton (Rick); son, Chris Stotts (Pamela); son-in-law, Todd Lamb; and several grandchildren.

Charleston, South Carolina - **Paul Harwood Millar Jr., MD**, passed away July 12, 2019, at MUSC Hospital in Charleston, SC. After graduating from Little Rock High School, he joined the U.S. Navy, trained to become a radioman, and served on the USS Rixey during World War II. Upon discharge from the service, he attended Hendrix College, where he completed the prerequisites for entry into medical school at UAMS. He graduated from medical school in 1951, interned at the University of Iowa, and completed his surgical residency at UAMS. Dr. Millar was legendary in Arkansas County as a brilliant and tireless surgeon. When he retired in 1994, he had performed 18,210 surgical operations at Stuttgart Memorial Hospital. Dr. Millar was preceded in death by his wife and his son, John Paul Millar. He is survived by his sister, Elizabeth Millar Rush; his daughters, Susan Millar Williams (Dwight) and Cathy Woods (Tom); his daughter-in-law, Anne Millar Williams (Chuck); and his grandchildren. AMS

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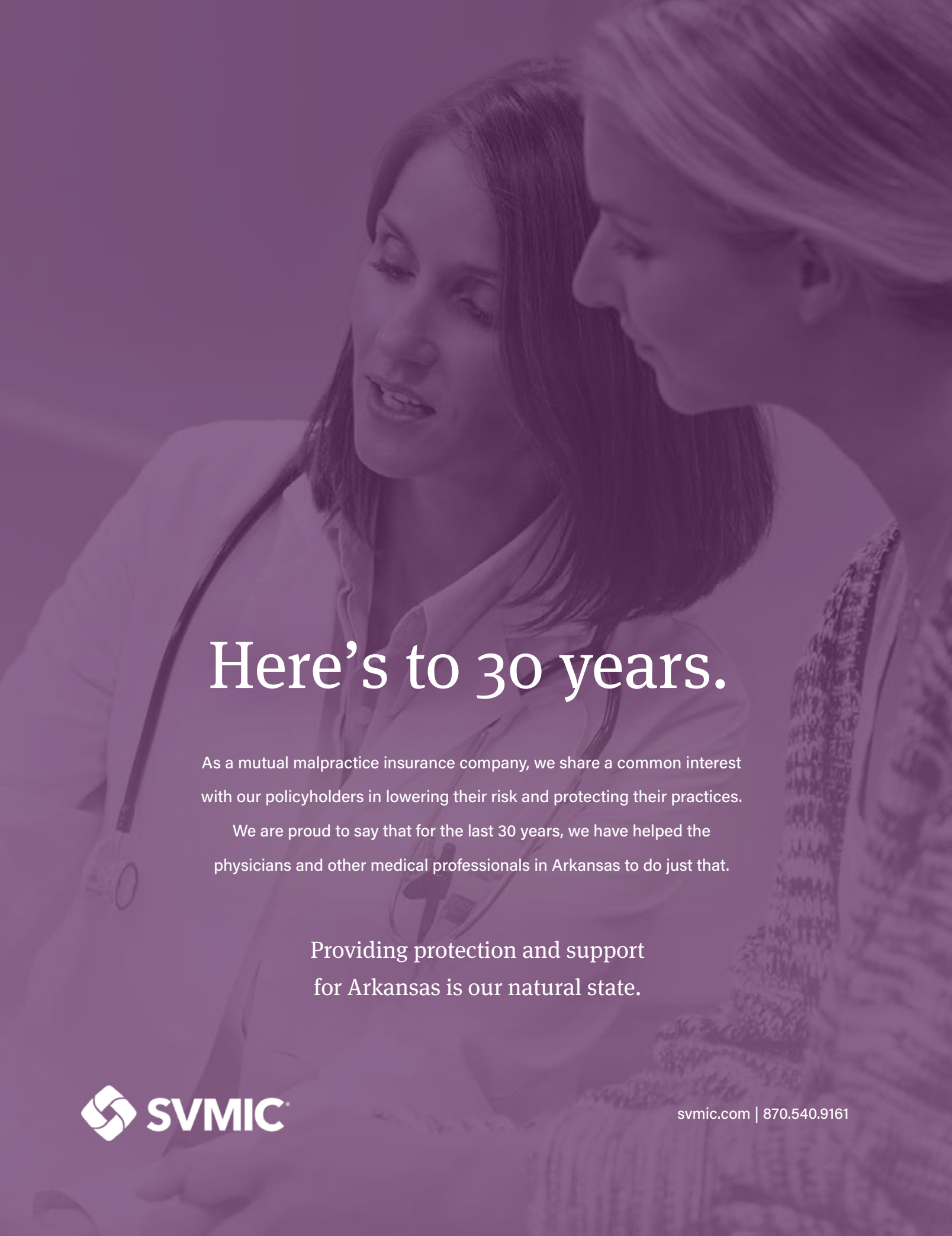

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