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The Journal of the Missouri State Medical Association www.msma.org/missouri-medicine September/October 2017



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Missouri Medicine

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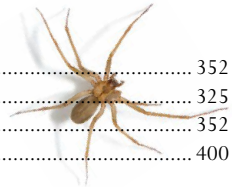
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Gallows-humor? Docs don't like the hang of it!

"Bad Medicine" Newspaper Beat Draws Rapid National Condemnation

by John C. Hagan, III, MD



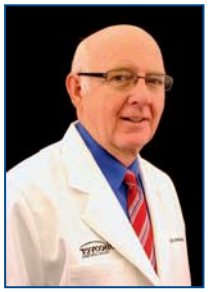
"*Kansas City Star* reporters are being given new assignments as part of parent company McClatchy Inc.'s "reinvention" of newsrooms across the newspaper chain. **The health beat has been transformed into the "bad medicine" beat……"**[1] *(emphasis added)*

-KCUR 89.3 radio website 8/21/2017 Dan Margolies Health News Editor

SPOILER ALERT!

For those of you who think like journalists at McClatchy Communications/*Kansas City Star* ('the *Star*') that good news is no news and adding dirt will never hurt, e.g., "Is Your Doctor Struggling with Addiction?" (9/16/17) and "Privacy of Medical Records is at Higher Risk in Missouri," (9/2/17)……This story has a happy ending.

The outraged emails started to pile up in my inbox shortly after the Margolies' "bad medicine" article appeared on the KCUR (KCUR 89.3 radio) website. To distill them down to their essence: this is inexcusable even for the Star. Don't let them get away with this pejorative "bad medicine" moniker. I decided to take these as marching orders from both members of MSMA and the Kansas City Medical Society (KCMS) on whose Board I serve.



John C. Hagan, III, MD, FACS, FAAO, MSMA member since 1975, is a Kansas City, Missouri, ophthalmologist and *Missouri Medicine* Editor since 2000. He is a multi-year Super Diamond Contributor to MMPAC.
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Many thanks to the leadership of these "good medicine" organizations for your prompt and effective responses. It was unprecedented. Here's hoping that similarly united, we will move forward on other substantive problems that face medicine and the health care professions.

As a responsible journalist, I read the article in its entirety several times. I noted that Margolies had attempted to contact two members of the *Star*'s leadership for confirmation but his calls were not returned. I emailed the *Star*'s leadership to ask if "bad medicine" was the new header for all health care news or a formal/informal designation of the direction their reporting would be taking? The *Star* response was the Margolies' story was vindictive, inaccurate, misleading and, "*We will hold those accountable where needed but our focus remains on keeping the community informed.*" Several follow-ups to *Star*/McClatchy leadership did not elicit any denials of the use of "bad medicine" for health care investigative reporting within their organization.

Also contacted confidentially were people working at the *Star,* and yes, they had heard the offensive term used to describe the work being done by *Star* reporters now covering health care. It was also obvious that at my paygrade the *Star* felt no further explanation was necessary. The Margolies' column was forwarded to Kansas City, Missouri, Kansas, and national health care organizations. What would be their read of the column and our profession being reported on as "bad medicine?"

I have been active in organized medicine in Missouri for 42 years and in this time, I have not seen such a rapid and effective response as occurred over the next two weeks. The *Star* and their owners at McClatchy Communications (Sacramento, Calif.) received letters of concern and objection from: The American Medical Association, The American College of Surgeons, The American Academy of Ophthalmology, The Missouri State Medical Association, The Kansas Medical Society, The Kansas City Medical Society, The St. Louis Metropolitan Medical Society, The Missouri Society of Eye Physicians & Surgeons, and The Greene County Medical Society. Other state and national organizations were also gearing up to respond.

After this glorious hue and cry, I then received an email from upper management at McClatchy Communications stating that "*I understand that you're concerned about the phrase "bad medicine," and I understand why you'd find that concerning. So I want to take a moment to explain. "Bad medicine" is a gallows-humor, shorthand way of referring to a beat that I think we can all agree is incredibly important: accountability in health care.*" I'm not an orthopedic surgeon but I know a lame excuse when I see it.

Subsequent conversations with the *Star* indicated that while no public apology will be issued they are no longer using "bad medicine" as an internal designation for dishing the dirt on health care. "We've learned our lesson" as one chastened, exasperated *Star* pooh-bah told me.

Many thanks to the leadership of these "good medicine" organizations for your prompt and effective responses. It was unprecedented. Here's hoping that similarly united, we will move forward on other substantive problems that face medicine and the health care professions.

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1. http://kcur.org/post/three-kc-star-veterans-accept-buyouts-newsroom-reinvention-gets-underway

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Is Marijuana Use for Pain Driving Negative Societal Effects?

by Kenneth Finn, MD

The problem of increased marijuana use has origin in its purported use for pain, but the medical literature is completely void of evidence for the treatment.

Pain is the most common diagnosis associated with marijuana being recommended for medical use[1]. With more states moving towards accepting marijuana use for medical purposes, there is a call from the medical and scientific community for more research and evidence that it actually works for common pain conditions.

Out of the top 20 medical diagnoses presenting to the primary care physician nationally, there are only three that are associated with a painful condition:[2] spinal disorders (i.e., lower back pain), arthropathies and related disorders (i.e., knee arthritis), and abdominal pain. There were no other pain diagnoses in the top 20 diagnoses that present to the primary care physician for treatment, including cancer pain or neuropathic pain.

What does the medical literature tell us about the use of marijuana for pain? In 2011, *The British Journal of Pharmacology* released a paper looking at the use for cannabinoids for the treatment of chronic non-cancer pain.[3] They narrowed a broad literature review to only 18 trials with a total of 925 participants. Most of the trials studied neuropathic pain (72%), including HIV neuropathy and multiple sclerosis related neuropathy (three trials), with single studies looking at arthritis and chronic spinal pain.



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There were four studies that looked at smoked cannabis and neuropathic pain only. Six studies evaluated synthetic cannabinoids (Dronabinol, Nabilione) for pain (off-label use).

From these trials, the average number of patients was 49 with average duration of 22 days, some of which were one week long. Despite their conclusion that cannabinoids may help for chronic non-cancer pain, they noted study limitations of small sample size, modest effects, and the need for larger trials of longer duration to determine safety and efficacy.

In 2015, the *Journal of the American Medical Association* (*JAMA*) released an article on cannabinoids for medical use.[4] Chronic pain was assessed in 28 studies, involving 63 reports and 2,454 participants. Thirteen studies evaluated nabiximols (not available in the United States), four smoked THC, six synthetic THC, three oromucosal spray, one oral THC, and one vaporized cannabis. The majority of studies looked at some form of neuropathic pain or cancer pain. Two studies were at low risk of bias, nine at unclear risk, and 17 at high risk. Studies generally suggested improvements in pain measures associated with cannabinoids but did not reach statistical significance in most individual studies. Despite these difficulties, the authors concluded there was moderate-quality evidence to suggest that cannabinoids may be beneficial for the treatment of chronic neuropathic or cancer pain (smoked THC and nabiximols). Note these are less common pain conditions presentimg to the physician for treatment nationally. The authors noted an increased risk of short-term adverse effects with cannabinoid use, including some serious adverse effects. Common adverse effects included asthenia, balance problems, confusion, dizziness, disorientation, diarrhea, euphoria, drowsiness, dry mouth, fatigue, hallucination, nausea, somnolence, and vomiting.

In 2017, the National Academies of Science, Engineering, and Medicine released a paper on the health effects of cannabis and cannabinoids.[5] It may be important to note that none of the authors had a background in Anesthesia or Pain Medicine. The authors felt the referenced *JAMA* article was the most comprehensive and that the medical condition most often associated with chronic pain in that article was neuropathy, and a majority of studies evaluated treatment with nabiximols, which are not available in the United States. The committee found that only a handful of studies evaluated the use of cannabis and that many of the cannabis products sold in state regulated markets bear little resemblance to the products available for research at the federal level in the United States. They also note that very little is known regarding efficacy, dose, routes of administration, or side effects of commonly used and commercially available products in the U.S. Despite this, they concluded that "cannabis is an effective treatment for chronic pain in adults."

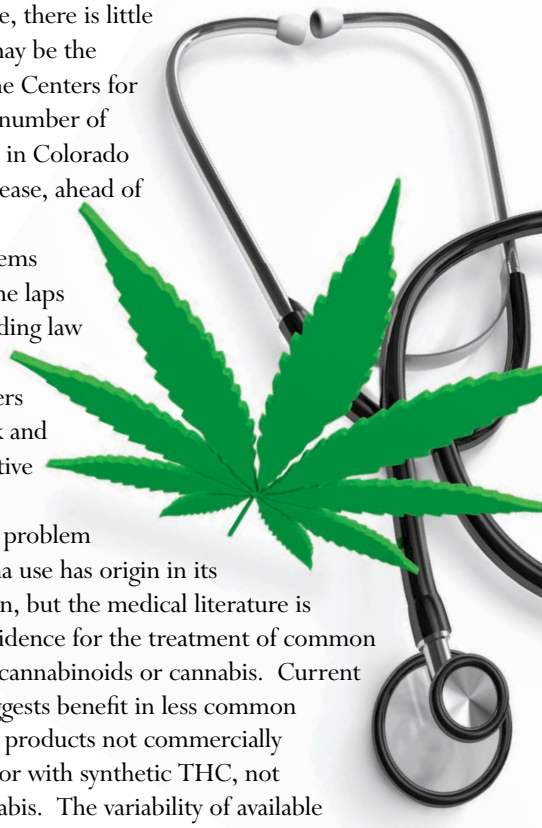
The above noted papers demonstrate the limited data available to the public and medical community, and represent the only information available regarding treatment of pain with marijuana. Despite that, the public has embraced that marijuana can treat all pain conditions, and state governments have followed suit, without scientific evidence, and have allowed an industry to prosper on the thin ice of what is currently and scientifically available.

It is important to understand that pain covers a broad spectrum of disorders and pain of different origins does not necessarily respond the same to different medications. Additionally, dispensary cannabis is considered a generic substance without defined or accepted dosing guidelines, and will vary in purity as well as potency. It may also contain hundreds of other compounds, some of which may have physiologic activity. Cannabinoids are purified components of the plant which have been isolated in a laboratory and have more scientific foundation, but are currently not available for study or use in pain conditions in the U.S.

Since *de facto* legalization in Colorado in 2009, there has been a significant increase in public health and safety concerns, which include utilization of the health care system, an increase in adolescent substance use treatment for cannabis, and an increase in marijuana-related driving fatalities.[6] The addiction rates are reportedly 9% in the adult and roughly 18% in the adolescent, which was based on the potency of marijuana from nearly 20 years ago. The potency has significantly increased in the past five years alone, so we are now in uncharted waters and unable to predict the long-term effects or addiction rates of currently available, highly potent products, with variable delivery systems.

As the number of medical marijuana patients increased in Colorado, there appeared to be a parallel increase in the number of adolescents needing substance use treatment, most often for cannabis. Colorado is now contending with a huge opioid and heroin epidemic, and despite the widespread availability of Narcan, does not appear to have leveled off or curbed the number of opioid or heroin deaths in the state which continue to rise.[7]

Although the concept of using marijuana to decrease opioid use is attractive, there is little data to suggest that may be the case. According to the Centers for Disease Control, the number of drug overdose deaths in Colorado has continued to increase, ahead of the national average.[8]



The above problems are now falling into the laps of other groups including law enforcement and mental health providers who are pushing back and straining their respective resources.

In summary, the problem of increased marijuana use has origin in its purported use for pain, but the medical literature is completely void of evidence for the treatment of common pain conditions with cannabinoids or cannabis. Current medical literature suggests benefit in less common pain conditions, with products not commercially available in the U.S., or with synthetic THC, not with dispensary cannabis. The variability of available products changes regularly and their use in medicine, particularly pain, is unproven. The end game is in the court of law enforcement, mental health providers, the medical community, and our educational systems, at unknown societal costs, which are only now becoming apparent.

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MM

THE LAST WORD

PRO CON

Should Missouri Have a Statewide Prescription Drug Monitoring Program?

In the July/August 2017 issue of *Missouri Medicine*, MSMA members Sam Page, MD, St. Louis, and John Lilly, DO, Springfield,discussed the pros and cons of a Prescription Drug Monitoring Program in Missouri. What follows is The Last Word.

THE LAST WORD

PRO

The Case for a PDMP in Missouri

by Sam L. Page, Jr., MD

The PDMP is not a panacea. It is one tool against a formidable problem. Doctor shopping is only one of the reasons for a PDMP. It is primarily designed to be sure that we do not accidentally over-prescribe, that we have a sense of the frequency of medication prescriptions from other providers, and to be sure that we do not inadvertently under-prescribe when faced with a patient we do not know well. In most states PDMPs are not designed as law enforcement tools. They are treated as protected health information resource for prescribers.



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Dr. Lilly rightly describes the alarming increase in opioid-related deaths occurring in the United States. The recent rise has been due to illegal sales of fentanyl and similar drugs. A PDMP has no effect on illegal drugs. However, a PDMP can help me to recognize problem use of prescription medication earlier for my patients. This helps me to ask if I have inadequately treated their pain and need to use other supplemental modalities. I can work to get them treatment if they are truly misusing pain medications. I have a tool to take good care of my elderly patients who don't always remember what medications they have been given by other doctors. A PDMP helps with all of these.

No matter what choice is made in Missouri, we must pledge to police our own prescribing habits and avoid introduction of opioids to naive patients whenever possible, use OTC medications and non-pharmacological therapies where we can, and prescribe the shortest and least intense form of opioids whenever possible. At the end of the discussion, Dr. Lilly and I want the same thing: the best practice of medicine possible in service of our patients and our community.

THE LAST WORD

CON

Prescription Drug Monitoring Program: Useful Tool or Government Control?

by John D. Lilly, DO

There are just two questions to ask about any government run program. First, is it a proper function of government that adheres to the Constitution? Second, does it work? The PDMP fails on both counts. It clearly violates Article I, Section 15 of the Missouri Constitution. The covered prescriptions that you give to the pharmacy go into a mandatory, involuntary database which is an illegal search and seizure of your property. As I proved in my original column, the PDMPs have not reduced the death rate, so they fail the second test.

If the government has a database, it will find a way mine it for information. In 2016, Scripps News found during a five-month investigation that law enforcement tapped into at least 344,921 prescription histories of Americans between 2014-2015 in the states that don't require a warrant or another form of court authorization. That is more than six times the number of searches that took place by law enforcement in states that have more privacy safeguards enacted.[1]

Dr. Page ended his column with, "We are both entrusted with and empowered to work for the safety and well being of the good people of Missouri." If this is for the safety of the citizens, then why stop at Schedule IV? Why not put all prescriptions in a database? If this is for safety's sake, why don't we let the Board of Healing Arts randomly search our patient files looking for improper treatment? If you are doing everything correctly, you have nothing to hide. Why not put all of the physician's scheduled prescriptions in a database and search for improper prescribing habits? Oh wait, that's the function of Gov. Greiten's PDMP. Now it doesn't look so good, does it? For safety's sake, let the police randomly stop vehicles to search them for anything illegal. For safety's sake, let the military randomly search our homes. That is what the British soldiers did to the colonists to make sure they had the proper "stamp" on their documents which sparked a rebellion (1765 Stamp Act). The "safety" argument always leads to a slippery slope which ends in expanded government control and the loss of personal liberty.



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1. Scripps News investigation led by Mark Greenblatt, senior national investigative correspondent, and Angela M. Hill, national investigative producer. http://www.thedenverchannel.com/longform/so-you-think-prescriptions-are-private



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À la recherche du temps perdu: Smoking and Genomic Imprinting

by Joel C. Eissenberg, PhD

Abstract

Tobacco smoking is the largest cause of preventable mortality and morbidity in the United States. Many of the pathological consequences of smoking result from mutations, but gene expression can also be modulated by genomic imprinting mediated by DNA methylation—so-called "epigenetic" regulation. Since genomic imprints, unlike gene mutations, can be reversed, it is of great interest what smoking-related imprints mean for smoking-related pathologies in smokers and their children, and the potential for imprint-targeted diagnostics and therapeutics.

Physiological Toll of Smoking

The practice of smoking tobacco leaves originated in Central or South America ca. 5,000 years ago.[1] It found its way to Europe in the 16th century, from where it rapidly spread around the world. Cigarettes—in which the tobacco is wrapped in paper for smoking—appear to have been invented in the 17th century.

While tobacco smoking was attacked and banned in some cultures, the evidence for its harmful physiological effects only gradually emerged. One of the signature pathologies associated with smoking is lung cancer, a disease that was rare prior to 1900, at which point only 140 case descriptions had been published.[2] Other medical conditions linked to smoking include cardiovascular disease, chronic obstructive pulmonary disease and osteoporosis.[3] In the U.S., the combination of cessation campaigns and legislative actions have led to a decline in smoking; there are now more former smokers than current smokers in the U.S..[4]



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Genomic Imprinting and Gene Regulation

For the purposes of this review, "genomic imprinting" refers to the inheritance of traits independent of classical Mendelian mechanisms. This mode of inheritance is also called "epigenetic." While the mechanism of epigenetic inheritance can vary for different genes, my focus will be on DNA methylation as an epigenetic mark. Specifically, the methylation of cytosine bases that immediately precede guanine bases (CpG) in the DNA sequence are usually associated with silencing of nearby genes. Thus, the gain or loss of DNA methylation can change gene expression in cells and can be stably transmitted during cell division and, in some cases, from generation to generation.

Methylation of DNA is catalyzed by two classes of methyltransferase enzymes. One class, the "*de novo*" methyltransferases, is capable of adding methyl groups at positions that were not previously methylated, thereby creating novel possibilities for gene regulation. The other class, the "maintenance" methyltransferases, only replace methyl groups at positions that were previously methylated but where new unmethylated DNA was recently laid down as part of DNA replication during cell proliferation. On the other side of the ledger, methylated cytosines in DNA may be lost passively by DNA replication when the maintenance methylases fail to restore methylation. Alternatively, a recently discovered mechanism of "active" demethylation targets specific methyl groups for chemical modification and elimination. The mechanisms of methylation and active demethylation are cartooned in Figure 1.

In humans, methylation patterns in the genome are established by early in embryogenesis, and with few exceptions are stably maintained through the rest of life. Genome-wide DNA methylation profiling finds higher variability between dizygotic twin pairs than between monozygotic twin pairs, demonstrating that genomic imprinting patterns are substantially genetically determined.[5] Nevertheless, the mitotic stability of cytosine methyl marks is lower than the stability of the underlying DNA sequence by a factor of 10-100.[6] This lability may make DNA methylation more vulnerable to modification as a result of environmental insults such as smoking.

Tobacco Smoke as a Genetic Mutagen

Like most combustion products, tobacco smoke contains a variety of chemicals that cause chemical changes in DNA structure leading to cancer (Table 1). The combustion products of burning tobacco includes chemicals that attach themselves directly to cellular DNA, interfering with accurate DNA replication and causing mutations that can lead to cancer.[7-10] In addition, tissue damage and inflammation in the lungs and elsewhere caused by smoking stimulates cell proliferation. Every time a cell divides, it makes a few mistakes in copying its DNA, so increased cell division is itself mutagenic. While the role of genetic mutation as a driver of cancer is well-established, the contribution of genomic imprinting and the mechanistic connection between smoking, DNA methylation and cancer is less clear.

Is Tobacco Smoke an Epigenetic Mutagen?

A growing body of literature supports a link between cigarette smoking and distinctive DNA methylation patterns.[11-14] Given (1) the broad physiological impact of sustained smoking and (2) that modifications in gene expression underlie these physiological changes, it should not be surprising to find changes in DNA methylation at specific genes. By analogy to genetic mutations caused by tobacco smoke, could smoking also produce "epimutations" that drive cancer and/or other smoking-associated pathologies? Or are changes in methylation status at particular genes a reflection of underlying genetic mutations and/or changes in transcriptional status of those genes driven by cell signaling?

Smoking and Fetal Programming

The "fetal programming hypothesis" holds that certain disease conditions are the result of fetal adaptations to adverse gestational conditions, and that these result in permanent, life-long changes in the body that predispose to cardiovascular, metabolic, and renal diseases.[15-17] Fetal exposure to alcohol has well-established pathological effects on development that result in permanent cognitive impairment.[18] Less well characterized is the impact of maternal smoking. In 2014, 8.4% of women smoked sometime during pregnancy.[19] There is a strong association between maternal smoking during pregnancy and elevated risk for a variety of peri- and post-natal outcomes (Table 2). Maternal smoking during pregnancy is associated with lifelong decreases

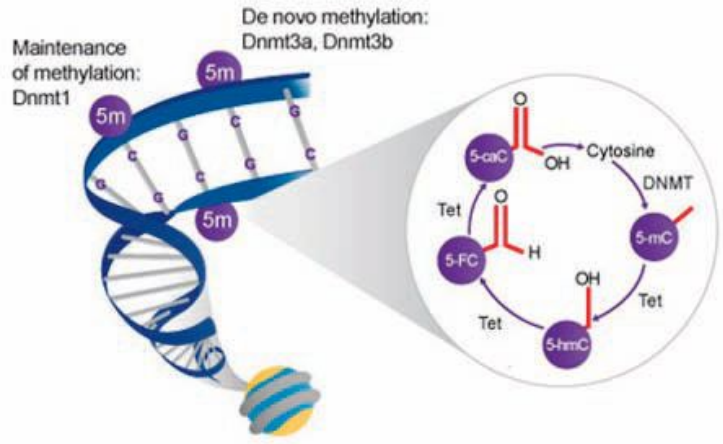


Figure 1
DNA methylation and demethylation overview
DNA demethylation involves the successive oxidation of 5-mC to 5-hydroxymethyl- (5-hmC), 5-formyl- (5-fC) and 5-carboxy- (5-caC) cytosine in a process that involves the Tet family of enzymes. A glycosylase of the base excision repair (BER) pathway, TDG, was also recently found to be involved in an alternative demethylation pathway, where it can repair the 5-hydroxymethyluracil which can result from deamination of 5-hmC.
From: http://a.static-abcam.com/CmsMedia/Media/dna-methylation-and-demethylation-1.jpg

Table 1.
The most genotoxic cancer causing chemicals in cigarette smoke

Compound	Micrograms per cigarette	Effect on DNA	Reference
Acrolein	122.4	Reacts with deoxyguanosine and forms DNA crosslinks, DNA-protein crosslinks and DNA adducts	33
Formaldehyde	60.5	DNA-protein crosslinks causing chromosome deletions and re-arrangements	34
Acrylonitrile	29.3	Oxidative stress causing increased 8-oxo-2'-deoxyguanosine	35
1,3-butadiene	105.0	Global loss of DNA methylation (an epigenetic effect) as well as DNA adducts	36
Acetaldehyde	1448.0	Reacts with deoxyguanine to form DNA adducts	37
Ethylene oxide	7.0	Hydroxyethyl DNA adducts with adenine and guanine	38
Isoprene	952.0	Single and double strand breaks in DNA	39

From: https://en.wikipedia.org/wiki/Tobacco_smoking

Table 2
Risks associated with tobacco smoke exposure in utero

Indication	references
Low birth rate	40
Pre-term delivery	40
Infant mortality	40
Decreased pulmonary function	20; 41, 42
Increased childhood asthma	21; 28; 41-43
Impaired fetal brain development	44-47
Immune system abnormalities	48
Obesity	49-53
Cardiometabolic disease	49

in pulmonary function and increased risk of asthma in offspring.[20,21] The mechanism by which maternal smoking affects later development remains unclear, but attention has turned to epigenetic changes in the fetus and placenta as contributory factors.

Genome-wide surveys of DNA methylation sites in 1,062 newborn cord blood samples identified four genes that showed methylation differences associated with maternal smoking during pregnancy.[22] One of the four genes is the aryl hydrocarbon receptor repressor (AHRR), which participates in detoxification of chemicals in tobacco smoke. A similar association of smoking with reduced AHRR methylation has been reported in blood cells and alveolar macrophages.[23-26] However, the physiological significance of this smoking-associated epigenetic change for the newborn remains unclear. Nicotine has negative effects on brain development mediated by acetocholine nicotine receptors in the fetal brain. While this pathway may also reprogram genomic imprints, the ways in which receptor signaling might drive DNA modification remain unknown.

The case for an epigenetic mechanism would be strengthened if paternal smoking were also shown to be associated with pathology in offspring, since the father contributes only DNA. In a survey of 1,456 Scottish Caucasian families consisting of 2,912 parents with 2,308 biological offspring (1,025 sons, 1,283 daughters), Han et al.[27] found: (1) maternal smoking history was associated with increased risk of metabolic syndrome in sons but not in daughters, while paternal smoking history was not associated with metabolic syndrome in offspring of either sex; (2) increased risk of high BMI ≥25 kg/m^2 was observed in sons, but not in daughters, if either fathers or similarly mothers smoked; (3) increased risk of high waist circumference above action level 1 (men 94 cm, women 80 cm) was associated with maternal smoking, both in sons and in daughters, but offspring waist circumference was not significantly correlated with paternal smoking; and (4) no associations were observed between maternal/parental smoking history and offspring blood pressure, lipids, diabetes or stroke. Thus, the evidence suggests at best a limited role for paternal smoking in metabolic disorders of their children, offering little support for the operation of epigenetic mechanisms.

Remarkably, there is evidence that grandchildren of smokers have increased risk for smoking-related pathology. Children of mothers who had experienced *in utero* exposure to maternal smoking have been shown to have an increased risk of developing asthma even if the child had not been exposed to maternal smoking *in utero*.[28] Note that this study controlled for secondhand smoke exposure as well. While the mechanism by which such multigenerational effects are transmitted remains unknown, smoking-dependent genomic imprinting remains a possibility.

Can Epigenetic Changes Associated With Smoking be Prevented or Reversed?

The physiological benefits of smoking cessation are well known and accumulate over time after quitting (Figure 2). Do the reversals of smoking's effects after quitting include restoring epigenetic modifications to non-smoking patterns, or is there an "imprint" of smoking encoded in DNA methylation? A genome-wide survey of methylation sites in the peripheral blood comparing smokers/ex-smokers to non-smokers indicated that the differences in methylation seen in smokers were partially reversed by three months after cessation.[12] A later study reported that the majority of the differentially methylated sites in current smokers compared to those who never smoked returned to the level of never smokers within five years of smoking cessation.[14]

A study of 35 subjects who reduced or stopped smoking over a six-month period showed a trend towards the restoration of normal (nonsmoking) methylation at the AHRR locus.[25] As noted above, AHRR encodes the aryl hydrocarbon receptor that participates in detoxification of chemicals in tobacco smoke. Increased methylation and decreased expression of AHRR would be expected as demand for detoxification diminished, although the methylation increase could be a byproduct of decreased AHRR



Figure 2
The benefits of quitting smoking accumulate over time.
https://i.pinimg.com/originals/8a/db/0b/8adb0b7057c7c3eee260543b622289a7.jpg

expression rather than a cause. Regardless, this study suggests that AHRR methylation status could serve as a quantitative marker for progress in smoking cessation.

Interestingly, 500 mg of daily vitamin C supplements starting at ≤ 22 weeks of gestation given to women who continued to smoke during pregnancy was associated with improved newborn pulmonary function and decreased incidence of wheeze through the first year of infancy.[29] A recent study found that maternal supplementation with vitamin C during pregnancy was associated with a reduction or reversal in smoking-related genome methylation imprints.[30] While the mechanism of the vitamin C effect is unknown, vitamin C is known as an essential cofactor for the teneleven translocation (TET) enzyme family that catalyzes DNA demethylation.[31] This suggests that vitamin C and potentially other interventions could be used to blunt the long-term consequences of *in utero* smoking exposure.

Genomic Imprinting and Smoking: Correlation or Causation?

While the intriguing correlations between genomic imprinting and smoking continue to multiply, the significance of these correlations remain in question. Are changes in imprinting patterns that accompany smoking a byproduct of physiological responses to smoking? If so, they are useful as biomarkers for mechanisms leading to pathology and in tracking recovery after cessation. Or are smoking-related changes in genomic imprinting themselves drivers of pathological responses? If that is the case, therapy aimed at attenuating and/or reversing such epigenetic marks could mitigate the personal and societal costs of smoking.

In other cases that have been studied in detail, many reported correlations between gene expression and DNA methylation are probably a byproduct of gene activation and not the cause of activation.[30] Surprisingly, demethylation has little effect on the expression of most genes.[32] Thus, for any genomic imprint associated with smoking, it is far from clear that the imprint is a driver for disease or dependency. Of course, this doesn't diminish the value of such imprints as diagnostic tools.

It is currently unknown whether any smoking-associated genomic imprints are associated with tobacco addiction. If this were the case, and more importantly, if the imprints were mechanistic drivers of addiction and not merely markers, this could lead to imprint-targeted pharmacology aimed at promoting the best outcome—smoking cessation.

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Disclosure

None reported.

MM

E-Cigarettes: Current Evidence and Policy

by Kate Lichtenberg, DO

For now, the evidence does not support recommending e-cigarettes over FDA-approved smoking cessation treatments.



History of Electronic Cigarettes

The Surgeon General's landmark report on smoking and tobacco celebrated its 50th anniversary in 2014. Since its release, there have been great advances in reducing the rates of smoking. A recent analysis has quantified the effect of tobacco prevention and control interventions since the release of that report. It is estimated that eight million premature deaths have been averted and 175 million years of life have been saved over the last half century as a result of those interventions. Yet, tobacco use continues to cause 443,000 premature deaths a year and $96.8 billion in productivity losses in the United States alone. Health care spending on smoking-attributable illnesses accounts for 5-14% of total health costs in this country.[1]

The first electronic cigarettes (e-cigarettes) were developed in 1965 and were patented in 2003. They were introduced in North America in 2007. Since then, multiple versions have been developed, and it is estimated that there are more than 400 different brand names available on the market. E-liquids are now available in more than 7,000 unique flavors, including kid-friendly flavors like cherry, bubblegum, and chocolate. E-liquids contain nicotine along with flavorings, propylene glycol, glycerin, and other ingredients. The liquid is heated by the device and aerosolized for inhalation. The vapor has been shown to contain lead, cadmium, nickel, formaldehyde, and hydrocarbons, among other chemicals.[2,3]

Several sources estimate that 30-50% of e-cigarette sales occur over the internet.[4] Until the FDA announced in April 2016 that it would begin regulating e-cigarettes and its component parts, there had been no regulation of the devices or the liquid. There was no way for the consumer to know how much nicotine they were inhaling or what other chemicals might be in the e-liquid they were utilizing. Once the new rules are fully enacted, packages will be required to list what the product contains.

Prevalence

Recent epidemiologic surveys estimate e-cigs are the most commonly used tobacco product in U.S. adolescents in the past 30 days at 13.4%. This is followed by hookah, traditional cigarettes, and cigars.[5] In 2014, there were an estimated 2.46 million middle and high school students that used e-cigarettes. The rate rose to more than three million in 2015. Availability of appealing flavors was the primary reason for use in 81% of current youth e-cigarette users.[6]

Between 2011 and 2015, e-cigarette use rose 900% among high school students.[7] These products are now the most commonly used form of tobacco among U.S. youth.



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Missouri Prisons Go Smoke-Free

A recent federal court decision has ordered the Missouri prison system to go smoke-free on or before April 1, 2018. The case was brought by an asthmatic inmate who was paired with cellmates who smoked. Although indoor smoking has already been prohibited inside the state's prisons, the rule was commonly violated. Missouri now joins the majority of other state prison systems in banning smoking. The federal prison system also prohibits smoking.



At least 21% of US adults use tobacco products occasionally. In 2014, an estimated 4% of U.S. adults used e-cigarettes every day or some days. Many of them are dual users of both regular tobacco cigarettes and e-cigarettes. Up to 52% of cigarette smokers also used e-cigarettes in an attempt to lower their cigarette consumption or as a cessation aid. This increases the risk of potential nicotine overdose and toxicity.[8]

Costs

Sales were expected to exceed more than $3.5 billion in 2015 in the United States.[9] A pack of name-brand cigarettes in Missouri runs approximately $5.50. E-cigarette devices start at $10 and can run upwards of $100. Disposable devices are less expensive, but even rechargeable devices may need to be replaced periodically. A pack of flavor cartridges or a refill tank of e-liquid costs $10-15 and may last as long as 150 cigarettes. A pack a day smoker might spend $2,000 per year on cigarettes, but if using a mid-range priced e-cigarette ($20) and a refill tank a week ($15), that cost could be just $800 per year.[3]

Missouri continues to have the lowest cigarette tax in the nation, so annual costs would vary based on the state tax rates.

Smoking Cessation Aid or Gateway to Other Drugs?

Proponents of e-cigarettes tout their value as cessation aids, although evidence supporting this is lacking. A review of e-cigarettes commissioned by Public Health England (an executive agency in the United Kingdom's Department of Health) published its review in 2015 declaring vaping is at least 95% safer than smoking.[10] This statement is being used in marketing campaigns in the U.S. and billboards proclaiming this have been seen along Missouri interstates.[11]

E-cigarette use is strongly associated with the use of other tobacco products in youth and young adults.[7] Advertising may also be "re-normalizing" nicotine addiction. In addition to the advertising, the media and social influences play important roles in teens' experimentation with "vaping."[3]

There has been great interest in e-cigarettes over the past seven years, and much research has been conducted. Many studies have looked at the chemical components of the e-liquid and others at use patterns. There have few randomized, controlled studies looking at e-cigarettes as cessation aids. To date, the evidence has shown

that e-cigarettes may be as effective as other forms of nicotine replacement, but only the e-cigarettes require the user to inhale nicotine along with other chemicals. No studies have demonstrated e-cigarettes to be safer or more effective than any currently FDA-approved smoking cessation treatment.[12,13,14,15,16]

The lack of studies documenting potential harms of e-cigarette use has led to a perceived safety of the devices. Advertising campaigns have promoted e-cigarettes as safer alternatives when it comes to cardiac and lung disease. Analyses have shown that the vapor exhaled by users contains variable levels of formaldehyde, acetaldehyde, isoprene, acetone, propylene glycol, and nicotine in the air. It is unknown if the ultra-fine particles of the vapor affect indoor air quality or have the same effects as tobacco second hand smoke. Because of the relative newness of e-cigarettes, there is very little information on long-term effects and safety, especially among chronic users.[15]

Calls to poison control centers continue to concern public health experts. Nationally, from January 1 to October 31, 2016, there have been 1,292 exposures (ingestion, inhalation, absorption) to liquid nicotine across all age groups. Not all exposures have resulted in overdoses or poisonings, but there have been a number of children who have required emergent care.[17] In 2014, more than half of all reported exposures occurred in children under the age of six. A one-year old child died in late 2014 as the result of liquid nicotine ingestion.[3]

Other health concerns related to e-cigarettes include explosions due to malfunctioning batteries leading to thermal injuries of the face and hands. Some of these have been extensive. No safe levels of inhalation have been established for the nickel, lead, and cadmium that can be found in e-cigarette vapor. Lead exposure is known to cause neurologic damage, especially in children, and can also cause hematologic dysfunction.[3]

Federal, State, and Local Laws

In 2016, the FDA finalized a rule that grants regulatory authority over all tobacco products including all types of Electronic Nicotine Delivery Systems (ENDS). Beginning in 2018, product packages and advertisements of all of the newly-regulated covered tobacco products must include the warning statement: "WARNING: This product contains nicotine. Nicotine is an addictive chemical."[6]

New regulations are being phased in between 2016 and 2019. If a vape shop or other retailer mixes or prepares e-liquids, mixes or modifies vaporizers, or mixes loose tobacco and then sells any of those products, they will be regulated as both a retailer and manufacturer.

Beginning August 8, 2016, retailers were required to begin the following:

- Check photo ID of everyone under age 27 who attempts to purchase e-cigarettes or other ENDS.
- Only sell e-cigarettes and other ENDS to customers age 18 or older.
- Do NOT sell e-cigarettes or other ENDS in a vending machine unless in an adult-only facility.
- Do NOT give away free samples of e-cigarettes or other ENDS, including any of their components or parts.

Further, beginning May 10, 2018, the following will be enforced:

- Do NOT sell or distribute e-cigarettes or other ENDS without a health warning statement on the package.
- Do NOT display advertisements for e-cigarettes or other ENDS without a health warning statement.[21]

State Laws

State laws vary across the country and include everything from a ban on all tobacco products indoors to no law at all.[22]

Local County/City Laws

Many counties and cities across the country have enacted local Clean Air Acts. In Missouri, several cities are smoke-free, and recently the age to purchase tobacco products, including e-cigarettes, has been raised to age 21. Columbia led the way in December 2014, and since then, Kansas City, Independence, Gladstone, Grandview, and Lee's Summit have followed. St. Louis County voted to increase the age in September, and St. Louis City is expected to follow soon.

Table 1. Summary of Statewide Smoke-free Laws

Some Type of Statewide Smoke-Free Law	No Statewide Smoke-Free Law
AZ, AR, CA, CO, CT, DE, DC, FL, HI, IL, IA, KY, ME, MN, NH, NJ, NM, NY, NC, ND, OH, OK, OR, SC, SD, TX, UTZ, VT, VA, WA, WV	AL, GA, ID, IN, KS, LA, MD, MA, MI, MS, MO, MT, NE, NV, PA, RI, TN, WI, WY

Future Considerations and Action

There are environmental concerns with disposal of the devices, the batteries that run the devices, and incompletely used liquid cartridges. Nicotine and heavy metals may pollute both land and water. We can only wait to see what the environmental effects will be.[3]

In 2016, the MSMA House of Delegates adopted Substitute Resolution 6: Minimum Age for Tobacco and Vapor Product Purchase. The substitute resolution reads: "Resolved, that MSMA support legislation to raise the state's tax on tobacco and nicotine-containing vapor products and to raise the age required for the purchase of those products from 18 to 21."[23]

In December, 2016, the Surgeon General released his report "E-Cigarette Use Among Youth and Young Adults." Action can be taken at all levels (national, state, local) and can include incorporating e-cigarettes into smoke-free policies, preventing access to e-cigarettes by youth, price and tax policies, retail licensure, regulation of e-cigarette marketing likely to attract youth, and educational initiatives targeting youth and young adults.[7]

Summary

For now, the evidence does not support recommending e-cigarettes over FDA approved smoking cessation treatments. As more research is done and manufacturers are required to disclose the ingredients in their products, a clearer picture may emerge. Keeping middle-school and high school students from starting to use these devices remains imperative and accidental exposure or ingestion of e-liquids will continue to be a concern for children, but especially those under the age of six.

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Concussion Care: Moving Beyond the Standard

by Amanda Keenan, MS & Brian Mahaffey, MD

Introduction

The world of concussion has changed dramatically. With increased media coverage, parents, and athletes are more aware of concussions. This is positive change, but can also lead to an increase in anxiety and misinformation about the condition. At the same time, the approach to treating concussions has shifted in very recent years. We are now moving past "basic" concussion care for a better understanding of treatments that are showing great promise. Incorporating an integrated, whole-body approach to treating concussions, including specialized therapy, early exercise, nutritional support, and psychological evaluation is effective. In addition, neuromuscular, vestibular, and visual assessments are key to improved outcomes.[1]

Evaluation and Return to Play

The standard of care for concussions is moving away from complete brain rest for an extended period of time to a controlled and gradual introduction to activities of daily living (including school and social activities) as tolerated.[1] Slow, controlled physical activity, such as walking or riding a stationary bike, below symptom threshold is now encouraged to help improve symptoms and aid in recovery, especially in cases of prolonged symptoms.[1,2,3] A discussion of this along with the most recent clinical research and an updated Sport Concussion Assessment Tool version 5 (SCAT 5) is available in the new Consensus Statement on Concussion in Sport.





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Additional useful evaluation measures include reaction time, balance assessment, and oculomotor screening.[1, 4]

When returning a concussed athlete to play, ensuring that they are completely recovered is vital to minimize the risk of re-injury and serious complications. Graded exercise testing is a beneficial tool to ensure complete recovery. The Buffalo Concussion Treadmill Test (BCTT) uses a graded exercise protocol to take the athlete to full exertion.[5,6] When the athlete completes this without an exacerbation of any concussive symptoms, they are considered physiologically recovered.[2] If concussive symptoms are provoked by the BCTT, an exercise program is prescribed at 80 percent of the symptom threshold, and the test may be repeated until full recovery.[5,6] Then it is important to take the athlete through a gradual return to play progression, including re-introduction of sport-specific activities over a period of seven days before returning to sport competition.[1] Effective concussion management requires a team approach between medical providers and school officials, and return to play decisions should be made based on multi-faceted assessments including graded symptom checklists, neuropsychological testing (such as the SCAT5 or ImPACT test) and balance assessment.[3] See Figure 1.

Neuroplasticity and Concussion Recovery

At Mercy Sports Medicine, we have created a system of recovery to help with concussion patients that have severe or lingering symptoms. Our therapy philosophy is based off of the concepts of regional interdependence and neuroplasticity. We utilize this type of approach with all of our patients and have relied on the rehabilitative model created by the Movement Restoration Project, outlined in a recent article in this publication.[7,8] These concepts translate well to patients with orthopedic as well as neurologic complaints. The idea of neuroplasticity is examined in the book *The Brain that Changes Itself*, by Norman Doidge, MD. He writes that "the brain changes its very structure with each different activity it performs, perfecting its circuits so it is better suited to the task at hand."[9(xvii)] The brain is remarkable in its ability to adapt in the presence of dysfunction, and concussion is no different. In rehabilitation, it is important to avoid using exercises that are simply a rehearsal of outputs and do not create neuroplastic change. To create real neuroplastic change,



Figure 1
Some of our commonly used post-concussion evaluation techniques. From left to right- Vestibular/ Ocular-Motor Screening (VOMS), Breathing pattern assessment, Cervical movement pattern assessment, vestibular screening using the Modified Clinical Test for Sensory Interaction in Balance (mCTSIB)

there must be a novel experience that is learned with highly intense focus, and the brain must be given "the right stimuli, in the right order, with the right timing."[9(88)] With these concepts in mind, we can create rehabilitation methods to decrease pain and physical symptoms, improve posture and movement and aid in a patient's recovery.

Post-Concussion Therapy and Rehabilitation

A full post-concussive evaluation includes multiple body systems and functions. Post-concussive symptoms are not related exclusively to brain injury, but have multi-factorial causes.[10] Patients may have symptoms related to cervical, vestibular, oculomotor, biomechanical and autonomic (breathing) dysfunction, and often a combination of these.[2,11] We assess the breathing pattern of every patient that comes through our doors, regardless of diagnosis. A person's breathing pattern affects a person's neuromuscular tone, posture, core stability, emotional regulation, and overall health.[12,13,14] Breathing evaluation becomes even more essential in concussion because of its effect on autonomic regulation and heart rate variability.[15] Both are contributing factors to exercise intolerance following concussion.[2] The resulting imbalance between sympathetic and parasympathetic activity in the autonomic nervous system may also contribute to impairment in cognitive abilities and emotional regulation.[15] Teaching a patient diaphragmatic breathing can help decrease pain, muscle tension, improve posture, and even lessen or eliminate physical and cognitive signs and symptoms.[14] Our experience with patients with oculomotor and vestibular dysfunctions is that these issues often normalize in less than five minutes of diaphragmatic breathing practice. More long-term practice of diaphragmatic breathing may contribute to overall symptom improvement and clinical recovery.

Treatment techniques vary based on the outcome of the evaluation, but typically include manual therapy, myofascial release, visual and vestibular training, and corrective exercises. See Figure 2. The Selective Functional Movement Assessment (SFMA) is an excellent tool that we use to seek out and diagnose movement pattern dysfunctions. This looks at more than simply range of motion and strength, but the pattern of movement and postural control as well.[16] With concussion, special attention is paid to the cervical spine. Neural receptors in the cervical spine have important connections to the vestibular and visual systems as well as alter afferent input to the central nervous system.[17] Dysfunction in the cervical spine can have effects on multiple areas of post-concussive symptoms. If a patient demonstrates dysfunctional cervical movement patterns, they are taken through further testing (SFMA "breakouts") that will isolate specific dysfunctions. These can be a joint mobility, tissue extensibility dysfunction, or a stability/motor control problem. With this knowledge we can target the specific dysfunction and improve the patient's symptoms. In our experience, many concussion patients present with spasm and pain in the sub-occipital muscles. We have had success in eliminating oculomotor and vestibular dysfunctions, as well as cervical pain, with a simple and quick sub-occipital muscle release and other manual therapy techniques.

While targeted cervical spine treatment is often successful, it is also important to look at the rest of the body. A concussion patient with dysfunction involving their shoulder complex, spine, core, hips, or even ankles/feet will demonstrate compensations that could affect their condition. We isolate these dysfunctions using the SFMA and breakouts, and correct using the Movement Restoration system. A case in point: a patient who had suffered a concussion came



Figure 2
Some of our commonly used post-concussion treatment techniques. These are just a small sample of the many techniques and exercises used to treat concussive symptoms and complications.

Top row: Manual therapy techniques (left to right) - Suboccipital release, Positional Release Therapy (PRT) of the cranium

Middle row: Visual/Vestibular training (left to right) - Ocular convergence training - Pencil push up exercise, Vestibulo-ocular reflex (VOR) training - gaze stabilization exercise

Bottom row: Movement and postural corrective drills (left to right) - Half kneeling head turns, Kettlebell deadlift

in with a complaint of dizziness upon running. She was able to complete other low impact aerobic activities to full exertion. Upon evaluation, it was found that her vestibular and oculomotor systems were normal, but that she had poor foot and ankle mobility and demonstrated poor lower body running mechanics which affected proper force absorption. This led her visual system to have to "over-compensate" to keep her visual field level. These dysfunctions likely pre-existed the concussion but her healthy brain had compensated easily. She was given a few simple lower body mobility and stability exercises, and this patient was able to return to running and sports without symptoms.

New Evidence

The newest evidence that we have began to implement is nutritional considerations to limit the metabolic effects of concussive injury and provide neuroprotective effects. Studies show that humans may be more susceptible to brain injury due to "diminished brain resilience syndrome," or a disrupted homeostatic state due to functional nutrient deficiency. This may lead to increased concussion risk and potential severe metabolic consequences following a concussive injury, leading to increased neuronal loss and more severe or longer lasting symptoms.[18] Functional nutrient deficiencies may include zinc, magnesium, omega 3 fatty acids, vitamin D, polyphenols, and flavonoids.[18] Much of the neurological dysfunction that occurs following a concussive injury is due to a secondary metabolic cascade involving glutamate-mediated exitotoxicity, intracellular calcium overload, mitochiondrial dysfunction, and the creation of reactive oxygen species. This mechanism is similar to features of other classical neurodegenerative disorders, such as dementia and ALS.[20] Magnesium levels in the brain fall rapidly following a traumatic brain injury and replenishing these levels has been shown to prevent and reverse neurological injury.[19] Nutritional supplementation with lithium and zinc may also be helpful during acute and chronic phases of concussion to stimulate the healing process and decrease effects of oxidative stress and inflammation.[19] A ketogenic (high fat) diet has been shown to provide neuroprotective effects in Alzheimer's and Parkinson's disease patients.[20] This may also be beneficial in traumatic brain injury.

Chronic issues after a concussion may be related to persistent neurologic and systemic inflammation. Although

Chronic Traumatic Encephalopathy (CTE) has been proposed to be related to a buildup of tau protein in the brain, recent studies have found the cause to be more multi-factorial and related to persistent neuroinflammation.[21,22] Treatment strategies aimed at decreasing systemic inflammation include nutrient supplementation and lifestyle modifications such as the ketogenic diet, as discussed previously. Further research is needed regarding long term effects of repetitive concussions or sub-concussive head impacts, and whether CTE represents a unique pathologic syndrome. An understanding of comorbid health problems, psychiatric disorders and other factors that contribute to a patient's risk for cognitive decline is essential.[23]

Conclusion

The concussion evaluation and treatment methodology has moved far beyond watchful resting. While rest and time will always be a vital component of treatment, it is not enough for every patient and it is important to consider the whole person that is being treated and thorough evaluation of the entire body. The methods described above allow the patient to be an active participant in their recovery and have produced very positive results. We hope that this information will allow clinicians to more thoroughly evaluate and treat patients with concussion and help patients to me more informed and empowered in their recovery.

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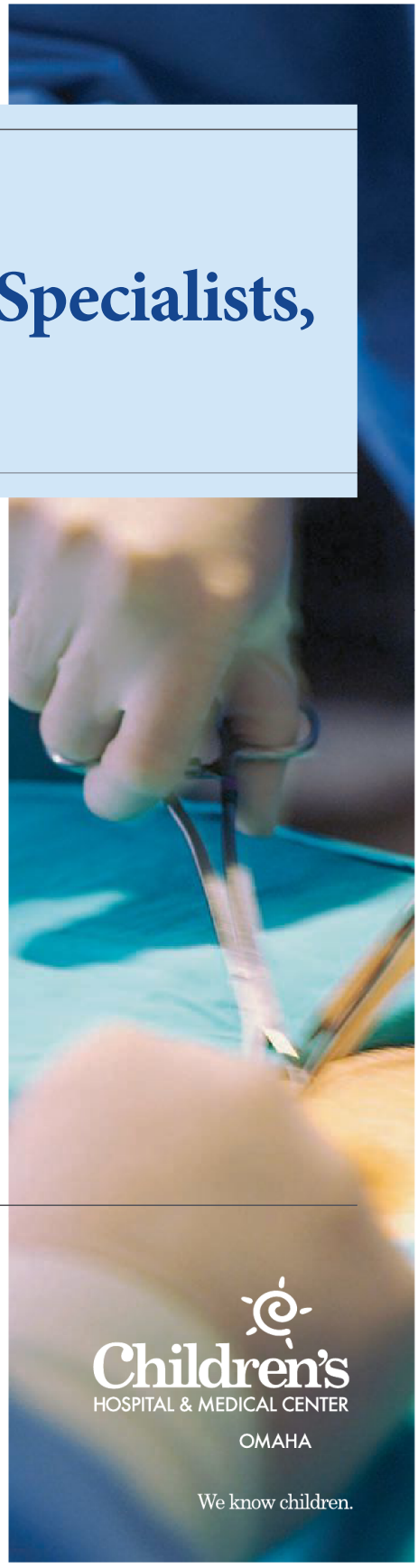
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Project Apache: Bringing Pediatric Care to an Arizona Reservation circa 1972

by Bobbette K. Ranney, MD



The author auscultating a male Apache toddler.

After graduating from Stanford Medical School, I went to the University of Colorado-Children's Hospital for my pediatric internship and residency, a rigorous and competitive program under the leadership of the renowned C. Henry Kempe, MD. Neonatology and pulmonology were my favorite subspecialties but all were exciting and taught by excellent faculty.

Early in my second year there, Joe Daily, MD, a brilliant neonatologist at Stanford who had moved to Phoenix with Belton Meyer, MD, to set up a neonatal intensive care unit (NICU) and neonatal transport system for Arizona, recruited me for a United States Public Health Service (USPHS) grant they had secured for the Fort Apache Reservation. Their infant mortality rate was 110/1000, one of the highest in the nation. My vision of Arizona was mostly of hot arid desert and I had always intended to complete my three years of internship/residency uninterrupted. Not deterred, Dr. Daily offered to arrange a visit.

I was flown into Whiteriver Indian Reservation ("the reservation") on a single engine plane. I was honored to be met by the tribal chairman, Lester Oliver, who was my personal escort for two days. The White Mountains, home of the proud and historic White Mountain Apaches, are lushly forested and rise majestically to more than 11,500 feet. On that October 1971 sojourn a foot of snow had freshly fallen. Chairman Oliver took me to the tribe's year-old Sunrise Ski Area, then to their Fort Apache Timber Company, and lastly to the Whiteriver Indian Health Service hospital. There I met with the hospital administrator, retired Army Colonel Bill Baker who tried very hard to discourage me from interrupting my training with vivid descriptions of alcoholism, violence, primitive housing, negative attitudes of Apaches toward 'white man's medicine,' and the resulting poor health and medical compliance. It all sounded daunting but a unique challenge I decided to face. There was the bonus of living in a very remote and spectacularly beautiful place.

Our USPHS grant was designated "Project Apache." Our group started work in July 1972, with a team of three pediatricians, of which one was a strictly non-clinical administrator, one nutritionist, three trained RN prenatal care practitioners, several Apache women whom we instructed to be field health prenatal aides, plus various Apache office staff. Bob Fukuchi, MD, the other clinical pediatrician, and I served as hospital consultants to the five freshly minted USPHS physicians serving after a lone year of internship following medical school graduation. Bob and I also ran weekly clinics in two more remote communities and attended every delivery at the hospital. One of us was on call all the time.

The Apache women resisted going to the hospital for prenatal care and more so to being examined by male physicians. We devised a plan to find out, via the reservation grapevine, who was pregnant. We then provided home prenatal care visits by the RN practitioners and their female Apache aides. We developed an effective slide show presentation for Apache women about breastfeeding. Breast feeding had been discouraged by previous

Bobbette Kraft Ranney, MD, FAAP, is from Kirkwood Missouri. A brilliant scholar all her life, she was the first person to graduate from the University of Missouri with a perfect 4.0 grade point average in sciences (physics), and was valedictorian of her medical school class at Stanford University Medical School. (See sidebar). She went into pediatrics and trained at the University of Colorado medical center where she describes in the following article her participation in Project Apache. Severely injured in an automobile accident in 1986, she is retired from medicine but farms and plays viola in the Brighton Colorado Orchestra.
Contact: goosetrailfarm@q.com



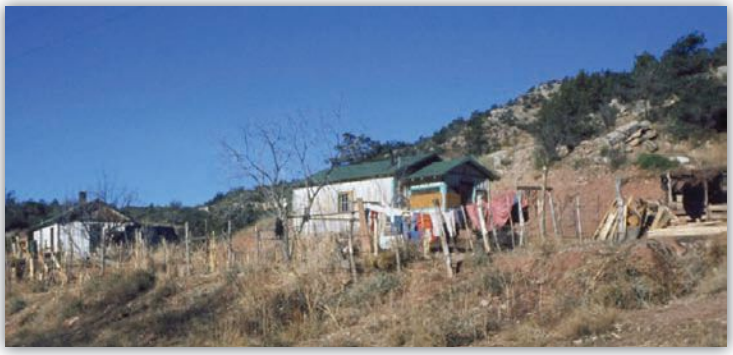
Project Apache

Images from Project Apache, counterclockwise from top: Apache women in usual traditional dress/camp dress; baby in cradleboard; Project Apache employees 1974; typical housing and shacks on the reservation; and Apache toddler. Badges/seals are representative of the area.









physicians and by misguided donations of formula. The number of tribe women breastfeeding greatly increased.

Child mortality was pervasive and oppressive. All forms of tuberculosis, trachoma, and Hepatitis A were endemic. Most of the infant mortality was due to gastroenteritis causing subsequent fatal dehydration and severe respiratory infections mainly pneumonia. The prevailing attitude of the stoic Apaches was that the hospital didn't help much when their babies were sick. Consequently they didn't bring them in until they were moribund. That first 1972 summer Project Apache introduced pediatric expertise of starting IVs (very difficult in Apache infants) and proper rehydration. Our team demonstrated we could save lives thereby winning the trust of most of the tribe. Survival increased as children were brought in at an earlier stage of their illnesses. Our reservation field nurses and aides were ultra-important communicators to the 8,000-plus Apache population. Word soon spread among the people themselves that good things were happening at the reservation hospital with the newly arrived children's doctors.

A physician group from Johns Hopkins medical school led by Norbert Hirschhorn, MD, who had previously worked in Bangladesh, arrived to work with us that 1972 summer. I collaborated with them doing unique research on oral rehydration of Project Apache children. That work resulted in a publication[1] in the *Journal of Pediatrics* that introduced the rehydration formula that with slight modification is still used by the World Health Organization (WHO) to the present time.

Winter brought increased respiratory disease most ominously bronchiolitis which at the reservation's mile high altitude caused significant hypoxia. Project Apache provided the hospital lab with a blood gas analyzer. Bob Borchardt, the IHS lab/x-ray tech, with his willingness and sincere interest in learning new techniques was an important contributor to our success. His diligence salvaged many lives. We were able to draw arterial blood gas samples (pre transdermal oximeters) and deliver oxygen appropriately with nasal cannula.

Among the many lives we saved one in particular stands out. A very cyanotic moribund five-month old presented with a completely opacified chest X-ray and almost no breath sounds. I intubated him and selectively suctioned four of the five lobes and opened all but the right upper lobe. Very bold, but successful and lifesaving.

An even bolder procedure I did was to evacuate a subdural hematoma form a near-dead nine-year-old girl who had fallen in the river and struck her head on a rock. To do this I had to perform some life-saving scavenging. I borrowed a hand drill from maintenance and sterilized the ordinary hardware bit. I used these to do skull trephinations and hematoma evacuation. She did come out of her coma. We flew her to Phoenix for follow up care where as I recall she did recover.

Generally, Arizona reservation hospitals had a delivery room but no operating room. Deliveries that required emergency caesarean sections, or anything else requiring urgent surgical intervention, had to be evacuated by the legendary Cessna Skymaster 337 a tiny 'push-pull' aircraft. The Skymaster belonged to the U.S. Indian Forest Service who used it as a spotter for the C-130 fire-fighting slurry bombers based in Whiteriver. I flew at least 50 medivacs as the only medical person on the plane for the seriously ill patient(s). Most flights were for emergency C-sections. I once delivered a single footling breech in the cramped plane quarters. Other memorable flights were a five-year-old GI bleeder (pneumonia and duodenal ulcer) and an ultimately fatal gunshot wound to a three-year-old. He died in the ambulance in Phoenix. The daily summer monsoons and frequent winter snowstorms made many flights risky and sometimes impossible. We did the best we could for the critical patients while waiting for a break in the weather. Phoenix was over 200 miles away by rugged highway.

The days and nights were long but the experience impossible to duplicate and everything I hoped it would be. There were many challenging pediatric illnesses, memorably an infant with adreno-genital syndrome who had wrongfully been assigned male gender. I consulted University of Colorado Endocrinology about her. With the help of the Assembly of God Church in Canyon Day village we put on a baby shower and celebrated with the family a re-baptism. Her parents were very thankful. She later had some reconstructive surgery at Colorado University Medical Center. An infant with Tetralogy of Fallot and absent pulmonary valve I sent to world famous cardiac surgeon and personal friend Norman Shumway, MD, at Stanford. I joined the local Navapache Medical Society to try to establish a working and collegial relationship with the off reservation physicians in Lakeside, 30 miles "up the hill." Some slow progress was made and I understand that today there is relatively good cooperation.

Because of the depth and breadth of my experience on the Reservation, Dr. Kempe obtained credit for my third year of residency from the American Board of Pediatrics. I thus became Board eligible. After four years, the infant mortality rate had dropped from 110/1000 to 30+/1000. Almost all of those deaths occurred in very hard core alcoholic families. Our USPHS grant ran out after four years and was replaced for one year with a Robert Wood Johnson Foundation grant. Five months into my fifth year I was twice left stranded in Phoenix after medivac flights. With Dr. Fukuchi continuing on, I resigned and picked up my off-the-reservation life. I have been blessed to live a fantastically rich and varied life both professionally and personally. Project Apache was among the most rewarding experiences of my life, and I feel so fortunate to have taken that opportunity when Dr. Joe Daily offered it to me.

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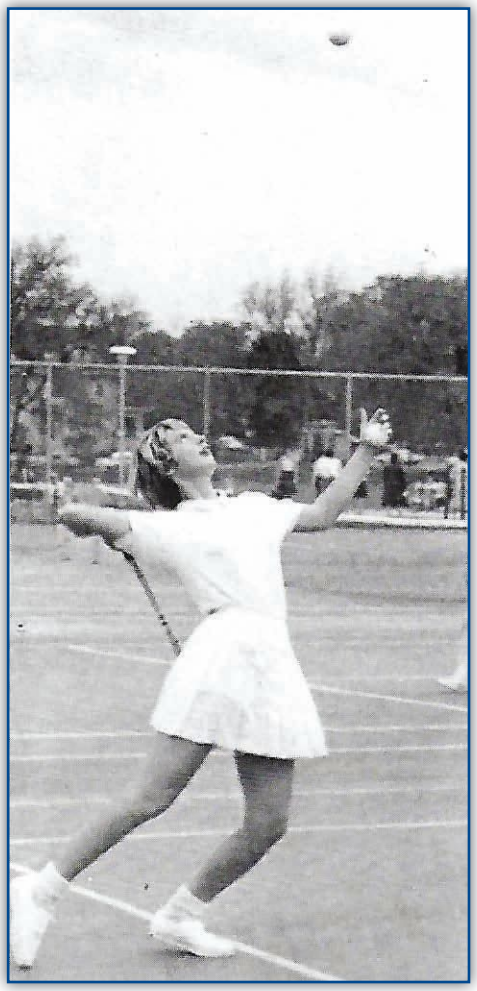
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University of Missouri's Most Distinguished Record of Scholarship: Bobbette K. Ranney, MD

by John C. Hagan III, MD

Grade point inflation is even more pervasive and pernicious than monetary inflation. The most common grade in two- and four-year colleges is now an 'A.'[1] At four-year universities the number of A grades has risen 5-6% per decade, and is over 300% higher than in the late 1960s when the regrettable phenomenon began.[1]

For better or for worse, at one time competition was felt to be one of the most effective methods of selecting the best and brightest for medicine and science. Grading was rigorous and grades allocated "on the curve." That meant approximately 10-15% of a college science class might expect to get an A grade in the time frame of 1961 to 1965 when Bobbette Ranney and I were in pre-med at the University of Missouri. A perfect grade point average (GPA) was 4.0 and no one had graduated from MU with straight As in every class they took. That is, until Bobbette graduated Phi Beta Kappa, Summa Cum Laude in 1965 with a 4.0 GPA in physics. While at MU she excelled in sports competing in women's tennis while on a full academic scholarship. She played viola in the University orchestra. After a summer of working as a lab technician at St. Louis County Hospital she decided to be a physician rather than a theoretical physicist.



Besides being Missouri University's first 4.0 GPA student, Bobbette Ranney starred on the MU women's tennis team.

I had several biology and math courses with Bobbette and she was modest with a good sense of humor and could explain solutions to our course problems better than most of the professors. Of course any class she took she was sure to get one of the coveted and highly contested "A" grades.

After graduation from MU she spent her summer on Pike's Peak with seven other female MU grads as high altitude research subjects for the Army Physiology and Nutrition Laboratory. She entered Stanford Medical School where she did original research including study of the properties of toxins used on poison arrows derived from Central American frogs; studied obstetrics in Scotland; and solo backpacked from Lake Geneva to Lake Lucerne. She was selected to the national medical school honor society Alpha Omega Alpha as a junior, and graduated first in her Stanford class.

In the nearby article she describes a singularly unique experience after her pediatric residency at University of Colorado. Dr. Ranney continued her brilliant career in both academic and private practice of pediatrics. In 1986 she was almost killed in a head-on collision on a one-lane rural road with a large pick-up truck. She had multiple surgeries including an aorta repair in which she twice had cardiac arrest. She was left partially paralyzed and uses Canadian crutches. She became a distinguished disabled athlete enjoying swimming and competing in golf tournaments. She played with the Denver Pops Orchestra, and presently the Brighton (Colorado) Orchestra. She maintains an active farm and raises livestock.

I think a strong case can be made that Dr. Bobbette Ranney created the most distinguished scholarship record of any graduate of the University of Missouri-Columbia, and without doubt a world class level of sustained personal, professional, and athletic achievement.

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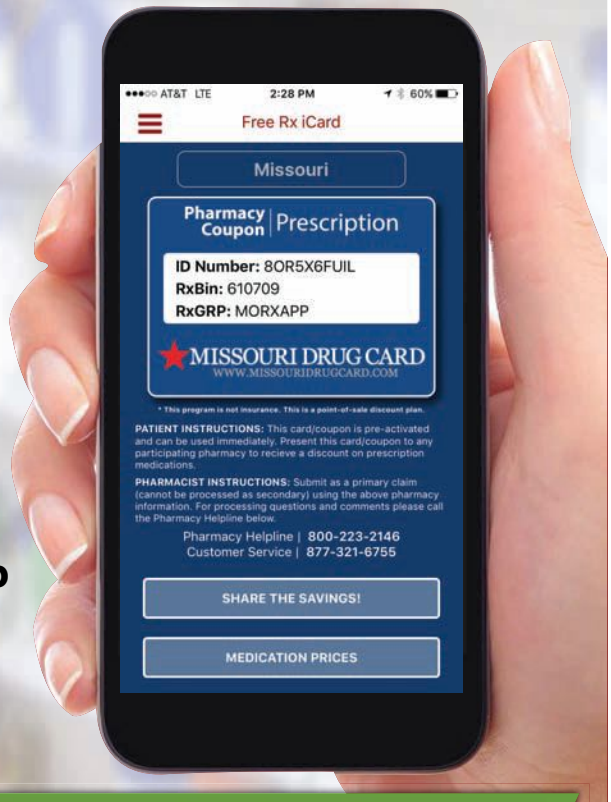
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A Lifetime of Service

by Warren C. Lovinger, Jr., MD



158 years of practice in Missouri. From left, William Haynie, MD, Butler, 54 years of practice, MSMA member since 1977; Curtis Long, MD, Butler, 53 years of practice, MSMA member since 1977; and John Torontow, MD, Nevada, 51 years of practice, MSMA member since 1970.

As physicians, we are given many opportunities to provide service to our patients, our communities, and our profession. Some of us do this for an exceptionally long time. Three doctors in the West Central Missouri Medical Society are particularly inspirational having served their patients for a total of 158 years, with all three continuing to practice medicine! William Haynie, MD, (Butler), Curtis Long, MD, (Butler), and John Torontow, MD, (Nevada) have all received their "50-Year Pin" from MSMA and are still serving their communities.

Dr. Haynie, a native of Butler, Mo., graduated from the University of Missouri School of Medicine in 1962, and moved back to Butler to open his Family Practice in 1964. He has also served in many additional roles – as a hospice medical director, physician for the Bates County Jail, president of the medical staff at Bates County Memorial Hospital, and president of the Butler Rotary Club. At age 88, Dr. Haynie is thankful to "be in good health and continuing to practice medicine."

Dr. Long, a native of Ironton, Mo., graduated from the University of Missouri School of Medicine in 1963, and opened his Family Practice in Butler in 1964. He has achieved many milestones in his long career: 50,000 hospital admissions, 10,000 surgical procedures, and 3,000 babies delivered. He is particularly proud to have done "the first laparoscopic procedure in Missouri" in 1974. In addition to a busy, ongoing medical practice, Dr. Long is active in several local and national organizations, and has been a generous benefactor to the MU Medical School.

Dr. Torontow was born in England, and remembers being evacuated to the countryside during the Battle of Britain. He graduated from Trinity College Medical School (Dublin, Ireland) in 1962, and came to the University of Missouri Medical Center to do an Internal Medicine residency. In 1969 he and his family moved to Nevada, Mo., to co-found the Nevada Medical Clinic—subsequently recruiting an entire generation of Nevada physicians (myself included). He has served on 10 medical mission trips to Haiti. He continues to provide primary care services in El Dorado Springs, Mo., and observes that "medicine is still the best career in the world!"

During the past several weeks, I have continued to travel around our state, visiting physicians, hospitals, and component groups as the representative of the MSMA. Usually accompanied by my wife, Marilyn, we have logged almost 10,000 miles in my green Chevrolet truck. We have now visited 108 of the 114 counties in this state and have met many wonderful people while enjoying the diversity of Missouri's communities and geography. We have also appreciated the hospitality of adjoining state medical associations, when we have visited in Iowa, Nebraska, Kansas, Oklahoma, and Arkansas for their annual meetings. We have been consistently impressed by the positivity and enthusiasm of Midwest physicians who are "Happy Unsung Heroes of the Hinterland." I certainly agree with Dr. John Torontow that we are blessed to be part of this great profession.



Warren C. Lovinger, Jr., MD, MACP, MSMA member since 1979, and President for 2017-2018, is an Internal Medicine physician, Nevada, Missouri.
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Ben Wilson, MD, Nevada, MSMA member since 2016, New President of West Central MO Med Society and Bar-B-Que chef extraordinaire!



White Coat Night at Cardinals Game: left to right, Marilyn and Warren Lovinger, Nevada, MSMA member since 1979; Cindy and Gary Olson, Cape Girardeau, MSMA member since 1994; and Kathy and Joseph Hazan, St Louis, MSMA member since 1977.



Elizabeth Wilson, MD, MSMA member since 2001, Columbia, Obstetrics and Gynecology at Boone County Hospital and Dr. Lovinger.



Palmyra Clinic, Palmyra: left to right, Dr. Lovinger, Gina Pontius, MD, MSMA member since 2011, Family Practice, and David Knorr, DO, MSMA member since 2001, Family Practice.



Texas County Memorial Hospital, Houston: left to right, Linda Milholen, MD, MSMA member since 2005, General Surgery, and Cory Offutt, MD, MSMA member since 2009, Family Practice.



John Memken, MD, MSMA member since 1984, Hannibal, Family Physician at the Hannibal Clinic.



Dr. Lovinger and Muhammad Faisal Khan,MD, West Plains, Cardiology at Ozarks Medical Center.



Lisa Rollison, DO, Memphis, General Surgeon at Scotland County Hospital.

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MSMA Members in the News

Did you make the news? Submit your success story and photo to hwansing@msma.org.



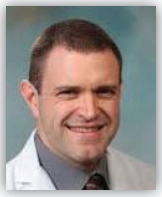
Three cheers to Jennifer Allen, MD, for being named the new medical director at New Haven Care Center. In July, she opened her own direct primary care practice in Hermann, New Freedom Family Medicine. MSMA appreciates her membership this past year.



George Bohigian, MD, made a presentation in July on "Differential Diagnosis of Keratitis" at the 25th Armenian Eye Care Project Conference in Yerevan, Armenia. He is a Professor of Clinical Ophthalmology, Washington University School of Medicine.



MSMA member since 2011, Matthew A. Brown, MD, of Houston, Mo., has earned the "Recognition of Focused Practice in Hospital Medicine" by the American Board of Internal Medicine and the American Board of Family Medicine.



MSMA commends John Bustle, MD, member since 2010, on being named Interim CEO for Bates County Memorial Hospital.



Christina Goldstein, MD, of Columbia, MSMA member since 2015, has been chosen as one of four U.S. physicians to participate in the North American Traveling Fellowship tour hosted by the American Orthopaedic Association.



Daniel Hoernschemeyer, MD, MSMA member since 2015, is one of three U.S. physicians chosen to travel with the Pediatric Orthopaedic Society of North America international fellowship, visiting multiple hospitals throughout South America.

Congratulations, Joseph Mayo, MD, and the team at Carthage Pediatrics, on moving to your new practice location at 2425 Fairlawn Ave.





Peter Perll, MD, MSMA member since 1996, has expanded his practice to include both Mexico and Louisiana, Mo.



MSMA is proud to call Evan Stout, MD, a new MSMA member this year. Congratulations on joining the team at Bothwell Regional Health in Sedalia.



Philip Wilson, III, DO, has joined the team at Jefferson City Medical Group, and MSMA is grateful to have him as a new member.

ERRATA

In the July/August 2017 issue of *Missouri Medicine*, an author was inadvertently omitted from the article entitled, "Femoroacetabular Impingement Syndrome: A Cause of Hip Pain in Adolescents and Young Adults." The correct authors are Christopher M. Shaw, MD, and Michael Harvey, MD.

In the July/August 2017 issue of *Missouri Medicine* MSMA member Max Heeb was inadvertently listed as having been a member since 1977. The correct year is 1958.

CORRESPONDENCE

Double Drat - Diagnosis of Brown Recluse

I read the excellent article by Troy Major, MD, on the treatment of 20 patients with brown spider bites. I was reminded of a simple bed side diagnostic method to diagnose the bite of a brown spider. Skin temperature is related to arteriolar circulation, while skin color is related to capillary circulation. The toxin of the brown spider constricts the arterioles and dilates the capillaries, therefore the bite results in a cool erythema.

The examiner touches the erythema and compares it to the surrounding skin. If it is cooler, you have a brown spider bite. If it is warmer than surrounding skin, you look for another spider or an insect bite.

This simple touch test may avoid extensive and expensive treatment. As an aside, the arteriolar damage is the cause of necrosis.

Max A Heeb, MD, FACS
MSMA member since 1958
Benton, Kentucky

Kansas City University: A Private University with a Very Public Mission

by Marc B. Hahn, DO

This is a time of exciting growth and great opportunity for osteopathic medicine, which continues to gain recognition and prominence in our country. During the past three decades, the number of DOs in the U.S. has increased by 276 percent, from 27,146 in 1986 to 102,137 in 2016[1]. Enrollment in osteopathic medical schools has led this positive trend. Between 1977 and 2015, first-year enrollment grew 521 percent, from 1,163 students to 7,219 students, and is expected to follow its upward trajectory through at least 2020[2]. Nearly one in four medical students in the U.S. is now in an osteopathic program[1].

This recent emergence of our profession, combined with its holistic philosophy and emphasis on primary care and rural health, bode well for our country's ability to make significant inroads in addressing the projected shortages and maldistribution of our physician workforce. The Association of American Medical Colleges estimates the need for up to an additional 43,100 primary care physicians by 2030[3]. At the same time, nearly a fifth of U.S. residents live in rural areas, yet less than a tenth of primary care physicians practice there[4]. Indeed, these shortfalls pose greater disparities in access to high-quality medical services and threaten to leave many of our most vulnerable patients unable to get necessary care and treatment.

Since 1916, Kansas City University of Medicine and Biosciences (KCU) has graduated more than 10,000 osteopathic physicians, making a significant, long-term impact on meeting workforce demand nationally. Today, KCU has nearly 8,000 graduates practicing medicine in every state in the country. With more than 1,500 alumni currently in practice in Missouri, the University is the second-leading producer of physicians for the state. Nearly 60 percent of KCU's graduates practice in a primary care specialty in Missouri, with 43 percent practicing in a rural or underserved area. The economic impact on the communities they serve is more than $2.4 billion annually, and they sustain more than 16,000 jobs.

Over the years, KCU has adapted and innovated to best prepare medical students for success in our country's ever-evolving health care landscape and to further our mission of "improving the well-being of the communities we serve." We have incorporated new models of care delivery and are expanding opportunities for interprofessional education to provide students with the learning experiences, knowledge and skill development that are essential for the growing trend toward team-based care. Critical public health issues facing our state, region and nation have driven key updates to our curriculum, as we prepare tomorrow's physicians to better understand and cope with complex issues of the day, such as widespread opioid addiction crisis, the challenge of emerging infectious diseases, increases in antibiotic resistance, and determinants impacting the health of populations.

During the past decade, KCU also began training medical scientists and ethicists. Our College of Biosciences has grown exponentially since its inception, with applications increasing more than ten-fold, and a class size that has more than quintupled to over 120 students today pursuing a Master of Science in the Biomedical Sciences. Our Master of Arts in Bioethics trains health professions students in addressing critical moral, ethical and humanistic issues they will face in today's increasingly sophisticated, technology-driven health care environment. The program continues to grow, with 102 students currently enrolled — more



Marc B. Hahn, DO, MSMA member since 2012, is the President and Chief Executive Officer of the Kansas City University of Medicine and Biosciences.
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than twice the number in 2012. And, we began training clinical psychologists at the doctoral level (PsyD), as our inaugural class entered the University's new program this year. By offering the only PsyD program in Missouri or Kansas, KCU will help address the growing need for behavioral health services in the region.

As KCU begins our second century, we are sharpening our focus on further identifying critical workforce needs and gaps, and developing greater solutions to improve access to health care. This summer, with a class of 150 medical students, we opened our second medical school campus in Joplin. This is the first new medical school in Missouri in nearly 50 years, further demonstrating our commitment towards positively impacting access to medical care (especially primary care) in the rural regions of southwest Missouri. KCU-Joplin is the culmination of hard work and perseverance by area civic and business leaders, government officials, hospitals, medical professionals and members of the community to meet the needs of the area's growing, aging population. Once fully enrolled, KCU-Joplin will infuse an estimated $120 million annually into the regional economy, representing an innovative and collaborative approach that will serve as a model for other parts of the country.

Graduating a greater number of highly skilled, compassionate physicians is part of the strategy for addressing the medical workforce needs for our state and our region. Key to ensuring an adequate number of graduates, we must continually develop clinical training sites for third- and fourth-year medical students to align with the growth in Missouri medical school enrollment. To that end, KCU recently formed a collaboration with HCA Midwest Health to provide additional clinical training opportunities for our medical students. In addition, we are working throughout the region to develop novel primary care and specialty graduate medical education (GME) programs in both urban and rural areas to train physicians in Missouri to care for the citizens of our state.

Looking ahead, KCU will continue to become a more comprehensive health sciences university, while remaining true to our foundation of osteopathic medicine. We will pursue opportunities for further growth, build additional strategic partnerships that add value for our constituents, and develop new academic programs that align with both our mission and the unique workforce needs of our two campus locations and the populations we serve.

We are using new technologies as a lever in providing leading-edge training to improve student learning, patient safety and population health. We look to break ground this year on a new 41,000-square-foot, state-of-the-art Center for Medical Education Innovation. This facility will provide the latest in virtual reality, haptic technology, and simulated clinical experiences, serving as a resource for our students and other health care providers throughout our community and state.

As part of our mission in academic medicine, KCU is dedicated to positively impacting patient outcomes through the development of a robust research program, intent upon the pursuit of new therapies and treatment options, with a key area of focus on neuromuscular and neurodegenerative diseases. Our research success has come from cultivating key strategic partnerships that leverage important synergies and funding opportunities. KCU has been part of a unique partnership with the Kansas City Consortium on Musculoskeletal Diseases, a growing collaboration between Kansas City University, University of Kansas Medical Center, University of Missouri-Kansas City and University of Missouri-Columbia, which serves as a model for bringing together the best scientific minds and available resources to build teams and advance research in musculoskeletal and neurodegenerative diseases.

Clinical service through unique clinical partnerships helps provide both important training opportunities for medical students and much-needed health care to underserved populations in our communities. KCU embeds physician faculty and students in a number of Federally Qualified Health Centers in the area, where they deliver important primary care to underserved populations. In addition, we have a long history of extensive outreach and service through our flagship Score 1 For Health program, which provides pediatric health screenings to more than 13,500 children annually in Kansas City's urban core.

Our vision to become the most student-focused medical university in the nation drives our commitment to addressing key issues of importance to our students' health and well-being. As tuition costs and student

debt continue to rise, KCU remains focused on medical school affordability, and we are proud to be recognized by *U.S. News & World Report* as the sixth-least-expensive private school of medicine in the country. Medical students, like many students in professional programs today, also face mental health issues, with stress, burnout, and depression being reported in increasing numbers. In response, KCU has introduced systematic changes to address these concerns, including implementing an intentional, multi-faceted program dedicated to student wellness, day in and day out.

As health care continues to evolve, so do we in health sciences education, continuously monitoring, measuring and adapting to provide education that prepares the next generation of physicians and other health sciences professionals to meet the health care needs of tomorrow. KCU's ability to innovate and proactively respond to the changing environment has allowed us to succeed and will sustain us as we educate students for the next 100 years. As we open our second medical school in Missouri, committed to educating physicians in rural primary care; as we develop new programs to address critical needs in our state, such as clinical psychology; and as we help to develop novel GME programs; KCU remains a private university with a very public mission.



KCU's newly installed monument signage provides an iconic entrance to the campus in Kansas City's Historic Northeast Neighborhood.

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Acknowledgment

Kansas City University of Medicine and Biosciences and *Missouri Medicine* would like to thank Jill Bagby, Executive Writer, for her coordination and editing expertise for this theme section. **MM**



At the center of the Joplin campus, an indoor/outdoor quad provides students with a communal social and study space.

System-Based Models of Care Influencing Population Health Outcomes

by Darrin D'Agostino, DO

The health care system in the U.S. has developed uniquely compared to other health care systems globally. Drivers of our system are based in capitalism and, thus, much of our commercial health care delivery is geared toward profit margins and market share in order to be sustained. The resultant competition has created a very aggressive and technologically advanced system of delivery, which is very expensive.

Based on World Health Organization data and reports from numerous sources, the U.S. ranks very low in comparison to other countries when evaluated on life expectancy, health care system efficiency, and cost of care. In one report from Bloomberg, the U.S. ranked 50 out of 55 countries evaluated. The U.S. is only the third most expensive country to provide health care at $9,403/capita, falling slightly below Norway ($9,522/capita) and Switzerland ($9,674/capita). Our life expectancy in the U.S. is 78.94 years (combined men and women). What is interesting, Norway and Switzerland have higher life expectancy rates at 81.75 years and 82.85 years, respectively.[1] The U.S. has, in fact, dropped in ranking (from 49 to 50) in the last eight years, which is fascinating given the attention to health care expenditure, access for the uninsured, and legislative change that has occurred in an effort to improve health outcomes. When compared to France, which is ranked fourth on level of health in the country and first in overall health system performance, we see large gaps in care. Is it possible that our technological, legislative, and political health care developments are not focused on the correct outcomes? Is it possible that the driver of health care favors technical diagnosis rather than a physical encounter and intellectual problem-solving?

According to the Commonwealth Fund report of 2014, the U.S. ranks last in "efficiency, equity and outcomes" among the 11 developed countries that were compared. The lack of "universal health care" in the U.S. was cited as the main factor accounting for the differences in access and quality among the evaluated countries. Disparities in care and access in the U.S. have become the targets claimed to be responsible for our falling rankings.[2] It can be argued that these disparities in care have developed, in part, due to our third-party payer system contributing to the increasing costs of care. These costs are driven by technology, administrative expenses, hospital costs, lifestyle choices, and chronic disease conditions.[3] Our capitalist society has allowed our system to make some of the most dramatic and important discoveries the world has ever known, saving lives that otherwise would have been lost. But this comes at a cost, and only in a country founded on the principles and laws that we have, could these advances be driven more than in any other country. These cost drivers have contributed to the creation of a caste system for health care, limiting access for many.

Euphemistically, it is said, "In God we trust, all others bring data." So how is data being used to guide medical care? Estimates of the body of evidence used in medical practice are difficult to calculate. Suffice it to say, the use of research-derived data regarding patient care has driven many health care systems to foster exceptional outcomes. These outcomes in health care endpoints require common and collaborative efforts to create health in our communities. Population health initiatives and systems of practice, pioneered in Canada, have demonstrated system-based care and improved patient outcomes. The metrics used to identify success are defined not by individual successes, but rather by improved health of a community and the improved health of society, ultimately decreasing utilization of high-cost, low-efficiency health care delivery.

Systems-based efforts are developing slowly in this country. Interestingly, the U.S. currently has 180 active medical schools. We are one of four countries with greater



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We inherently focus on and understand that illness pays the bills and ensuring wellness does not.

than 150 medical schools (shared with China, India and Brazil).[4] Almost 27 percent of the world's organized public health schools or departments are in the U.S., and these are made up of either accredited public health schools (59) or public health degree programs (113).[5] We are a country which arguably has the greatest opportunity to create a systems-based health care model that focuses on patient safety, quality health outcomes and population health. Yet, our health care system and public health system are the least integrated worldwide. The tools and expertise of our public health system are uniquely geared to offer guidance to the delivery of our limited health care resources. What is needed is a partnership between medical schools, medical practices, and public health programs that is organized around health care systems, with a focus on improving community and population-specific health care outcomes.

Focusing on and including the determinants of health during a medical visit can impact a patient and the community in which they live. Most of the chronic disease burden in the U.S. is driven by determinants of health, such as poor socioeconomic factors, built environments forcing isolation and inactivity, genetic predisposition, and aberrant individual health behaviors. If we add to this the limited access to clinicians, especially in emotional and mental health care, we can see how these factors form the "perfect storm" that is impacting an individual's health, as well as our nation's health. The most powerful tools to help improve the wellness of our population are not in the holster of the physician, but rather in the hands of policymakers, community leaders, and cultural influencers. Interventions that address social determinants of health have the greatest potential public health benefit. Action on these issues requires the support of government and civil society if they are to be successful.[6]

Currently, there is a movement in the U.S. focusing on providing quality health care that is affordable and targets the improved health of communities. This triple aim is guiding program development and outcomes-driven care, helping to prevent disease. Although there have been practices and health care systems around the U.S. attempting to do this, our current payment systems have hindered the wide-scale acceptance of population health care. New, population-based payment models need to develop, moving our system away from fee-for-service payment models.[7] Given the majority of payment plans utilize a fee-for-service model, It is fair to say that this premise has enhanced the development of innovative technologies (some of the most advanced in the world) geared to care for the sick and infirmed. Said differently, our system of health care focuses on, and invests in, secondary and tertiary prevention (whereby illness and disease has presented itself) but for the most part ignores primary prevention (whereby illness and disease has not presented itself), since reimbursement is lacking for wellness.

Health care is ever changing in the U.S. Winston Churchill once said, "You can always count on Americans to do the right thing - after they've tried everything else."[8] These words have never been more true, especially when referring to health care. As we move through new programs to help improve health care quality, efficiency, and effectiveness, we learn a little more about what works and what does not. What has always been interesting to this author is that the most powerful influencers of our health and wellness are those things that members of our society influence and our culture allows. Physicians and the health care workforce have an obligation to address those elements that impact the health of their patients. Addressing the determinants of health with population health-based strategies has the potential to be "… the right thing."

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Innovations in Training the Next Generation of Physicians for Missouri and the Nation

by G. Michael Johnston, DO

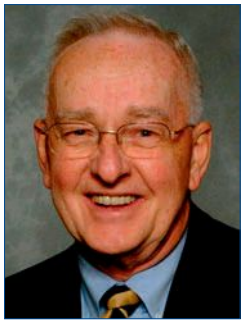
Building on History

Medical education today must be innovative for our current medical students, as well as for generations of physicians to come. Continued evolution in educational training is essential in order for young physicians to meet the expectations and demands of our country's changing health care and delivery systems.

Innovation occurs in curricular philosophy, methods of teaching and in settings beyond the classrooms or labs. During the last century, medical schools have been slow to transition from the traditional curriculum of two years of basic science and two years of clinical clerkships. Yet, it is through such innovative changes to the curriculum that students gain the greatest opportunity to better understand concepts, learn how to work through problems and develop practical differential diagnosis.

At the same time, because the history of medical education spans hundreds of years, it must effectively bridge multiple generations. Indeed, those involved in medical education today include Traditionalists (before 1946), Baby Boomers (1946-1964), Generation X (1965-1981) and Generation Y (1982-2000), better known as Millennials.[1]

Medical educators must foster generational gap closure for both faculty and students through innovation to the curriculum, incorporating academic resources, technological advances and utilization of medical informatics. These changes are essential components to a dynamic curriculum. Most importantly, these changes are necessary in order to ensure that high-quality educational content continues to be delivered to our students.



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Recognizing Today's Challenges

Based on current demands of the U.S. health care system, the Association of American Medical Colleges predicts a significant physician shortage by 2025.[2] To meet this challenge, there has been a growth in the number of accredited osteopathic and allopathic medical schools over the past 15 to 17 years. At the same time, class sizes have increased, resulting in higher faculty-to-student ratios and concerns about sufficient time to ensure individual students receive a high-quality education. Faculty are not only responsible for teaching the students, but also for serving in other roles, including advising, counseling, mentoring, interviewing applicants and supporting the University's internal committee structure and external professional obligations.

As class size increases, student engagement decreases, with less interaction between the student and teacher. Today's students prefer a blend of classroom didactics, a review of reading assignments, or small group discussions, for example, discussing a video they've watched the night before. Such a combined approach leads to engaging discussions that may occur in the classroom or in small breakout areas. This form of training is more active and learner-focused. The benefits of earlier pre-clinical experiences reinforce these concepts and lead to the retention of students' knowledge and increased confidence.

Those involved in medical education include both faculty and students from different generations. Each generation has its unique characteristics, preferred teaching-learning styles, and technological skills. Often, the older generation (Traditionalist before 1946) and Baby Boomers are teaching medical students born in the decades of Generation X, Generation Y or at the turn of the millennium, with intergenerational differences and associated challenges.[3]

For example, challenges arise when Traditionalists prefer to use a lecture hall format and are reluctant to use advanced technology. In contrast, Millennials grew up with and often thrive on technology, and prefer active learning and student engagement in small groups as opposed to large classrooms. They are a generation that responds well to



Dr. G. Michael Johnston leads students in learning osteopathic manipulative treatment methods.

change, enjoys group problem-solving, wants mentoring/coaching, and prefers to communicate through emails, texts or chatrooms. Traditionalists prefer face-to-face dialogue or written correspondence.[4]

Other characteristics of Millennials include a focus on outcomes and achievements rather than structure and process. Millennials tend to request regular feedback, periodic compliments, and clear instructions. They enjoy working with a diverse group of people and different cultures. They expect a balanced life between their job and family. Both generations, however, share a respect for having a deep understanding of the material.[5]

Challenges also exist with the measurement of academic performance. The evaluation of a student's progress has traditionally been measured by grade point average (GPA) and board scores. New methods of measuring academic performance embrace additional means to measure progress that focus on outcomes, such as Osteopathic Core Competencies and Entrustable Professional Activates (EPAs). These measurements reflect the student's proficiency and competency in fundamental skill sets that are essential before graduation and prior to starting post graduate training.

There is no doubt that high expectations are being placed on our students during a time of rapid change in health care. As noted in the *International Journal of Teaching and Learning in Medicine*, "the provider of tomorrow must be self-aware, self-directed, resource-effective, technologically savvy, and a team player.[6]

Enhancing Academic Performance

In 2014, Bruce D. Dubin, DO, former provost and dean of the KCU College of Osteopathic Medicine (KCU-COM), introduced a new curriculum to faculty and students. These changes were detailed in the May/June 2016 issue of *Missouri Medicine* in the article "Innovative Curriculum Prepares Medical Students for a Lifetime of Learning and Patient Care." The curriculum took two years to fully implement and is a "modified systems-application based approach."[7] A concise explanation of the different types of curricula (discipline-based, systems-based, problem-based learning) and their incorporation into the new model are discussed in the article.[8]

The new KCU curriculum contains both traditional classroom lectures, plus out-of-classroom reading assignments (DSA – Designated Student Assignments). In addition, the model highly encourages and promotes student engagement through dialogue with the faculty, along with the application of problem-solving and critical thinking in the classroom. This process integrates knowledge from lecture material, readings and discussions, which stimulates an overall better understanding of the subject matter.

Since its implementation in 2014, the new curriculum continues to be reviewed and evaluated through ongoing inquiry. Is this the ideal curriculum for the COM to meet students educational and experiential needs? Will this curriculum prepare the next generation of physicians to meet the demands of the evolving health care system? Does this modified systems-application based curriculum model work?

Our preliminary analysis is a resounding "yes!" Although only one cohort of students has trained for two years using this curriculum, the class performance on the College of Osteopathic Medicine Licensing Exam (COMLEX Level 1) was outstanding. The pass rate

for first-time takers was 98.8 percent, a distinctive academic accomplishment. This performance is a tribute to the hard work of the students and faculty, as well as the vision of administrative leadership. Additional evaluation of the curriculum will continue as students are evaluated on Osteopathic Core Competencies and Entrustable Professional Activates (EPAs).

The current curricular philosophy and content will continue, with the understanding that periodic revision will be necessary. As summed up by Dr. Ed Hundert, "A good curriculum is never finished."[9] As such, the model will evolve to provide the most up-to-date training in areas of health care systems, resources and delivery.



KCU's future Center for Medical Education Innovation will provide new opportunities for advanced medical education for KCU students as well as local and regional health care professionals.

Expanding Clinical Training Opportunities — Now and for the Future

In addition to ongoing curricular updates, ensuring optimum clinical training opportunities are critical for the continuation of a highly qualified physician workforce. Through an innovative new collaboration between KCU and HCA Midwest Health, up to 100 third-year medical students in the COM will be able to experience clinical rotations in some of the region's finest hospitals, clinics and surgical centers. The partnership provides an excellent opportunity for the next generation to be trained by some of the best physicians in the area, while also providing the foundation for new graduate medical education training programs in the future.

Advancing Simulation and Medical Innovation

KCU's planned Center for Medical Education Innovation also provides a new opportunity for learning for students. The Center will be a new, 40,000-square-foot state-of the-art facility for educating students and providing opportunities for interprofessional training with community partners. The new center will contain high-fidelity equipment such as haptic tools (to appreciate touch and sensation of resistance) and programmed mannequins for specific task training (procedures including spinal tap, chest tubes, central lines, injections, and joint aspirations). Students will benefit from practicing procedural skills before starting clerkships. The center will create an environment as realistic as the trainee will experience in real-time clinical situations. The next generation of physicians will train utilizing virtual patients, virtual or augmented technology, and smart-glasses headsets, as well as simulators and standardized patients. The simulation center will provide training opportunities for medical students from both our Kansas City and Joplin campuses, allowing opportunities to collaborate with local and regional health care professionals (nurses, therapists, paramedics) who will also benefit from this educational experience.

Placing Wellness at the Forefront

KCU-COM has always been committed to the health and well-being of our students. In 2016, we began developing an enhanced wellness program dedicated to addressing the issues of student burnout, depression and anxiety. Nationally, medical schools have seen sharp increases in the number of students who are depressed, anxious, and burned out during their

four-year medical student career, with evidence that these experiences transition with the student to residency. The University is working to proactively identify and support students who may be struggling personally while at KCU. Key elements of this innovative program include a student-led wellness council, student wellness checks to assess students at high risk, and enhanced programming that addresses wellness of the mind, body and spirit. Read more about our model wellness program in the detailed article in this section by Vice Provost of Student and Enrollment Services Rick Winslow, PhD.



Students join Dr. Barth Wright in exploring the University's anatomage table–an advanced virtual dissection tool that allows students to study the full human anatomy without the use of a cadaver.

Measuring Outcomes

There are three significant areas of measurable and meaningful performance that are predictive of success for the next generation of physicians. These areas are national board examination scores, graduation rates and residency placement (the match) in graduate medical education (GME) training sites.

As briefly mentioned, KCU-COM performed very well on the national board examinations. COMLEX Level 1 is taken upon completion of the second year of medical school. Innovative changes to the curriculum were introduced in 2014, and meaningful results are reflected in the performance scores on COMLEX Level 1. The first-time pass rate is 98.8 percent, compared to a national pass rate of 92.76 percent. KCU-COM's mean score of 551 is 32 points higher than the national mean score of 519.[10]

The performance on the COMLEX 2-CE (Cognitive Examination) for first time takers is 96.8 percent, again above the national pass rate of 93.23 percent.[11] COMLEX 2-PE (Performance Examination) yields a first-time pass rate of 91.63 percent.[12] Passage of all three examinations is required in order to graduate with a Doctorate of Osteopathic Medicine.

Although not required, KCU-COM students who take the United States Medical Licensing Examination (USMLE) do very well on first-time pass rates. On USMLE Step 1, our pass rate is 96.9 percent compared to the national pass rate of 96 percent.[13] On USMLE Step 2, the first-time pass rate for KCU-COM students is 97.18 percent.[14] The national pass rate is not available. Performance on the national boards is a significant indicator of whether students will be successful in matching into the residency program of their choice.

Graduation rates from KCU- COM during a four-year curriculum have varied over the past 11 years but remain an indicator of the University's focus on student success. The class of 2016 graduation rate was 92.13 percent. The total graduation rate, including those students who needed five years to finish, is 94.25 percent.

Before graduation from medical school, students become candidates for residency training by participating in the match. By 2020, the Single Accreditation System

(SAS) will be fully implemented with oversight from the Accreditation Council for Graduate Medical Education (ACGME) for all GME programs. Several programs will have the unique distinction of Osteopathic Recognition (OR). The match is a very competitive process for which the University prepares all candidates to be "ready" in order to successfully begin residency training on day one.

Historically, residency placement rates have been very strong for KCU-COM's graduating classes. One hundred percent of COM graduates who have completed academic requirements and are eligible to participate in the match have successfully placed into residency training sites for the past three years. Through collaborative efforts with the Clinical Education Department, associate and assistant deans, Residency Placement Coordinator, GME administrator, chiefs of Departments and Specialties Medicine, the University provides guidance and counseling to the candidates in preparation for the match. Support is provided to every candidate to discuss realistic goals for being successful in obtaining competitive residencies; a dean's letter or MSPE (Medical Student Performance Evaluation) is written on students' behalf, commenting on academics (GPA, class standing, board scores, clerkship evaluations, shelf examinations), professional achievements and unique characteristics of each candidate.

Looking to the Future

During our first 100 years (1916–2016), the Kansas City College of Osteopathy and Surgery (KCCOS) — now Kansas City University College of Osteopathic Medicine — has graduated more than 10,000 doctors, approximately 8,000 of whom are still practicing, predominantly in primary care. Projections for the next 100 years suggest even more opportunities for growth and development of the University and its current and future generations of physicians and alumni who will have a significant impact on health care.

New generations of KCU students and graduates will continue to benefit from technological advances and will recognize the importance of medical informatics in their training and practice. They will receive innovative training in accessing resources, databases, current guidelines and treatment that will impact the quality of patient care they deliver. These advances in available resources will provide graduates a pathway to pursue a career that is dedicated to lifelong learning.

Evaluation of today's and tomorrow's students will always involve academic metrics; in addition, emphasis will include training focused on competency-based performance and achievements. The educational environment will continue to provide a state-of-the-art academic center for didactic presentations and break out rooms for small group discussions. The training in the new simulation center will enhance their clinical skills and depth of knowledge.

The future is bright for generations to come to receive high-quality medical education from the University's faculty and clinicians within the community, and to reap the benefits from rotating at some of the finest facilities in the region and nation. It is through these collaborative efforts that graduate medical education (GME) programs will develop to provide training in areas most needed, namely primary care. The quality of the medical school applications we receive and the quality of the medical education we provide will continue to produce well-trained, competent osteopathic physicians who will help meet the demands for delivering the health care our country needs.

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Addressing Rural Health Challenges Head On

by Marci Nielsen, PhD, Darrin D'Agostino, DO & Paula Gregory, DO

Abstract

Providing health care to patients and families living in rural America presents significant challenges, but comes with unique rewards. The physician who chooses a rural life typically cares for an underserved and aging population, which is often less healthy and affluent than its urban and suburban counterparts. At the same time, rural clinicians feel deeply connected to their patients and their communities. Physicians cite strong doctor-patient relationships as a primary motivator to practice in a rural setting, in addition to lower cost of living and slower pace of life[1]. Those who choose primary care specialties also enjoy the challenge of caring for multiple, interrelated aspects of health for their patients and community.

During Kansas City University of Medicine and Biosciences' (KCU) century-long history, we have offered our osteopathic medical students the opportunity to learn in rural areas during the third and fourth years. As our new, state-of-the-art medical school campus opens in Joplin, Missouri, we will build on our commitment to rural health by offering first- and second-year KCU-Joplin students training opportunities in rural settings, and expanding third- and fourth-year rural clinical rotations. The rich experience to learn rural medicine offers the potential to connect medical students, patients and community in new and exciting ways, building on the firm foundation of osteopathic medical training grounded in strong patient-centered primary care.



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Challenges of Rural Health

Health Professions Workforce Shortage

About 20 percent of Americans live in rural areas, but barely one-tenth of physicians practice there[2]. The federal government projects a shortage of over 20,000 primary care physicians in rural areas by 2025.[3] Primary care physicians in rural areas often do not have the support of sub-specialists, hospitalists, or emergency physicians, and thus treat a wider range of conditions with limited access to sophisticated technology. Most are required to admit and take care of patients in community-based hospitals, many of which are gravitating toward an emergency room and short-stay models of care[4], moving more complex patients to larger medical centers. This reduces clerkship training sites at small hospitals and can impact medical students' specialty choices in the future.

Limits of Rural Health Training Opportunities

Physicians are more likely to locate in the area where they train. Most U.S. medical schools and residencies are located in urban and suburban areas, resulting in fewer physicians choosing to locate in rural settings. Indeed, 99 percent of residencies are located in urban or suburban areas[5], and thus even those interested in rural practice may feel inadequately prepared for the challenges of working in rural communities. For middle- and high-school students interested in science, a dearth of rural physician role models limits exposure to medicine as a career choice. Moreover, students in rural settings may have fewer opportunities to receive the prerequisite math and science courses in undergraduate education curriculums that prepare them for medical school[6].

Population Health Challenges Among Rural Communities

In addition to the challenges of recruiting students to train in rural settings, rural physicians treat patients that tend to be older, sicker, and less well insured. Populations in rural communities are increasingly elderly; the average age for hospital admissions in rural

settings is over 65, and these older patients comprise one-half of all admissions. In contrast, older patients in urban settings account for just 37 percent of hospital admissions[2]. Many patients in rural communities also suffer from multiple chronic diseases and acutely feel the various social determinants of health that impact their well-being — from social isolation; to lack of access to affordable, nutritious food; to the impact of rural poverty. A recent large national study found that although those living in rural areas had a lower incidence of cancer than those living in urban areas, they suffered from higher rates of death. Researchers suggested that differences in cancer death rates might reflect disparities in access to health care and timely diagnosis and treatment, as well as behaviors related to tobacco use and obesity[7].

Delaying Care

Rural patients must often travel farther for their care and are reluctant to take time off from work. As a result, rural patients often delay seeking care, which can lead to a more complex illness and a sicker patient. For those in the self-employed farming community, who may live hours away from needed health care services, the challenges of caring for livestock and crops must be factored in, creating stresses unique to rural populations.

Missouri Demographics

Although flanked by large cities on opposite sides of the state, Missouri has 25 percent of its population living in rural areas[8]. Those living in rural Missouri earn less than those in urban areas ($33,078 vs $42,300[9]) and have higher rates of poverty (18.7 percent vs 13.5 percent). In addition, rural Missourians are more apt to drop out of high school (16.4 percent vs 9.9 percent) and have higher unemployment rates (5.5 percent vs 4.3 percent)[10]. The relationship between socioeconomic factors and health are well established, with those at the lower end of the income scale suffering worse health outcomes[11]. Accordingly, in terms of health status rankings by state, Missouri ranks 35th for women and children's health, 36th for general population health and 40th for senior health[12].

Role of Medical School and Graduate Medical Education in Addressing Physician Shortage

Kansas City University is one of six medical schools operating in Missouri. We are the number-one producer of primary care physicians for the state, with nearly 60 percent of our alumni practicing in a primary care specialty in Missouri, and 43 percent practicing in rural or underserved areas[13]. Our role is to train medical students during their first four years of medical education or undergraduate medical education (UME).

While UME and a number of factors impact the overall supply and distribution of physicians in each state, graduate medical education (GME) -- commonly known as residency training -- is also a significant determinant. Most GME is publicly funded through the Medicare program, which does not currently direct the $15 billion spent on GME to those areas of the country where health professions shortages exist. Instead, GME residency "slots" are determined by a federal formula that has been capped since 1997[14]. Although the number of students in U.S. medical schools (UME) has grown steadily to try to keep up with physician workforce demands, the number of GME residency slots has generally not been keeping pace. The majority of residency slots are currently found in the northeast United States (69 percent), are slotted for non-primary care (or specialist) training (86 percent), and are located in urban areas (99 percent).[15]

Leadership of KCU and Joplin Community

The health workforce shortages facing rural communities will require attention from business, government, philanthropy, universities, community colleges, and local community leaders, who must work together to recruit health professionals to care for their communities. Although the needs of caring for rural populations can be daunting, many physicians find the rewards of caring for underserved rural communities as a meaningful professional calling. Building on a history of more than 100 years of training osteopathic medical students to improve the well-being of the communities we serve, KCU has partnered with entrepreneurial leaders from across the Joplin region to open its new campus in Joplin, Missouri – our second campus in more than a century.

With a class size of 150 students, the unique partnership between KCU and Joplin leaders (highlighted elsewhere[16]) seeks to expand the rural physician workforce for the entire Midwest region. In addition to increasing the number of medical students trained, KCU-Joplin will feature cutting-edge technology

in the classroom. In light of its particular focus on primary care and rural health, the curriculum at KCU-Joplin will expose medical students to rural clinical settings earlier in their training (during their first and second years) and expand the number of rural clinical rotations in years three and four. The curriculum will also utilize innovative models of care including: telemedicine; distance learning; a team-based integrated approach to patient-centered primary care; and the creation of new clinical partnerships across the region to expand graduate medical education opportunities for our students.

Encouraging Rural Students

Encouraging medical students to practice in rural Missouri can be enhanced by recruiting and admitting qualified and motivated students from rural areas, and training them in rural settings across the state. One study found that students from a rural background were 10 times more likely to prefer to work in rural areas when compared with students from non-rural areas[17]. Of the 121 hospitals across the state of Missouri, 36 are considered to be rural (otherwise known as Critical Access Hospitals). Providing primary care services to Missouri communities are 367 Rural Health Clinics and 29 Federally Qualified Health Centers at 215 sites across the state[18]. Nearly a third of the first cohort of KCU-Joplin medical students grew up in the surrounding area and have expressed plans to remain in the region in order to help address inadequate access to high-quality primary care in the four-state rural region.

Training with New Technology

KCU will use state-of-the-art technologies to teach students, connect the curriculums on the Kansas City and Joplin campuses, and enhance the use of patient-centered telehealth services. New technology that reinforces clinical skills is on the forefront, and universities like KCU are working with the business sector to explore innovative avenues for student education, especially at distant rural sites. In the classroom, students will benefit from: new anatomy and osteopathic medical manipulation labs; advanced robotics for clinical simulation and standardized patients; distance learning technology to provide lectures and standardized curriculum; and newer blended educational models that use part online and part real-time clinical information to train students. For example, a student learning neurology would be able to access a stroke patient's mini mental status exam, imaging readings, and other relevant clinical information important to the patient, in addition to didactic course materials on neurology and stroke. This allows the preceptor physician to instruct students and residents with information similar to that assessed during a clinical rotation.

The use of telehealth and mobile health applications is expected to increasingly connect patients and their health care providers. Communication between physician and specialist has changed over time, from informal discussion to virtual consults and beyond. Technology will help patients who must travel significant distances to receive care and will be key to providing rural health services over the next 10 years. However, the use of technology does not replace the needed personal connection between patients and physicians, and more progress on the interoperability of health information technology is sorely needed. In Joplin, one health system has created a vast network of technology supporting physicians and assisting patients. KCU will train our students on the use of these technologies to care for patients as part of their medical school curriculum.

Expanding Early Clinical Experiences

Medical schools are typically part of a network of safety-net health care institutions. At KCU-Joplin, students will be afforded the opportunity to work with physicians in rural settings in years one and two in medically underserved communities. This will foster experiences in patient care and physician mentorship early in the students' education, with the goal of exposing them to patient-centered team-based care that embraces a whole-person perspective of health, addressing socioeconomic factors that affect patients' well-being and impact community health. Students report they enjoy these experiences and look forward to building healing relationships with patients and learning about health disparities, particularly the challenges facing rural communities with patients who suffer from multiple chronic conditions and barriers to care. With deep connections to the local health

care network not typically seen in urban settings, medical schools like KCU have the opportunity to partner with rural local and regional physicians and hospitals to guide, train and motivate students to consider rural health opportunities after medical school graduation.

Increasing GME in the Joplin Region

Historically, Kansas City University has had a robust process of assisting medical students with residency placement. Through collaboration with local Joplin hospital systems and leaders, KCU will help to foster growth in the number of residency programs and expand the number of residency slots in the region. We will work with area hospitals and clinics to take advantage of the various federal and state programs designed to expand much needed GME residency slots in rural and primary care settings. Currently, these programs range from incentivizing hospitals to expand the number of residency slots, to supporting the development of Teaching Health Center GME programs, to partnering with Veterans Affairs GME expansion programs, to expanding GME funding through Medicaid[19]. Since the distribution of residency programs favors non-rural settings, placing new residency programs in rural areas could further ensure that physicians remain connected to these areas of need.

Conclusion

Kansas City University has taken the bold step of opening an additional campus in Missouri in partnership with regional leaders from across the Joplin, Missouri, area. As the first new medical school in Missouri in nearly 50 years, we seek to improve health and wellness by training and retaining physicians for Missouri, with a particular focus on rural health and primary care. By instilling in our students an understanding and appreciation for the unique challenges of caring for rural communities, we hope to inspire our students with a whole-person perspective that improves the health of the region and the state. As our new osteopathic medical school campus opens in Joplin, KCU is proud to build on our more than 100-year history of training medical students grounded in strong patient-centered primary care. By offering first- and second-year KCU-Joplin students training opportunities in rural settings, expanding third- and fourth-year rural clinical rotations, and working to expand GME residency opportunities in the region, we remain committed to our mission of improving the well-being of the communities we serve.

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MM

Flagship Program Provides a Model for Early Clinical Exposure, Service to Community

by Ray Newman, MD, Anne VanGarsse, MD & Annette Campbell, RN

History

For nearly a quarter of a century, a large-scale health screening program, now known as Score 1 for Health®, has served elementary school children in the urban core of the Kansas City metropolitan area. This program, sponsored by Kansas City University of Medicine and Biosciences (KCU), illustrates the unique role a medical school can play in improving the health of the community it serves.

The program began in 1993, when a local nurse set out to assess if the health needs of school children were being met. She completed a community needs assessment of the neighborhood surrounding the former Park Lane Medical Center and discovered that a significant number of children enrolled in local elementary schools had unmet health needs. Following this discovery, the nurse implemented a program aimed at performing health assessments on children enrolled in two elementary schools near Park Lane. During the first year of the program, 240 school children from the area included in the initial needs assessment survey received free health screenings.

Following these early strides, the program began to experience significant growth. By 1996, it had grown to include nine schools in the Raytown School District, necessitating the addition of a second nurse. This was also the year in which Dr. Bob Ricci, chief of staff at Park Lane Medical Center and dean of the University of Health Sciences (UHS) — now KCU — saw an opportunity to involve second-year medical students from UHS. He incorporated the medical students into the program by having them perform the physical assessment portion of the health screening. By this time, the program had formed partnerships with local nursing schools and the University of Missouri-Kansas City (UMKC) School of Dentistry, leading to increased manpower, the provision of additional services and further growth.



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Community support for the program began early on, when it caught the attention of former Kansas City Chief, Deron Cherry. Through the generosity of the Deron Cherry Foundation, proceeds from the Deron Cherry Celebrity Invitational golf tournament began to help support Score 1 for Health. His association with the program also led to grants from other NFL Charities for the purpose of supporting Score 1.

By 1999, 3,700 children in 13 schools were being served annually by Score 1 for Health. In 2000, as a result of Park Lane Medical Center's closure, UHS absorbed Score 1 for Health, adopting a formal mission of "serving the underserved." In 2001, with strengthened support from the University and a grant from the Kauffman Foundation, the program more than doubled in size. This growth included a new partnership with the Kansas City Missouri Public Schools, adding eight schools in 2001 alone. In 2005, the program expanded across the state line to include schools from USD 500, a large urban school district in Kansas City, Kansas. By 2007, nearly 13,000 children were being served by the program, and a follow-up component was developed to reach out to parents in the days following the health screenings to answer any questions regarding screening results.

The years following 2008 have been years of growth in terms of grant funding, continued outreach, service

to the community, staff, and technology. Additionally, the program has been able to provide valuable and unique information back to the community and to community leaders regarding the health status of children living within the program's boundaries. The Score 1 for Health program is a unique and special program that is now deeply engrained in the culture of KCU and the community in both academic and community service sectors.



Score 1 for Health's CHAMPS program, which pairs KCU students with local families to provide healthy lifestyle coaching, celebrates a successful cohort.

How the Program Works

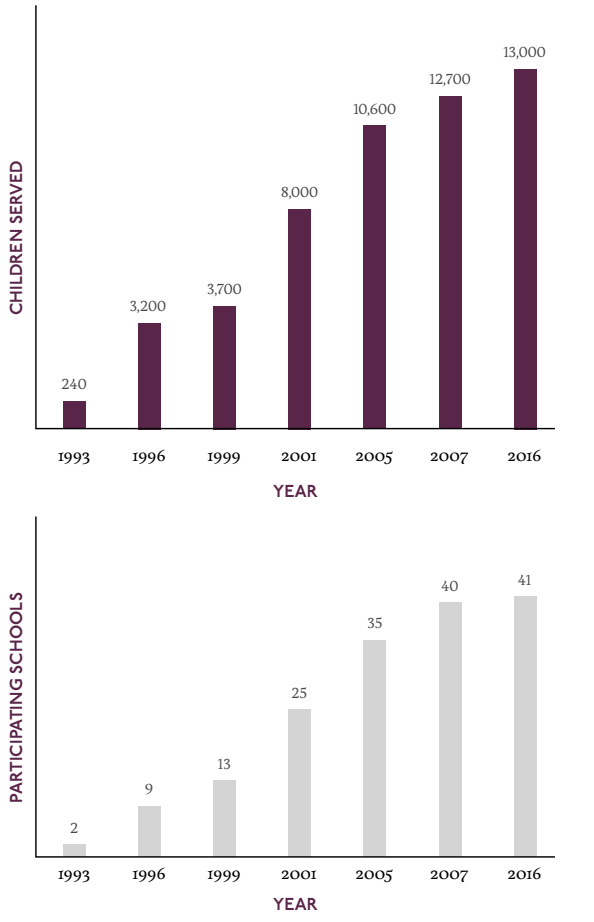
The program would not exist if it were not for a supportive University, a supportive community and an incredibly dedicated Score 1 team.

Nearly all of the elementary schools participating in the Score 1 program have a very high percentage of students enrolled in the free/reduced school lunch program, and the families of these students face more challenges than most in terms of finances, transportation and equitable access to health care. The elementary school nurses (when there is one) and the principals at these schools are instrumental in engaging the teachers and families in Score 1 and making the value of the program known. Prior to a screening day, all children participating in the program must have a consent signed by their parent or guardian. While it is made clear to the family that the Score 1 screening is not meant to take the place of well-child visits, teachers report that Score 1 provides the only medical assessment some of their students receive.

Today, the Score 1 team is led by a group of full-time registered nurses in the roles of director, school/community outreach coordinator and screening coordinator. Also included on the team are an office coordinator, registered dietician, community health worker, program coordinator, data entry specialist and data entry clerk, and 10 PRN nurses who help on screening days. A pediatrician (a member of the clinical faculty) serves as the medical director of the program. On screening days, nursing students from area nursing schools and dental students join the medical students at screening sites. Members of the KCU clinical faculty, along with several community physicians, serve as supervisors for the medical students. Nursing instructors and the Score 1 nurses supervise the nursing students, and the dental students receive supervision from the faculty of the UMKC School of Dentistry.

On approximately eight afternoons scattered throughout the first and early part of the second semester, the approximately 250 second-year medical students at KCU board buses and are transported to elementary schools throughout the urban core and close suburbs of both Kansas City, Missouri, and Kansas City, Kansas. They are met at the schools by the nursing students, dental students, Score 1 team and supervising faculty. There are approximately 45 elementary schools that participate in the program, with between four and six schools visited on each screening day. The nursing students measure and weigh all the students,

SCORE 1 PROGRAM GROWTH



calculate the BMI and screen everyone's vision. The medical students obtain a blood pressure reading and perform a modesty-protecting physical exam. Finally, the dental students along with some of the medical students screen everyone for tooth decay and other dental issues. Kindergarten classes through fifth or sixth grade participate and all findings are documented, with positive findings confirmed by a supervisor. If it is determined a child needs to see his/her physician, a note is sent home with the student that includes the findings and the recommendations of the screener.

After the day of the screening, the Score 1 team goes to work. A letter is generated and sent to the parents with height, weight, BMI, results of the vision screen, and findings of the physical exam and dental screening. This letter contains educational information about BMI, what it is and what it means. If students have failed vision screens or have abnormal blood pressure measurements, a Score 1 nurse will return to the school to repeat the screen and make appropriate notifications and arrangements. The last step is a phone call to the families of screening participants several days after the event to answer any questions they may have about the Score 1 letter. Again, if follow-up with a physician was recommended, they are encouraged to seek appropriate care. If they do not identify a primary care provider, recommendations are given. If the school has a nurse, he/she is made aware of any findings needing further attention and becomes an important liaison in the effort to communicate with and educate the family.

Score 1 collaborates with many community organizations and has developed several programs and services in response to the needs identified by families. For example, finding adequate and affordable support to combat obesity is a need many parents of obese children have reported. Score 1 designed the CHAMPS program, currently grant-funded by a local community health foundation, to help meet this need. In this program, medical students are first trained by a pediatrician and a dietitian. These medical students are then matched, one-to-one, with a child and his/her parents to provide education and coaching for healthy lifestyle modifications. The program is free, flexible for families, and provides a rich opportunity for medical students to actively engage with the community. They learn how to assess and counsel children and parents from culturally diverse and mostly low-income households, educating them on how modification of lifestyle and changes in behavior can have a positive impact on health.

Why Score 1 for Health?

The benefits of Score 1 for Health are multifaceted. First and foremost, it benefits the children of the community in several ways. Because schools that participate in Score 1 serve families and neighborhoods in which the social determinants of health could be described as poor to fair[1], for some children it provides an interface with the health care system they might not otherwise experience. On screening days, it is not unusual for the screeners to identify a physical finding needing further evaluation, a dental condition requiring dental care, or a social situation needing further investigation.

For example, consistent with published literature on the childhood obesity epidemic and its disproportionate effect on children in an urban-core setting, 40 percent of the children screened by Score 1 are found to be overweight or obese upon calculation of their BMI.[2] Score 1 provides the opportunity to educate the families about the BMI, what it means, and how obesity increases the risk of hypertension, Type 2 Diabetes and heart disease. Dental caries can be a cause of school absence, poor nutrition and pain in children. Oral health exams performed on screening days demonstrate untreated dental caries in 27 percent of the children whose families are then instructed to seek dental care for their child. If a child fails his/her vision screen on the first attempt, it is repeated at a later date. On average, 19 percent of children whose vision is screened are referred to a vision care specialist. The goal of the Score 1 program (and the desired result) is to connect families to health care services and promote good health in children, helping them reach their full potential.

Score 1 for Health screenings give the elementary school children an opportunity to interact for a short time with a diverse group of young, energetic medical students and nursing students. This interaction occurs in a safe, familiar and non-threatening environment. Although these children are not yet likely planning their future careers, exposure to health professions students could plant the seed of interest in a health care career that, if nurtured, would grow as years pass.[3] The medical and nursing students can often be heard asking their young elementary school counterparts, "What do you want to be when you grow-up?" Hopefully Score 1 is inspiring at least a few who will become the health care professionals of the future.

Score 1 for Health is also beneficial to the medical students at KCU. Score 1 gives them the unique opportunity to see a community from the vantage point of those who actually live there. It provides a real-world lesson on the impact that social determinants can have on the health of children and families, and it serves to remind the students of the immense challenges many families face on a daily basis. This program provides extensive experience in how to approach, examine and communicate with pediatric patients. This pre-clinical pediatric experience is unique among medical schools in the US and helps prepare KCU students for their third-year pediatric clerkships. Moreover, Score 1 provides an opportunity for medical students to see themselves as part of a team-based approach to care, highlighting the importance of professionalism. Having medical, nursing and dental students working together to accomplish these screenings provides an educational opportunity for valuable inter-professional interaction and inter-professional coordination and cooperation.

Score 1 provides an early clinical experience for medical students, and while it involves children and is particularly inspiring to those interested in pediatrics or family medicine, the experience is beneficial to all of the health professions students. The nursing, dental and medical students are an essential and valuable part of the entire Score 1 effort. Unlike most early clinical experiences in which students merely observe and listen, students at Score 1 weigh, measure, obtain vital signs and examine the children and then document their findings. There is great value to the work they do, and their contribution is vital to the overall goals of the program. Their efforts impact both the children being screened and Score 1 for Health as a whole. The feeling of being a contributing member of a medical team has been shown to combat the "burnout" sometimes experienced by health care learners, and it helps bring meaning to the extraordinarily hard work of medical school.[4]

KCU is proud of Score 1 for Health, as it is a very unique program in both the academic and community sectors. Currently, scholarly efforts are underway to more objectively assess the benefits of this program for the children screened, the collaborating schools and the professional students involved in the screenings. It is hoped that Score 1 for Health will become a model for other academic institutions and communities wishing to develop their own large-scale childhood health screening programs.

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MM

How Kansas City University is Creating a National Model for Student Wellness

by Richard Winslow, PhD

I was sitting in a presentation at the 2016 conference of the American Association of Colleges of Osteopathic Medicine in Washington, D.C., when the student presenters shared the data that they had collected from osteopathic medical students nationwide. And I almost fell out of my chair.

Ten thousand medical students responded to the Council of Osteopathic Student Government Presidents (COSGP) survey designed to measure levels of depression and anxiety. The conclusion they had reached was that, nationwide, 54 percent of osteopathic medical students self-reported being clinically depressed and/or anxious at some point during their four years in medical school. Fifty-four percent.

Recent studies, such as Rotenstine, Ramos, Torre, et al. (JAMA. 2016;316(21):2214-2236), had provided conclusions that 20 to 27 percent of medical students nationwide were clinically depressed at some point during their medical school years. My own professional experience working with medical students on a daily basis led me to believe it was somewhat higher than 25 percent, a number already substantially above the general population. But when you begin to consider that over half of our medical students are depressed and/or anxious, that is an overwhelming number.

If we as medical professionals and educators were confronted with over half of our patient population having the flu or meningitis, for example, we would label it an epidemic, declare a public health crisis, and begin emergency procedures to treat and care for the sick. Yet, historically, medical educators have accepted that being burned out, unhappy and even depressed is just part and parcel of the gauntlet that is medical school and medical training. And in many cases, medical educators have even actively encouraged systems, traditions and practices designed to frustrate future physicians to, in essence, "toughen them up."

Four years ago, we began a discussion at KCU about how we could place student wellness at the heart of our Student Services philosophy. We began planning for how we could systematically address burnout, stress levels, depression, suicidality and general wellness.

There is a clear need to do this in a way that is different from the status quo at most medical schools. National research is unequivocal in demonstrating that the medical educational philosophies of the 1960s and 1970s simply don't work with this current generation of students. And achieving these changes is possible without breaking the bank. The following is how KCU set about focusing on student wellness.

Systematic Changes to Student Services

Five years ago, Student Services at KCU was a diffuse group of administrative offices that had individualized missions, visions, and goals. We changed that by bringing all student-related services — Admissions, Financial Aid, Registrar, and Student Affairs — under one department, run by a single vice provost.

This approach allows us to work toward a single mission and a single set of common goals for all four offices and provides for more collaboration in how we offers programs and services to our students, in both our College of Osteopathic Medicine (COM) and our College of Biosciences (COB).

Secondarily, we place our singular focus on making sure we're positively enhancing students' experiences on a day-to-day basis. Customer service has become a natural priority, and in a couple of our offices, we have changed cultures that previously were focused on saying only "no" to students, to a culture that now



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Activities such as yoga, held here as a sunrise session during a Wellness Week, bring students together to release the stresses of academic rigor.

emphasizes saying, "Let me see how I can help you solve your problem…"

These cultural changes allow us to more clearly and effectively emphasize the osteopathic foundation of insuring that our students' minds, bodies and spirits are cared for on a daily basis.

Enhancing Counseling Services

One of the major additions we made to Student Services was creating an on-campus, full-time Office of Counseling Services. Prior to this decision, students were referred off-campus to clinicians through the University's employee assistance program (EAP).

We added two full-time, doctorate-level licensed psychologists to begin meeting with our students. The effects of this change were felt immediately. Students quickly filled the new 70 hours per week of counseling sessions that were available. And for student crisis situations, Student Affairs added two new staff who are available to assess potentially suicidal students on-campus, just a short walk away. This saves time and provides immediate care for our students in crisis.

In addition to the new on-campus resources, we kept our EAP contract in place, primarily so that we would have a nationwide network of providers for our third- and fourth-year rotating students. This provides them with mental health care and support while outside of the Kansas City metro area, via an easily accessible website and a 1-800 hotline.

Lastly, our Office of Counseling Services sponsors a year-long series of seminars focused on emotional intelligence. These seminars, available to our medical students, are shaped to provide both information on personal wellness and professional balance. Some of the topics of the seminars have included: "Emotional Wellness and Bioethics," "Emotional Wellness and Being a Trauma Surgeon," "Emotional Wellness on Clerkships," "Emotional Wellness in the Operating Room," "Emotional Wellness in the Emergency Room" and "Emotional Wellness in Internal Medicine," to name a few. These seminars are taught by our own faculty and some of our KCU alumni.

Changes in Student Activity Programming

Each year, when the Office of Student Affairs is considering its budget requests for the upcoming fiscal year, the conversations around the table are no longer about "fun stuff" we can do for students. Rather, the conversations have focused on "What fun things can we do for students that emphasize personal wellness?"

As we have planned these events for students, we really have focused on how we can impact the whole student. Examples of programming include:

Mind

- Meditation and mindfulness classes taught by one of KCU's Buddhist faculty members
- Emotional intelligence workshops
- Motivational speakers such as Dayton Moore, general manager of the World Series Champion Kansas City Royals
- Regular interaction with certified therapy dogs that are brought to campus during stressful weeks

Body

- On-campus yoga classes
- Group runs around and near campus
- Core workouts
- Chair massages, on-campus, by certified massage therapists

Spirit

- Faith-based celebrations such as Ramadan, Christmas, and Hanukkah
- Support from student-organized and student-run religious organizations, such as our Muslim student organization
- Student access to a university chapel for daily prayer and reflection
- Peer encouragement programs, which tap students to identify and communicate positive reflections with their medical student and master's degree peers

Consistent and Ongoing Student Well-Checks

As a proactive step to identify at-risk students as early as possible and apply effective interventions with those students, KCU has begun administering the Maslach Burnout Inventory (MBI) to our medical students and master's-level students. This nationally recognized tool allows the University to gauge each student's personal level of burnout, which is often predictive of levels of depression and anxiety.

The MBI is sent to students at the midpoint of each of the fall and spring semesters. All students are required to take the MBI. Once individual results are available, students are then placed in three separate categories based upon their inventory scores: 1) a high-risk category, identifying students who need immediate intervention; 2) a moderate-risk category, identifying students who need follow-up, but not immediately; and 3) a low-risk category, including students who do not need any follow-up at the time. Each of the students in categories one and two is assigned to a Student Affairs staff member for personal follow-up.

Interventions with students may include a visit to Counseling Services, a referral to an off-campus psychiatrist, and/or an appointment with one of our Learning Specialists to assist the student with academic problems. Each intervention is specifically tailored to the individual student's needs.

Development of Student Wellness Council

KCU has formed a Student Wellness Council, which fosters a culture of advocacy, promoting students' personal growth, wellness and resilience.

Our Wellness Council meets once a month and consists of students from each of our COM classes, as well as representatives from our COB class. Each meeting is student-driven and focuses on: programming for students outside of class; our curriculum and ways we can improve student wellness from an academic perspective; and the opportunity to talk about University systems, policies and procedures.

As administrators working with the Wellness Council, we take student concerns and ideas to other administrators and faculty and serve as a bridge between the Council and the University administration. So far, we are seeing positive results.

Intentionality

"Wellness" has become one of those trendy words within higher education and especially within medical education during the last year. Ultimately, the success of any program designed to ensure students' health and happiness should not be based upon trendy words. The success of any program should be based upon intentional effort, every day, to promote student well-being through the University's mission, vision, values, goals, decisions, planning and actions.

Remember that nationally, 54 percent of our medical students are telling us that they are clinically depressed because of the educational experience we are providing for them. This should be a call to action for all medical educators to no longer continue the status quo. If we are able to change this paradigm now, what we will find in the future are healthier students, healthier residents and healthier physicians in our communities. And each of them will be modeling to their patients how to find wellness in their own lives. **MM**

Training Medical Scientists of the Future

by Robert White, PhD, Larry Segars, PharmD, Marshall Andersen, PhD & Margaret Kincaid, PhD

Introduction

Kansas City University (KCU) established the College of Biosciences (COB) in 2004 to offer a graduate education to students wishing to pursue a Master of Science (MS) in Biomedical Sciences. Since the graduation of the first class in 2006, there has been significant growth in the number of graduates. The College's vision is to educate graduate students from diverse backgrounds in an environment that allows students to develop into critically thinking innovators in research and health care professions. Students interested in pursuing a MS degree in Biomedical Sciences can enroll in either the one-year non-research or two-year research program. Beginning in fall 2017, a new addition to the COB will be the Doctor of Clinical Psychology (PsyD) program.

To meet the College's mission of fostering intellectual development and scholarly training, students complete advanced coursework in various required and elective biomedical sciences. Graduates of the MS in Biomedical Sciences degree programs are prepared for careers in research, teaching or service in the life sciences and health care fields. Our COB alumni have successfully entered into graduate and doctoral training programs in various health care professions, including medicine, dentistry, pharmacy and nursing.

Graduate Education in Biomedical Sciences

The largest student enrollment in the COB is in the one-year non-research (non-thesis) track culminating in a Master of Science in Biomedical Sciences degree. This degree program began with seventeen students in 2005 and has grown to over 100 students today. The program track is structured to provide graduate students with advanced education in the biomedical sciences, including core courses in anatomy, physiology, biochemistry, molecular biology, immunology, cell biology, and epidemiology. Students also select from elective courses, including microbiology, histology, human development, and human genetics. This program track culminates in graduate students developing and presenting a scientific seminar lecture to faculty and peers and the successful completion of a comprehensive examination.

Training Laboratry Research Scientists

Graduate students who select the two-year research (thesis) track conduct studies under the mentorship of a primary investigator, who serves as the students' thesis committee chairperson. Current research-track students are studying neurodegenerative diseases (Parkinson, Alzheimer), musculoskeletal diseases (Duchenne muscular dystrophy), virology (Zika virus) and hematological diseases (iron overload and leukemia). Student research activities occur on the main KCU campus in laboratories in the Dybedal Research Center, as well as at partner institutions within the Kansas City area, including Midwest Research Institute (MRIGlobal). The students' research culminates in a written thesis and a public thesis defense of their project. Student research is presented at national biomedical conferences, including the American Society of Human Genetics, American Society of Hematology and American Association of Cancer Research. Many of the graduate students in the two-year track are interested in becoming future physician-scientists, and KCU's master's program effectively prepares them to become premiere research physicians.

Programmatic Support and Successes

To support career selection among all graduate students, KCU has added a dedicated Career Counselor to the staff, who serves the Student Services division in guiding students to career options, including subsequent educational training in the fields of medicine, pharmacy, nursing, physician assistant, optometry, physical therapy and health care law, to list just a few examples. For the



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Inside his on-campus lab, Dr. Abdulbaki Agbas guides a student researcher in leading-edge research techniques.

COB Class of 2016, 68 percent transitioned into doctoral training programs, with the majority entering medical school at either KCU or national medical schools. An additional 6% of this graduating class found careers or jobs that were related to the biomedical sciences.

One of the exciting examples of KCU-COB's mission of generating the scientist of tomorrow is two-year research student Macy Potts (Class of 2018). Potts has a promising opportunity to work on understanding how the Zika virus leads to disease. She is actively working in partnership with a nationally recognized researcher at MRIGlobal, Dr. Carl Gelhaus. For Potts, this means being involved in unique and vital research, and learning from a premier researcher in Kansas City involved in the fight against a major threat to global health. This team of biomedical scientists is working hard to make a difference in understanding Zika, potentially leading to the development of a treatment for the disease and for the devastating medical outcome associated with it. KCU is extremely proud of this win-win collaboration. Our student has a career-defining research opportunity, and MRIGlobal has an outstanding and passionate student-investigator to mentor and train as a future biomedical researcher.

Future Programs

The COB has undergone tremendous growth in its enrollment, and now is moving forward with the development of new programs, such as the Doctor of Clinical Psychology, which will begin in the fall of 2017. Consistent with this approach, the College is exploring the development of a PhD in Biomedical Sciences program. This program will constitute a significant research engagement by doctoral students. Currently at KCU, areas of research include neurodegenerative disease, neuromuscular disorders, cardiology and hematology studies. In addition, graduate student research opportunities at partner institutions in the areas of cancer and infectious disease, along with research on endocrinology-based illness, such as Type 1 diabetes, will enhance the success of PhD research impacting these fields. With the further development of research at KCU and its partnerships with other institutions, KCU believes the time is right to explore this new program. The establishment of a PhD program also creates the opportunity to develop a dual degree DO/PhD program for the training and education of physician-scientists who would bring their biomedical sciences expertise to clinical health care in a translational fashion. The prospect of deriving findings in the clinic, which would drive research activities in the laboratory for development of studies and lead to information that could be returned to the clinic and bedside of patients for innovative treatments, would be the goal of this program. **MM**

Advancing Health Services Teams: KCU Launches Only Clinical Psychology Program in the Two-State Region

by Sarah E. Getch, PhD

Growing Need for Mental Health Providers

About 30 percent of the residents of Kansas and Missouri live in counties that are designated a Mental Health Professional Shortage (MHPSA) area. In fact, on average, Kansas has one mental health provider per 580 residents, while Missouri has one provider per 630 residents.[1] To put this in perspective, the average caseload for psychologists is between 25 and 45 patients, with most patients being seen on a weekly basis for 50-minute sessions.[2] Both states currently struggle and rank well below the top U.S. performers in responding to the mental health needs of their populations.

This shortage plays out on a national level as well, where it is projected that another 70,000 mental health providers will be needed nationwide by 2025 to meet the demand.[3] Although the Affordable Care Act includes provisions to ensure coverage of mental health services, how individuals access mental health services has put a spotlight on the relationship between primary care providers and mental health providers and their ability to work together. Primary care providers often act as the first line of response for their patients who present with mental health concerns. In addition, many individuals with chronic illness also suffer from behavioral health issues.[4] However, under the current reimbursement model, primary care providers frequently lack the time and training to be able to effectively diagnose and treat behavioral health issues. Thus, the field has moved to integrating behavioral health providers within primary care settings and the creation of health service teams.



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Geropsychology, a growing need for our nation's aging population, is offered as a specialty area of study within KCU's PsyD program.

Psychology programs are ubiquitous throughout higher education. There has been steady growth in the profession over the years, and the United States Bureau of Labor Statistics projects jobs in the profession will grow at a rate of 19 percent during the period 2014 to 2024.[5] Although most major institutions in Missouri and Kansas offer doctorate psychology programs, none of these institutions is currently offering the clinical practice-oriented PsyD program. In addition, existing PhD programs enroll very few students annually, and these students primarily focus on research. Considering the projected growth of the profession, the absence of direct competitors, and the shortage of mental health professionals in Missouri and Kansas, Kansas City University of Medicine and Biosciences (KCU) saw an opportunity to develop a robust and successful training program for clinical psychologists and has begun recruiting students for a new program that will open this fall.

PsyD at KCU

Clinical psychologists are trained to address the psychological needs of individuals from all backgrounds, ethnicities, races and ages. Students in the clinical psychology PsyD program at KCU will gain the knowledge,



An emphasis on interprofessional education helps prepare students from both KCU's College of Osteopathic Medicine and PsyD program for a future of team-based health care delivery.

skills and attitudes necessary to practice as highly competent, caring, patient-focused clinical psychologists who are able to pursue careers working with children, adolescents, adults and older adults. Throughout the five-year program, students will be exposed to a broad base of discipline-specific knowledge and will be trained in the following profession-wide competencies required by the American Psychological Association (APA): (i) Research; (ii) Ethical and legal standards; (iii) Individual and cultural diversity; (iv) Professional values, attitudes, and behaviors; (v) Communication and interpersonal skills; (vi) Assessment; (vii) Intervention; (viii) Supervision; (ix) Consultation and interprofessional/ interdisciplinary skills.

As we look to the future of health care, there are two growing trends. First, health care providers will be treating a growing population of older adults. In fact, this is the fastest-growing sector of the U.S. population, with adults over the age of 65 increasing from 13 percent of the population in 2010 to 16 percent in 2020.[6] And, unfortunately, while nearly 20 percent of older adults will suffer from mental illness, currently only 3 percent of psychologists are trained to treat them.[7,8] The APA has recognized the shortage of providers trained to work with older adults and made a call for more geropsychology training opportunities for psychologists. KCU has answered. In addition to establishing the broad foundation of knowledge and skills mentioned above, the PsyD program at KCU will provide students with two years of geropsychology coursework, along with geropsychology-focused training sites and geropsychology-focused research opportunities for those interested in pursuing a specialty in geropsychology.

The second trend in health care is the continued push toward integrated health care and the need for health care professionals to be able to deliver team-based care. As previously mentioned, primary care settings are often the first line of response for patients with mental and behavioral health concerns, thus prompting the integration of behavioral health providers and team-based approaches in primary care.

Research has shown that a team-based approach to care delivery can not only result in improved quality of care, productivity and efficiency, but also an increase in satisfaction among both patients and clinicians.[9,10] Increased support of health services teams — both in the literature and practice — places increased pressure on health professions education and training programs to incorporate interprofessional education in the curriculum early and often.

One way the KCU clinical psychology PsyD program has responded to this curricular need is to integrate courses, such as Psychopharmacology, Physiological Psychology, Integrated Health Care and Consultation into the current medical school curriculum. Our PsyD students will learn alongside medical school students in order to promote integrated health care and learn from each other. In addition to integrating students in the classroom, KCU provides an interprofessional education experience through our screening program, Score 1 for Health. Score 1 for Health provides 13,000 free pediatric health screenings and outreach annually for children from under-resourced neighborhoods and has grown to include KCU's medical and psychology students. By utilizing the Score 1 screening program as a platform for assessing interprofessional competencies, both psychology and medical students learn to develop the basic communication and professional skills necessary to operate effectively on a health care team.

Osteopathic physicians have long aimed to treat both mind and body, making the pairing of PsyDs with DOs a logical fit. Osteopathic medicine is defined as a complete system of patient-centered medical care focused on the whole person and based upon the idea that a person is the product of dynamic interaction between body, mind and spirit. Thus, osteopathic physicians are grounded in the mind-body connection: our mental health affects our physical health, and our physical health affects our mental health. Research confirms that behavioral and social factors cause or contribute to nearly every cause of death, illness and disability and directly cause approximately half of the deaths each year.[11] Indeed, an estimated 85 percent of physician visits are for problems that have a psychological or behavioral component.[12] Early interprofessional education between osteopathic and psychology students aims to strengthen the understanding of how psychological and physical aspects of health are interrelated. Psychology students will benefit from exposure to the medical model and biological basis of health that frames osteopathic student training, while osteopathic students will benefit from effective strategies that psychology students employ in practice that promote behavioral change.

Our work in building the KCU PsyD program is as complex as it is rewarding. We are establishing a high-quality curriculum delivered by expert faculty to provide excellent training opportunities and engage our students in interprofessional experiences, all with an eye toward the future of health care. At each level — curriculum, training, interprofessional education — we are laser-focused on creating opportunities for students to contribute to improved population health outcomes. From this perspective, KCU has not simply added another academic program to an already successful health sciences university. Rather, KCU has remained true to its mission, continuing to serve and keeping its promise to improve the well-being of the surrounding community.

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Leveraging Partnerships and Collaboration to Advance Research: Kansas City Musculoskeletal Disease Consortium

by Edward O'Connor, PhD, Robert A. White, PhD & William Duncan, PhD

Research at Kansas City University of Medicine and Biosciences (KCU) embraces the University's mission of "improving the well-being of the communities we serve" through scientific discovery and meaningful partnerships. As most scientists discover early in their careers, their endeavors cannot be accomplished alone. Partnerships and collaboration are primary ingredients of success in biomedical research. When researchers come together across institutions to share their ideas, resources and expertise, the results often exceed all expectations. KCU researchers are exploring innovative discoveries that may one day treat debilitating disease, expand the understanding of health and illness, and improve the health of our community.

A significant area of study at KCU focuses on understanding and developing innovative treatments for neurodegenerative and neuromuscular diseases. To that end, and in the spirit of collaboration, in 2015, KCU joined the University of Missouri-Kansas City (UMKC) and the University of Kansas Medical Center (KUMC) to develop the Kansas City Musculoskeletal Diseases Consortium (KCMD), a partnership dedicated to bringing together scientists and resources focused on these critical areas of research. Since that time, the University of Missouri-Columbia (MU) has also joined KCMD.

This unique consortium is the first initiative of its kind in Kansas City and provides opportunities to combine the individual strengths and resources of the four health sciences schools to advance translational research. Sometimes referred to as "bench to bedside," translational research harnesses knowledge from the study of basic sciences to produce new drugs, devices and treatment options for patients. The goal of this partnership is to build medical research teams that will focus on specific diseases of muscle and bone, thereby accelerating the process of turning discoveries into clinical treatments, while also improving research education opportunities for health sciences students.

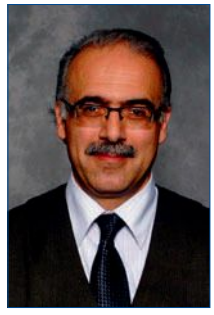


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For example, KCU's Dr. Jingsong Zhou is conducting studies in which she is helping us better understand the etiology of ALS (Amyotrophic Lateral Sclerosis), commonly known as Lou Gehrig's disease, so named after the legendary New York Yankees baseball player who contracted this disease. Zhou is advancing our knowledge as to how ALS arises and the cellular contributions to its development. She has focused on the role of mitochondria in the development of the disease. She also is examining novel treatments which someday may impact the treatment and well-being of these patients.

Zhou's work is being conducted in collaboration with several scientists who are a part of KCMD. Zhou shares: "KCMD brings scientists together from four universities who conduct research in neuromuscular diseases, and also provides grant support for joint projects among the universities. I am currently in the discussion phase with Dr. Barohn's group at KUMC for developing a potential grant application in ALS research."



Zhou's colleague, Dr. Abdulbaki Agbas, is also looking into the development of biomarkers for the detection of ALS and other

neurodegenerative diseases such as Alzheimer disease and Parkinson disease. In this latter research, he is working with investigators at KUMC where many of these patients are seen and treated. Agbas indicates, "I am also collaborating with researchers at KUMC to test the oxaloacetic acid treatment on the ALS –model G93A mouse. The preliminary data are so compelling that we have submitted another proposal involving clinical trials. It is the KCMD pilot project that has made these collaborative studies possible."

Another example of leading-edge research conducted at KCU in collaboration with scientists from UMKC can be found in the work of Dr. Robert White, dean of the KCU College of Biosciences. He has been working for years on a novel treatment idea for patients with Duchenne muscular dystrophy (DMD), a progressive muscle disease that leads to immobility, patients' use of wheelchairs by age 12 and premature death. Currently, there is no cure for DMD despite decades of research.



White discovered a "cousin" protein to the type of protein found missing in patients with DMD, and together with scientists at KCMD institutions (UMKC and KUMC), was able to perform gene therapy in mice, with positive results. White and his team of scientists from KCMD member institutions were able to show that mice with DMD were rescued from their severe heart disease and lived a normal lifespan compared to non-DMD mice. "The collaborative efforts with scientists at KCMD research institutions were imperative to our success," noted White. "Studies conducted in collaboration with UMKC histology labs, along with investigations with the Hoglund Brain Imaging Center and Transgenic Mouse Facility at KUMC, would not have been possible at KCU," he added. "Our ability to reach successful outcomes in this research would not have happened without these partnerships."

Dr. Asma Zaidi, a KCU investigator who focuses on neurodegeneration in Alzheimer's disease and in aging populations, has dedicated her life to understanding this complex illness. Her study is tackling the questions associated with understanding the foundation of these clinical diseases, specifically calcium channels and the proteins associated with them. Her efforts are also complemented by collaborative partnerships with scientists at KCMD member institution KUMC.



Consistent with an effort to understand neuromuscular disorders, another KCU scientist, Dr. Eugene Konorev, is studying the role of biological pathways in the development of microvascular defects in heart disease. Many American patients and their families are all too familiar with the devastating effects of heart disease, the leading cause of death in the United States. By the age of 40, the lifetime risk of heart failure in both men and women is one in five. Despite important advances in medicine, current treatments do not prevent or reverse the progression of the disease. KCU and Konorev have been awarded an NIH grant totaling more than $460,000 from the National Institutes of Health (NIH) to study how to stimulate new myocardial blood vessel growth that will alleviate the progression of heart disease.

The development of future scientists and physician scientists is a major goal of our institution. Critical to the neuromuscular research being done at the medical and graduate school is the involvement of students in the research mission. All KCU scientists have medical students conducting research in their laboratories, and many have graduate students conducting research for their thesis in labs that involve collaboration with other investigators at KCMD partner institutions. Several KCU students have received national and regional awards for their efforts.

At KCU, we continue to seek innovations in the treatment and understanding of disease to improve the lives of patients and their families. Indeed, leveraging research partnerships and seizing opportunities for collaboration will promote scientific discoveries that will further expand our research enterprise and support our mission to improve the well-being of the communities we serve. **MM**

Sleep and Parkinson Disease

by Pradeep C. Bollu, MD & Pradeep Sahota, MD

Patients with Parkinson disease can have a range of sleep disorders that can affect not just the quality of sleep but also the quality of life.





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Abstract

Sleep disorders are prevalent in Parkinson disease (PD), a disease with well recognized motor dysfunction. Sleep related problems received little attention until the last three decades. Sleep disorders seen in PD patients include insomnia, excessive sleepiness, restless legs syndrome, REM sleep behavior disorder. Some of these can have significant impact and lower the quality of life in these patients. An understanding of sleep issues in PD can help identify them early and result in optimal management.

Introduction

Parkinson disease (PD) is a neurodegenerative disorder first described by James Parkinson in his ' Essay on Shaking Palsy'[1]. It has predominant motor dysfunction. Its prevalence increases with age. In his description, Parkinson briefly mentioned the sleep disturbances seen in the terminal stages of PD. He described severe exhaustion and extreme sleepiness. Though motor symptoms dominate initially, the patients start experiencing non-motor symptoms as the disease advances. These include: dysautonomia (constipation, erectile dysfunction, impaired heat regulation, etc.), mood disorders (anxiety, depression) and sleep problems.

Sleep disturbances in PD are numerous, multifactorial, and result in a significant morbidity even contributing to earlier institutionalization[2]. Prevalence of sleep problems in PD can vary anywhere from 50%[3] to 81%[4,5]. Although nighttime sleep impairment and excessive daytime sleepiness were reported first, other sleep-related problems in PD received little attention until the last three decades. In this review article, we will discuss the sleep-related issues in Parkinson disease.

Sleep-Wake Architectural Differences and Circadian Variation of Symptoms in Parkinson Disease

With increasing understanding and analysis of sleep in PD, sleep architectural abnormalities are reported in this patient population.

Compared to healthy controls, PD patients have reduced total sleep time[6]. Sleep fragmentation is a consistent finding and may be seen early during the disease[7]. Sleep fragmentation is also a common finding in other neurodegenerative disorders[8]. Sleep efficiency is reduced with increased amount of WASO (Wakefulness After Sleep Onset). Nocturnal arousals are common complaint in PD patients. Up to 80% of PD patients report two to five nocturnal awakenings[9]. Coexisting problems like benign prostatic hypertrophy, diuretic usage, etc., may further worsen this. Some studies report increased amount of Rapid Eye Movement (REM) sleep with shortened onset to REM especially with coexisting depression[10]. Increased alpha activity has been noted in drug naive patients with Parkinson disease.

People with PD may show circadian variation of their symptoms[11]. Some feel better in the morning while some may feel worse. A small proportion may not have this circadian variation[9]. However, studies analyzing changes in the circadian rhythm in Parkinson disease population did not find any differences between patients and controls. One study showed increased melatonin secretion in patients with significant tremor compared to patients with just akinesia or rigidity. Treatment with levodopa is reported to cause phase advance of the nocturnal melatonin secretion[12].

Medications used in PD can also affect sleep architecture. Levodopa can result in REM suppression and increased REM latency[6,13]. Levodopa can also block REM rebound following REM sleep deprivation[14]. Dopamine receptors agonists can also suppress REM sleep. Anticholinergic drugs can increase REM latency and suppress REM sleep[15]. Similar REM sleep suppression is noted with Mono-Amine Oxidase Inhibitors and Catechol-O-Methyl Transferase inhibitors. Deep brain stimulation of subthalamic nucleus was shown to improve total sleep time and sleep efficiency and reduction in WASO[16].

Insomnia

Insomnia is persistent difficulty with sleep initiation, duration, consolidation, or quality occurring despite adequate opportunity/circumstances for sleep and resulting in daytime impairment. Daytime symptoms include fatigue, mood issues, irritability, malaise, and cognitive impairment. Some patients with insomnia may also experience physical symptoms like muscle tension, palpitations, and headache. Under the international classification of sleep disorders, insomnia with PD is categorized as "Insomnia due to a Medical condition." Female sex, disease duration, and presence of depression are associated with higher risk of insomnia in PD patients[17].

A variety of reasons are proposed for insomnia in PD. Insomnia is more prevalent in elderly and PD is a disease, typically of elderly. Inadequately controlled motor symptoms can interfere with sleep initiation and maintenance. Associated Restless Legs Syndrome (RLS) can result in sleep onset difficulties. Periodic leg movements in sleep can cause sleep fragmentation with resulting sleep maintenance insomnia. Nocturia is another frequent problem in elderly and can cause repeated awakenings from sleep. This can result from prostatic issues but can also be due to dysautonomia and fluctuations in responses to medication.

Co-existing mood problems contribute to daytime dysfunction and affect night sleep. In fact, depression is common and seen in up to 50% of PD population[17]. Identification of mood disorders should be part of evaluation of PD patients. Coexisting depression and anxiety can result in sleep fragmentation and early morning awakenings[10]. Addressing and alleviating depression and anxiety in these patients can improve the day time functioning and help with the night time insomnia.

Pain disorders cause sleep disruption and insomnia and increased prevalence of pain in PD patients may negatively impact sleep. Approximately 46% of patients with PD report chronic pain[18]. Nocturnal limb dystonia (discussed below) can also result in early morning awakening.

Sleep-Disordered Breathing in PD

Sleep-related breathing disorders include obstructive sleep apnea, central sleep apnea, sleep-related hypoventilation, and sleep-related hypoxemia.

A high incidence of central and obstructive apnea is found in moderate to severe PD[19] as compared to early stages[19,20]. Several factors may be contributory including rigidity, diaphragmatic dyskinesias, abnormal movement of glottis-supraglottic structures, and stridor. These in conjunction with increased tone in upper airways increase the likelihood of obstructive sleep apnea[21-23]. Sleep disordered breathing can cause chronic sleep deprivation and is a risk factor for cardiovascular and cerebrovascular disease. Untreated sleep apnea can result in sleep deprivation with daytime sleepiness, fatigue, early morning headaches, poor concentration, etc.

Treatment of sleep disordered breathing depends on the type of the disorder. Obstructive sleep apnea is treated with Positive Airway Pressure (PAP) therapies, mandibular advancement devices, positional therapy, and surgery in select cases. Treatment of central sleep apnea involves addressing the causative factors, advanced PAP therapies, and in some cases, respiratory stimulants like acetazolamide. Hypoxemia disorder is treated with supplemental oxygen while hypoventilation is treated with advanced PAP therapies.

Parasomnias and Other Sleep-Related Movement Disorders

Restless Legs Syndrome and Periodic Leg Movements in Sleep

Restless Legs Syndrome (Willis-Ekbom Disease) is associated with urge to move the legs due to unpleasant

and uncomfortable sensations. These sensations begin or worsen during periods of rest or inactivity and are partially or totally relieved by movement. The symptoms occur mainly in the evening or nighttime. Sometimes, symptoms may involve arms and very rarely, the whole body. RLS can result in significant distress to the patients. It can interfere with sleep onset and cause insomnia. Daytime fatigue and sleepiness are common associated complaints with restless leg syndrome.

Prevalence of RLS is estimated to be 5-10% of adult population in North America. It is twice as prevalent in women as in men. Prevalence increases with age. Iron deficiency, certain medications (sedating antihistamines, centrally-acting dopamine blockers, and most antidepressants), pregnancy, chronic renal failure, and prolonged immobility are associated with increased risk of RLS. There is a strong familial association especially with early onset RLS.

Multiple studies show higher RLS prevalence in PD patients than in general population[24]. RLS profile of PD patients, however, is different from general population. RLS in PD tends to start relatively late, tends to be milder with most patients having no family history of RLS[25]. The overall impact of RLS on PD patients seems modest in terms of day time sleepiness and quality of life[24].

RLS responds to dopaminergic medications especially agonists (pramipexole, ropinirole, rotigotine), already used for treatment of PD. Other medications like gabapentin enacarbil can help especially in patients with coexisting neuropathy. Opioidergic medications are a second line therapy in refractory RLS cases.

Periodic limb movements are repetitive, stereotyped, usually lower extremity movements in sleep, and may cause sleep disruption with daytime symptoms. Symptoms associated with periodic leg movement disorder may result from sleep fragmentation like daytime fatigue, daytime sleepiness, lack of energy etc. Periodic leg movements in sleep can also disrupt the sleep of the bed partner. They are commonly associated with restless legs syndrome.

REM Sleep Behavior Disorder

REM sleep is characterized by rapid eye movements and skeletal muscle atonia. Respiration is diaphragm–based during REM sleep. Dreaming during REM sleep tends to be vivid and detailed, compared to vague content of Non-REM (NREM) sleep. Muscle atonia is mediated by brainstem centers, pedunculopontine nucleus and locus ceruleus, and serves as a protective mechanism preventing dream enactment during REM. However, conditions resulting in disruption of this protective mechanism can lead to physical enactment of dream content during REM[26]. This phenomenon is called REM Sleep Behavior Disorder (RBD) [27].

Parkinson disease is very strongly associated with RBD. In fact, RBD can predate the initial motor symptoms by years[28] and is one of the best known biomarkers for PD. RBD is present in 25-50% of PD patients and is even more frequent in multiple system atrophy and Lewy body dementia[29,30]. Forty percent of the patients with idiopathic RBD develop a parkinsonian syndrome within a decade, and two-thirds within two decades[31-33]. Mild cognitive impairment[34] and dysautonomia[35] were seen in these patients with idiopathic RBD.

As PD advances, higher amount of phasic muscle activity is found in both REM and NREM sleep[36]. Patients experiencing RBD may have mild, low amplitude limb movements that are often overlooked. Some patients have vocalizations. These movements can be significant and violent with apparent goal directed behaviors that can cause injury with lacerations, ecchymosis and, even death[37]. Curiously, the motor activity in RBD appears smoother, faster and stronger than the patient's day time motor activity[38]. Patients may report falling from their beds during the night. Their bed partners may sometimes be able to understand the dream content based on the patient's behavior. Some episodes result in arousal from sleep. Usually, RBD episodes do not cause significant sleep disruption.

Management includes careful history from the patient and the spouse. The first step is to make the sleeping environment safe – e.g., putting soft pads around the bed to minimize the impact of falls, using pillows, keeping distance from the bed partner, and removing sharp and potentially injurious objects. Most common medications used in the treatment of RBD are Melatonin and Clonazepam. They should be started at low doses and increased if the RBD behaviors continue. Morning grogginess and day time somnolence are common side effects (especially with clonazepam) and should be part of patient counselling. Refractory cases may require combination of both medications. Of note, presence of medications like Tricyclic antidepressants and Selective Serotonin Reuptake inhibitors can increase the likelihood of causing RBD episodes. Discontinuation of these medications should be

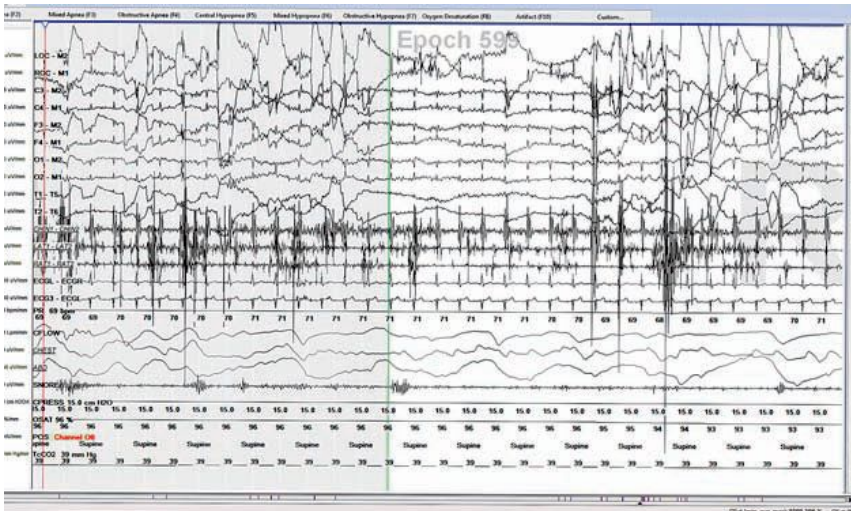


Figure 1
Increased EMG activity in the chin and the leg leads suggestive of RBD in a patient with Parkinson disease.

considered, especially if there is a temporal correlation between the initiation of medication and the onset of RBD. Unlike most other motor problems of Parkinson disease, RBD does not respond to dopaminergic therapy. See Figure 1.

Nocturnal Limb Dystonia

Limb dystonia may occur in the affected limb during the night as off phenomenon and can be painful. Painful extension of the great toe called 'Striatal toe' is an 'off phenomenon' and happens as the concentration of Levodopa declines during the night. It can cause early morning awakenings. Addition of long-acting Levodopa/ Carbidopa formulation or a dopamine agonist (which typically tends to have a longer effect than Levodopa formulations) can help.

Excessive Daytime Sleepiness

Excessive daytime sleepiness (EDS) is a common problem in PD patients. Up to one-third of the patients can have disabling sleepiness[39]. The incidence of excessive sleepiness increases as the disease advances[40] and can have a significant impact on the quality of life measures in PD patients. Early recognition and appropriate management is very important. See Figure 2.

There are multiple potential reasons for increased sleepiness in Parkinson disease. Based on the analysis of the PSG data, Arnulf et al. suggested sleepiness as an integral part of neurodegeneration in PD[41]. Neurodegenerative disorders in general tend to have EDS as a common feature. This is thought to be due to involvement of alerting mechanisms and reduction in the levels of neurotransmitters (like acetyl choline, dopamine, serotonin, and norepinephrine) that increase alertness. Reduction in some of the same neurotransmitters is also implicated in mood disorders seen in PD. Recently, it has been found that PD is associated with loss of orexin producing neurons[42,43] – same neurons that are lost in narcolepsy. These neurons play a critical role in alertness and wakefulness.

In addition, medications to treat PD may also contribute to the EDS. Dopamine agonists (DA) have a greater tendency to cause sleepiness than Levodopa formulations. This effect is dose dependent but it is not uncommon to see intolerable sleepiness in some patients even with low doses. Though these medications are used for addressing the cardinal symptoms of PD, they may also be started to treat RLS in this patient population. DAs may cause sleep attacks, which are episodes of sudden onset of irresistible sleep out of a relative alert state. These can be dangerous and potentially result in accidents and injuries, and should always be inquired in PD patients on dopaminergic therapy. They were first reported in eight patients taking non-ergot dopamine agonists at high doses[44]. Sleepiness in PD has been found to increase with the duration of dopaminergic therapy[40].

Though sleep attacks are less likely with Levodopa formulations[45], they may happen. Amantadine, another medication used in managing Parkinson disease, may be associated with sleepiness. Amantadine has both anti-NMDA and anti-cholinergic properties along with dopaminergic activity. Antagonism of acetyl-choline appears to be the main reason for increased sleepiness caused by amantadine. Tolerance to amantadine gradually decreases as people get older.

Another reason for daytime sleepiness is nocturnal sleep fragmentation causing chronic sleep deprivation. Insomnia may also contribute to daytime sleepiness and fatigue. Some patients may also have irregular sleep-wake routine causing sleepiness during the day and insomnia at night.

Clinicians should have a high index of suspicion for EDS. Addressing the EDS can sometimes be challenging. The dopaminergic medications that are helping the patient in alleviating the motor symptoms may be causing sleepiness. It is important to establish the temporal relationship between increased sleepiness and the initiation

of medication before the medication changes are planned. Younger patients tend to tolerate DAs better than older patients. When DAs are intolerable, levodopa formulations should be introduced for symptomatic treatment of PD symptoms. Sometimes, tremors may not respond to dopaminergic therapy and require anti-cholinergic agents. Sleepiness from anti-cholinergics may limit their use and in fact, centrally-acting anti-cholinergics are usually intolerable when used in adult patients making their use very rare (the exception is amantadine which is commonly used). At times, patients can't tolerate any of the symptomatic treatments due to disabling sleepiness, and DBS can be explored as an option in this select group. Appropriate patient selection for DBS is beyond the scope of this paper.

Figure 2
It is important to establish the temporal relationship between increased sleepiness and the initiation of medication before the medication changes are planned.



Other Miscellaneous Sleep-Related Issues

Sweating in Parkinson Disease

Thermoregulary and sweating disturbances are well recognized in PD patients. The disturbances in sweating can be both hypo- and hyperhidrosis, and are related to the spectrum of dysautonomia seen in this disease. Up to two-thirds of the patients with PD report a problem with sweating and this can have a considerable impact on the quality of life in PD patients. This may trouble the patients at night causing discomfort and arousals from sleep. Both central and peripheral mechanisms are thought to be involved[46].

Tremor and Other Motor Symptoms of Parkinson Disease in Sleep

The resting tremor of PD usually ceases with the onset of stage I sleep. Even when it persists, the amplitude of the tremor is typically reduced in sleep by up to 50%, compared to waking level[47]. However, it may result in sleep onset insomnia in some people. Unlike essential tremor which is predominantly an action tremor, PD tremor is predominantly at rest. If the tremor is bothering the patient causing sleep onset insomnia, medications may have to be used to address the symptoms during sleep wake transition. Sometimes, patients may also experience bothersome tremor when they get up in the middle of the night. A long acting dopaminergic agent may help to address this issue. In some patients, the tremor improves during the morning hours suggesting a beneficial effect of sleep on tremor.

Similar to tremor, other features of PD like rigidity and bradykinesia can cause discomfort to the patients and sleep initiation problems. Other motor abnormalities described in PD patients include increased muscle tone, simple and complex movements, repeated blinking, blepharospasm at the onset of REM sleep, and prolonged tonic contractions of limb muscles during NREM sleep[48].

Dreaming in Parkinson Disease

Parkinson disease patients on dopaminergic therapy report higher prevalence of dreams that are intense, unpleasant, frightening, and recurrent as compared to controls. Nightmares and nocturnal vocalizations are reported and increased with treatment. Patients who experience altered dreams frequently hallucinate and vice versa[9,49]. It has been suggested that a kindling mechanism consisting of progressive mesolimbic dopamine receptor hypersensitivity might be the reason for this strong association[50].

Summary

Patients with PD can have a range of sleep disorders. They may be a feature of the disease process, result of other motor and non-motor symptoms, related to medications, or represent a primary sleep disorder. They can affect not just the quality of sleep but also the quality of life in patients with PD. Their recognition and appropriate treatment can play a vital role in the overall management and functioning of patients with PD.

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Disclosure

None reported.

MM

Persistent Elevation of Thyroglobulin in Patient Treated for Differentiated Thyroid Cancer: A Ten-Year Review

by Sarah Khan, Roopashree Prabhushankar, MD, Emily Leary, PhD & Uzma Z. Khan, MD

All patients with persistent disease should have regular clinic visits, laboratory tests and imaging procedures, and may require multiple treatments with radioactive iodine ablation and surgeries.



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Abstract

Differentiated Thyroid Cancer (DTC) is increasing in prevalence due to better diagnostic tools and excellent long-term survival. This study is to understand the outcome of twenty-six patients with DTC over a period of 10 years after the initial treatment with surgery and radioiodine therapy. Our study analysis showed no deaths, and indicated that older men were more likely to have persistent disease. Further studies are needed to focus on cost effective long-term management of DTC.

Introduction

Differentiated thyroid cancer (DTC) comprises about 90% of all thyroid cancers in the world[1]. DTC can be further differentiated to include papillary thyroid cancer (PTC), follicular carcinoma (FC) and Hurthle cell carcinoma (HCC). In the United States, the annual incidence of DTC has increased nearly three-fold over 34 years from 4.9 per 100,000 in 1975 to 14.3 per 100,000 in 2009[2], mainly attributed to an increase in PTC. DTC has an excellent long-term prognosis, with a five-year survival rate of 97.9%[1].

In 1996, the American Thyroid Association (ATA) published guidelines for patients with thyroid nodules and DTC; these guidelines were updated in 2006, 2009 and most recently in 2015, and are widely used for management of patients with DTC. Many patients with DTC undergo total thyroidectomy with radioactive iodine ablation postoperatively. This procedure is followed by appropriate thyroid stimulating hormone (TSH) suppression, as well as long-term follow up[2]. The increasing incidence and high survival rate of DTC requires long-term monitoring of these patients for recurrence of cancer involving clinical exam, lab studies including TSH and thyroglobulin (Tg) levels, and imaging, if indicated.

The ATA guidelines recommend the monitoring of serum Tg as a tumor marker for DTC due to the high degree of sensitivity and specificity of Tg levels in detecting DTC recurrence or persistence after the initial treatment with total thyroidectomy and remnant ablation with RAI. Serum Tg is also utilized for risk stratification of patients with DTC[2]. Tg levels of <0.2 ng/mL, with a suppressed TSH or a Tg $<$ 1 ng/dl with TSH stimulation indicate an excellent response to treatment in patients treated with total thyroidectomy and RAI. A Tg greater than 1 ng/ml following thyroidectomy and radioactive iodine indicates an incomplete response to treatment and requires long-term follow up. These patients also require suppressive doses of levothyroxine to maintain a TSH below normal (0.27 – 4.2 mIU/ml). Tg levels should be monitored every 6-12 months[2]. Imaging, including ultrasound, diagnostic whole body scan, and in certain clinical situations, a neck/chest CT scan, neck MRI or a PET CT scan are performed at varying intervals to identify the focus of DTC. Patients with persistent disease may receive additional doses of adjuvant RAI therapy during the course of their disease.

According to Surveillance, Epidemiology and End Results (SEER) program data there will be an

estimated 64,300 new cases of thyroid cancer in the United States in 2016, and an estimated 1,980 people will die of thyroid cancer[1]. There is an ongoing debate focusing on the increasing incidence of DTC and factors that may be leading to this increase[3]. Most of this research focuses on low risk DTC, with only a few small studies focusing on patients who have persistent or progressive disease in patients with DTC.

The purpose of this study was to identify patterns in clinical course and management over a period of 10 years in patients with DTC and persistent elevated Tg levels, after initial treatment with surgery and radioactive iodine ablation (RAI) therapy. This study was a retrospective chart review of patients in a clinical setting and as such provides a "real life" picture of patients with thyroid cancer. The study will aid physicians in providing long-term, cost-effective management, focused on individualized care for these complicated cases, which comprise less than 1% of patients diagnosed with DTC.

Material and Methods

A retrospective non-randomized chart review was performed to assess long-term patient management at the University Hospital, Columbia, Mo.

Subjects

Patients receiving medical care from University Hospital, Columbia, Mo., between January 2004 and December 2014 who met the following criteria were included in this study: (a) patients with a diagnosis of DTC, including PTC, papillary thyroid cancer – follicular variant, FC, and HCC presenting to the multidisciplinary clinic during the study period; (b) underwent total thyroidectomy followed by RAI; and (c) at least two Tg measurements, including at least two unstimulated Tg measurements elevated above 0.2 ng/dl or two stimulated Tg measurements above 2 ng/dl. The care of most of the patients was based on ATA guidelines in 2006 and 2009. As a retrospective chart review, no specific protocol for testing or imaging was followed, but patient follow-up was based on "real life clinical management" in a tertiary care hospital. This study was approved by the Institutional Review Board of the University of Missouri School of Medicine. Informed consent requirement was waived because of the retrospective nature of the study.

None of the patients in our study showed secondary primary cancers from other organs. These are usually diagnosed more than 10 years after the primary thyroidectomy[3]. There were no deaths from thyroid cancer during the study period.

Measures

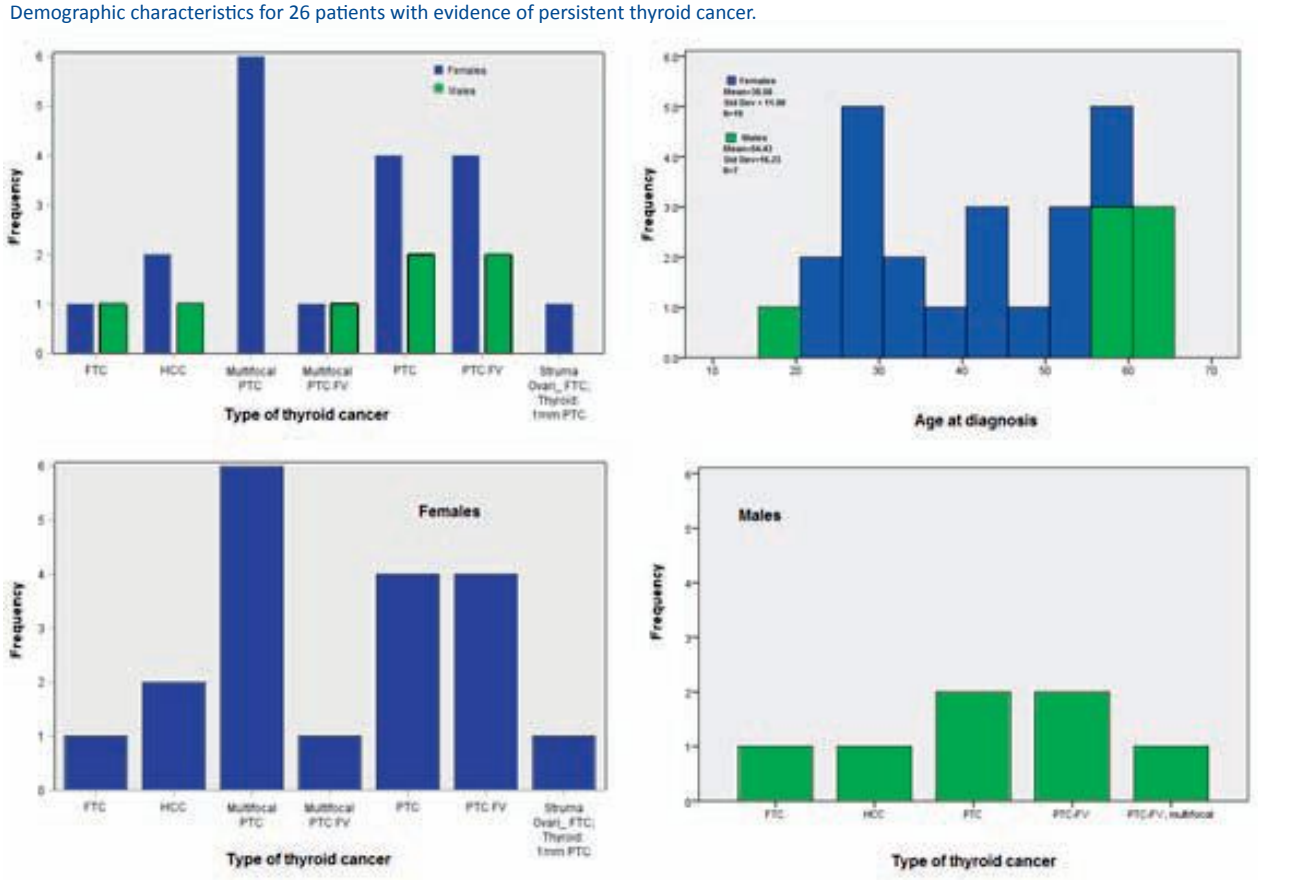
A retrospective chart review was performed and data collected included clinical history and patient demographics (e.g. age and sex). The clinical history included any known history of radiation to the head and neck area, hypothyroidism, Hashimoto's thyroiditis, Grave's disease, uninodular or multinodular goiter, family history of thyroid disease, preoperative laboratory studies including thyroid stimulating hormone (TSH), antithyroglobulin antibody (Tg Ab), and thyroid peroxidase antibodies (TPO), preoperative imaging (ultrasound, CT neck), fine needle aspiration findings, and histopathological findings (tumor size, pathological classification, extrathyroidal extension, intrathyroid multifocality, lymph node metastasis and presence of underlying Hashimoto's thyroiditis). All studies related to the long-term clinical course after diagnosis and treatment including Tg levels, imaging including CT, MRI, ultrasonography, PET scans were recorded.

Three patients with elevated Tg Abs were excluded from this study. Tg Ab are detected in 25-30% of patients with DTC[6]. In these patients with elevated Tg antibodies, Tg levels checked utilizing radioimmunoassays are unreliable. Some laboratories measure Tg by Liquid Chromatography-Tandem Mass Spectrography, which is reliable in the presence of Tg Abs[2, 4]. Some authors have suggested using Tg Abs trends as a surrogate tumor marker in patients with DTC[5]. However, we preferred to exclude patients with elevated Tg Abs due to lack of reliable data in this setting.

Initial Course

Between 2004 and 2014, 272 patients diagnosed with DTC obtained care at the University Hospital, Columbia, Mo., and were treated with total thyroidectomy. This was followed by radioactive iodine ablation, with I-131 whole body scan (131I WBS) six to twelve months after remnant ablation, as per ATA guidelines[2]. Patients underwent lymph node dissection if cervical lymph node involvement was noted on preoperative imaging or intraoperatively by the surgeon. Depending on clinical evaluation, imaging studies were performed such as neck ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), and flouro-18-deoxyglucose positron emission tomography (PET). External radiotherapy was performed if clinically indicated for distant metastases. All patients were followed in a multidisciplinary thyroid cancer clinic by the same endocrinologist during the study period (2004 – 2014). During the ten-year follow-up period, TSH and Tg using immunoradiometric assay results were followed at 6 to 12 month intervals. After a 10-year follow-up period, 29 patients had evidence of persistent thyroid cancer, as shown by either two or more unstimulated Tg measurements elevated above 0.2 ng/dL or two stimulated Tg measurements above 2 ng/dL, performed at least 12 months after remnant ablation. Of these 29 patients, 26 patients had at least two detectable Tg measurements with negative Tg antibodies. The long-term outcomes of these 26 patients were further analyzed to determine the clinical course specifically focusing

Figure 1
Demographic characteristics for 26 patients with evidence of persistent thyroid cancer.



on Tg level, use of imaging modalities and treatment offered including surgery or chemotherapy. The remaining three patients had elevated Tg antibodies and were excluded.

Data Analysis

Due to small sample sizes, only patterns of clinical outcomes and treatment were investigated. Based on at least two detectable Tg measurements with negative Tg antibodies, twenty-six patients of the 272 had evidence of persistent thyroid cancer and were further studied. These participants were followed and categorized into three distinct categories based on Tg levels (e.g. $<$10 ng/dL, 10ng/dL – 100ng/dL, $>$100ng/dL). Although primarily a descriptive study, the non-parametric Wilcoxon Rank Sum test was used to determine differences in the age at diagnosis and Tg levels between males and females.

Results

In this cohort of 26, there were 19 females (73%) and seven males (27%) (see Figure 1). Females were 21-58 years old with a mean age of 38.6 years ($\pm$ 11.9 years). Males were 18-64 years old with a mean age of 54.4 years ($\pm$ 16.2 years). Most females were between the ages of 20 and 30 years old and most males were between 56 and 65 years old[5,6]. Male patients were also older at diagnosis, on average, compared to women (p-value = 0.0134). Of the 26 patients, 20 patients had papillary thyroid cancer (PTC). Of these 20 patients, six patients had classical PTC, six patients had multifocal papillary thyroid cancer (MF-PTC), six had papillary thyroid cancer follicular variant (PTC-FV) and two patients had multifocal PTC-FV. Of the six patients that did not have PTC, two patients had follicular thyroid cancer (FTC), three patients had Hurthle cell cancer (HCC) and one patient had struma ovarii with a 1 mm micro PTC. In females, the most common type of DTC was MF-PTC in six females (31%) followed by PTC in four females (26%) and FV-PTC in four females (26%). In males, the most common DTC was PTC in two males (28.5%) and FV-PTC in two males (28.5%). Six patients had a family history of DTC.

Seventeen patients (Group 1), three males and fourteen females, had stimulated Tg levels less than 10 ng/dL (see Table 1). In Group 1, one person died of an unrelated cause and four patients were lost to follow-up. Therefore, the survival rate of Group 1 was 94% assuming that those patients who were lost to follow-up are included in the surviving group. Five patients underwent cervical lymph node dissection with postoperative follow-up Tg levels that were less than 1.6 ng/dL.

Table 1
Group 1: Patient progress for those with TG less than 10ng/dl

Age at Diagnosis (years)	Sex	Type of Thyroid Cancer	I -131 admin (age)	Imaging (Frequency)	Surgery	Status
52	F	Multifocal PTC	152 mCi (52)	CT neck (1) WBS (1)	Left neck dissection at age 56, 2 LN + PTC	Doing well at age 60 years, stimulated Tg: 1.5 ng/dL
18	M	PTC	33 mCi (18) 205 mCi (18) 263 mCi (19) 255 mCi (22)	WBS (4) CT scan (1)		Doing well at age 34, stimulated Tg: 0.4 ng/dL
36	F	PTC	Dose NK (36) 150 mCi (39)	WBS (2) PET (1)		Lost to follow up at age 40 years, unstimulated Tg : 0.7 ng/dL
38	F	PTC FV, Multifocal PTC	100 mCi (38) 150 mCi (43)	WBS (2) PET (1) MRI neck (1)	Left neck dissection age 44 years: 1 LN + PTC	Continues follow up, age 48 years, unstimulated Tg: 0.8 ng/dL
28	F	FTC	Dose NK (28) Dose NK (32)	WBS (2)	LN resection at age 29	Doing well at age 53, unstimulated Tg : 1.1 ng/dL
21	F	PTC	Dose NK (21) Dose NK (27)	WBS (1) CT scan (1)	Right neck LN dissection at age 31, 2 LN + PTC	Doing well at age 42 years, unstimulated Tg: 1.6 ng/dL
58	F	Struma Ovari_ FTC Thyroid: 1mm PTC	Pelvic XRT (58) 250 mCi (59)	WBS (3) PET scan (2) CT scan (4)		Lost to follow up at age 63 , stimulated Tg: 0.5 ng/dL
26	F	PTC	152 mCi (29) 152 mCi (35)	WBS (3) PET scan (3) CT scan (6)		Being followed at age 38, stable multiple pulmonary nodules, unstimulated Tg: 6.9 ng/dL
58	M	PTC	104 mCi (58)	WBS (1) CT scan (2) PET scan (1)	Right neck dissection at age 59 , 7 LN + for PTC	Being followed at age 63, unstimulated Tg: < 0.1 ng/dL
41	F	PTC	Dose NK (41)	WBS (1)		Deceased age 72, last unstimulated Tg: 1.1 ng/dL
44	F	PTC FV	103 mCi (44)	WBS (1)		Lost to follow up age 54, unstimulated Tg: 0.9 ng/dL
41	F	Multifocal PTC	150 mCi (41) 150 mCi (43)	WBS (3) PET scan (1)		Continued follow up, stimulated Tg:3.6 ng/dL
51	F	Multifocal PTC	153 mCi (51)	WBS (1) PET scan (1) CT scan (1)		Lost to follow up at age 56, unstimulated Tg: 2.5 ng/dL
30	F	PTC FV	Dose NK (30)	WBS (1) PET scan (1)		Being followed at age 82, unstimulated Tg: 0.6 ng/dL
47	F	PTC FV	100 mCi (47)	None		Being followed at age 49 years, unstimulated Tg: 0.2 ng/dL
31	F	Multifocal PTC	154 mCi (31) 150 mCi (34)	WBS (2) PET scan (2) CT scan (1)		Pulmonary nodules noted at age 34, being followed at age 35, unstimulated Tg: 5.7 ng/dL
62	M	PTC FV, Multifocal PTC	100 mCi (62)	None		Being followed at age 66 years, unstimulated Tg: 0.4 ng/dL

Table 2
Group 2: Patient progress for those with TG 10-100ng/dl

Age at Diagnosis (years)	Sex	Type of thyroid cancer	I -131 admin (age)	Imaging (Frequency)	Surgery	Status
35 years	F	Multifocal PTC	99 mCi (35) 150 mCi (37)	WBS (1) PET (1)		Continues follow up, age 37, unstimulated Tg: 12 ng/dL
29 years	F	Multifocal PTC	100 mCi (29)	WBS (2) PET scan (2) CT scan (1)		Lost to follow up age 33 years, stimulated Tg: 13.8 ng/dL
58 years	M	FTC	151 mCi (58) 150 mCi (62)	CT scan (1) PET scan (3)		Being followed at age 67 years, unstimulated Tg: 65 ng/dL
57 years	F	HCC	75 mCi (57) 130 mCi (58) 151.7 mCi (60)	WBS (1) PET scan (1)		Being followed at age 64 , unstimulated Tg: 30 ng/dL
59 years	M	PTC FV	152 mCi (59) 152 mCi (61)	WBS (2) PET scan (7) CT scan (7) MRI (6)	C-6 vertebral metastasis removed age 61, lung nodules noted age 62, right frontal metastases removed age 64	TKI started age 64, stable at age 65 years, stable pulmonary metastasis, unstimulated Tg: 59 ng/dL

Table 3
Group 3: Patient progress for those with TG greater than 100ng/dl

Age at Diagnosis (years)	Sex	Type of thyroid cancer	I -131 admin (age)	Imaging (Frequency)	Surgery	Status
64 years	M	HCC	100 mCi (64)	WBS (2) PET scan (5) CT scan (2)		Regular follow up, unstimulated Tg: 443 ng/dL, multiple FDG avid lung nodules
24 years	F	HCC	203 mCi (73)	CT scan (5)		Unstimulated Tg: 8981 ng/dL, multiple pulmonary nodules treated with TKI, deceased age 74 years from unrelated renal disease
54 years	F	PTC FV	200 mCi (55) 200 mCi (56)	CT scan (1) MRI (2) PET (1)		Pulmonary and brain metastasis, TKI started age 57 years, being followed at age 58, unstimulated Tg: 2185 ng/dL
62 years	M	PTC FV	Dose NK (62) 151 mCi (65)	PET (1) CT Scan (2) MRI (1) WBS (1)	Right neck LN dissection , 2 + LN for PTC age 65	Pulmonary metastasis noted in 2014, TKI started age 68, continues follow up at age 69, unstimulated Tg: 2061 ng/dL

Five patients (Group 2) had stimulated Tg levels between 10 and 100 ng/dL, two males and three females (see Table 2). Of these five patients, one patient had cervical vertebral metastases that were removed and was later noted to have pulmonary and brain metastases requiring surgical removal. This surgery was followed by treatment with tyrosine kinase inhibitors (TKI).

Four patients, two males and two females, had stimulated Tg levels greater than 100 ng/dL (see Table 3). In Group 3, all four patients were noted to have pulmonary metastases; one patient opted for continued surveillance, the other three patients were treated with TKI. Although our sample size was much smaller, we found that more males were in groups 2 and 3, and were also significantly older compared to the females in our cohort (p=.0134).

All patients received radioactive iodine ablation (RAI) and more than half of patients (n=15) received RAI at least twice. The mean dose given was 148.31 mCi, which includes all doses given to all 26 patients. Eleven patients received only a single dose of RAI (42%). The mean doses for Groups 1, 2 and 3 were 151.3 mCi, 131.07 mCi and 170.8 mCi respectively. For three patients, I-131 doses for RAI ablation were not known. All patients had multiple imaging studies during the 10-year study follow-up period. Most patients had two imaging studies in Group 1 (n=6) and Group 2 (n=2). One patient in Group 2 had pulmonary, brain and cervical vertebral metastasis and had 22 imaging studies performed during the 10-year period. In Group 3, most patients had five imaging studies (n=2), one patient had four studies and one patient had nine studies performed for follow-up.

Tyrosine Kinase inhibitors (TKI) treatment was used in four patients, one patient was in group 2 and three patients were in group 3. One patient in group 3 opted for continued clinical surveillance of pulmonary nodules rather than undergoing TKI treatment.

Discussion

This study included patients treated at a single center. It highlights the management of thyroid cancer patients in a "real life clinical situation" outside of the confines of a preset research protocol. Our study shows that the management of thyroid cancer has changed significantly since 2004. Many patients were managed with total thyroidectomy and RAI using previous guidelines in 2006 and 2009. Despite the small size of the sample, we were able to gain some insightful knowledge about patient management. Unlike the prevalence of thyroid nodules and cancer in the general population, where significantly more women are affected compared to men, there was a higher proportion of men with thyroid nodules and cancer in this study. Male gender has been significantly associated with disease-specific mortality in thyroid cancer and males generally show more advanced disease at clinical presentation and have poorer prognosis after therapy [6]. Although our study utilized a small sample, there were proportionally more males in Groups 2 and 3 (40% and 50%, respectively), compared to Group 1 although statistical significance was not demonstrated. Male patients were also older at diagnosis, on average, compared to women (p-value = 0.0134). Patient age has been shown to be an independent negative risk factor for survival in DTC[6, 7].

There is no consensus for the long-term clinical management of patients with DTC who have an elevated serum Tg[8]. Tg levels in patients with DTC are reliable indicators to identify recurrence based on elevated Tg levels[9]. Studies have shown that most patients with PTC and histologically proven lymph node metastases treated with I-131 ablation are rarely free of detectable disease[10]. Retrospective studies in DTC patients designed to assess the long-term course of Tg positive patients with negative imaging without any therapeutic intervention have shown spontaneous remission in the majority of patients with a minority showing persistent disease[11]. In patients with persistent disease, therapeutic interventions achieve remission only in some patients, with most patients continuing to harbor persistent disease and a few patients showing progression of the disease leading to their death[12]. A small case series by Kwong et al. showed that in select patients with PTC and distant metastasis, long-term survival could be achieved by close follow-up without aggressive treatment[13]. Several recent case series have tried to highlight the clinical course of DTC with distant metastasis. Lin et al. looked at the survival time after diagnosis in patients with DTC and distant metastasis and found a disease-specific mortality of about 70% after a mean follow-up of 10.1 years[6]. They found that older patients and male patients with distant metastasis needed more aggressive treatment. It is known that recurrent or persistent disease may not be localized and patients undergo different imaging studies to localize the recurrence. In our study, we found that patients had an average of 1.38 imaging studies. We did not analyze the cost of these studies or any anxiety that may have been caused to the patients. The clinical use and cost-effectiveness of different imaging modalities has not been widely studied but may be a question for future research[14].

Interestingly, none of the patients in our study showed underlying Hashimoto's thyroiditis. Some studies have shown an increased prevalence of DTC in patients with Hashimoto's thyroiditis, especially in the setting of increasing TSH levels[10]. Some authors have noted that even though the prevalence of DTC has increased, Hashimoto's thyroiditis may have a protective effect and be associated with better prognostic factors including younger age, smaller tumor size and female sex[14, 15]. Although some studies have shown increased risk of DTC with

hypothyroidism[16], none of our study patients had a previous diagnosis of autoimmune hypothyroidism. One patient in Group 1 had been treated for Grave's disease with RAI ablation six years prior to diagnosis resulting in post ablative hypothyroidism.

Our study has several limitations including a small patient population limited to a single provider in an academic tertiary care setting. The higher percentage of patients with persistent disease in our study may be due to referral bias to the tertiary care center and hence may not be representative of the general population. In addition, a study that assesses mortality and secondary primary cancers in DTC patients will likely need a longer follow-up period, beyond ten years. However, obtaining consistent data for a longer period of time is quite challenging. No specific protocol for long-term treatment of thyroid cancer was followed during the study period. The management of thyroid cancer in a clinical setting may have changed based on thyroid cancer guidelines from the ATA changed in 2006 and revised in 2009. Further, few of our study patients were treated with TKI, a treatment option that has only become available in the last few years. Cellular mutation profile of thyroid cancer was not included in our study. This testing is now included in management of thyroid cancer patients, but was not widely used between 2004 and 2014.

Conclusion

Thyroid cancer is increasing in incidence in the United States and worldwide. Though most patients with DTC have an excellent survival, older men may be more likely to have persistent disease. Patients with persistent disease after initial therapy can be followed long-term with observation and lab tests. Of these patients, a small number will develop progressive disease requiring targeted therapy. All patients with persistent disease should have regular clinic visits, laboratory tests and imaging procedures, and may undergo multiple treatments with RAI and surgeries. Sialadenitis resulting from RAI as well as other side effects resulting from other interventions may add to increased cost and morbidity in these patients. Further studies are needed to better define management in this small group of patients to decrease morbidity during long-term follow-up. Future guidelines for management of persistent thyroid cancer should address the cost of care and encourage providers to review long-term cost effective management, especially in the lower risk groups.

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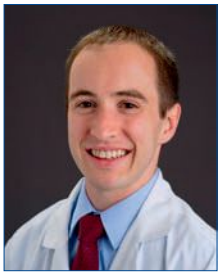
Author Contribution Statement

All authors had significant contribution to this manuscript including drafting, revision, and final approval of the manuscript. Sarah Khan contributed with data acquisition and interpretation; Roopashree Prabhushankar contributed with design and concept, data acquisition, and interpretation; Emily Leary contributed with data analysis and interpretation; and Uzma Khan contributed with design and concept, data acquisition, and interpretation. **MM**

Uveitis Following Treatment of Verruca Vulgaris with Intralesional *Candida* Antigen

by Nicholas J. Crowley, MD, John C. Hagan, III, MD, Jonathan A. Dyer, MD & Tyler F. Brundige, MD

Dermatologists and ophthalmologists should be aware of uveitis as a potential, though apparently rare, side effect of intralesional *Candida* for the treatment of warts



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Abstract

This is a first literature report of a case of uveitis along with severe systemic symptoms following verruca vulgaris treatment with intralesional *Candida* antigen. We believe the *Candida* injection was causative.

Introduction

Intralesional immunotherapy with *Candida* antigen is a commonly used, effective and safe treatment for verruca vulgaris (VV). Stimulation of cell-mediated immunity, via increased production of IL-2 and IFNy, contributes to the immune response against the human papilloma virus.[1] Febrile reactions and constitutional symptoms such as chills and aches are reported side effects.[1] We report a case of uveitis along with severe systemic symptoms following VV treatment with intralesional *Candida* antigen.

Case Report

A 47-year-old male with a history of penicillin allergy and narrow angle glaucoma previously treated with laser iridotomy presented to his dermatologist for the treatment of plantar warts. Intralesional *Candida* antigen was injected into three plantar warts on his left foot. He noted mild discomfort at the injection site. Five days following treatment, he reported generalized fatigue with migratory arthralgias and myalgias in addition to difficulty walking due to swelling and pain of his left foot. He also reported subjective fevers with generalized lymphadenopathy. Two weeks later he presented to an ophthalmologist with redness, pain, blurry vision and photophobia of both eyes. Inflammatory cells and flare were noted in the anterior chamber with no keratic precipitates in either eye. He was diagnosed with bilateral anterior non-granulomatous uveitis and treated with dexamethasone 0.1% eye drops and dilation using cyclopentolate 1% solution.

Nearly three weeks later the patient underwent a second treatment of intralesional *Candida* antigen on both feet as his warts had improved. After this treatment he developed similar, more severe, earlier onset systemic symptoms including nausea, headache, fever, chills and generalized lymphadenopathy. He again had difficulty walking due to pain and swelling of the treatment sites. He did not report ocular symptoms; however, he was still medicating with a tapering dosage of dexamethasone 0.1% eye drops.

Due to the bilateral nature of his uveitis and his significant systemic symptoms, a second ophthalmologist theorized his uveitis could be related to his treatment with *Candida* antigen. Testing by ophthalmology revealed elevated antibodies to *Candida* (*Candida* IgG 62 U/mL, normal 0-29 U/mL; IgM 43 U/mL, normal 0-9 U/mL; IgA 28 U/mL normal



Example of Verruca Vulgaris
Source: http://www.regionalderm.com/Regional_Derm/RD_Large/Wart33.jpg

0-9 U/mL). Additional testing included the following which were normal: CBC, ACE, ESR, ANA, RPR, FTA-Ab, Lyme IgG/IgM Ab, HIV, HLA B-27. His systemic symptoms resolved and his ocular exam normalized. His verruca improved. As this paper went to press he was using duct tape occlusion therapy for residual foot warts.

Two uveitis experts consulted about the case also suggested the injections were the cause and advocated for its publication. An adverse reaction report was filed with the manufacturer HollisterStier Allergy.

Discussion

This report describes uveitis as a newly recognized side effect of intralesional *Candida* therapy during treatment of warts. Worsening (and improvement) of uveitis and systemic symptoms following injections of *Candida* extracts are reported in the ophthalmologic literature, although not in the setting of wart treatment or without a preexisting history of uveitis.[2]

Previous studies of patients with uveitis noted an abnormal cellular response to *Candida* antigen with increased circulating levels of CD69 $CD4^+$ T-cells.[3] Uveitis following immunotherapy with intravesicular BCG for bladder carcinoma has been reported in patients with HLA-B27 positivity and in one with HLA-B27 negativity.[4]

The mechanisms of anti-*Candida* immune responses have been extensively studied. Exposure to *Candida* antigens triggers pattern recognition receptors of local phagocytes and epithelial cells leading to the production of T cells which then initiate signaling through the IL-17 pathway. In this case it is tempting to speculate that systemic exposure to *Candida* antigen led to activation of local ocular immune responses resulting in uveitis.[5,6]

Conclusion

Dermatologists and ophthalmologists should be aware of uveitis as a potential, though apparently rare, side effect of intralesional *Candida* for the treatment of warts.

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MM

Comparison of High-Fidelity Medical Simulation to Short-Answer Written Examination in the Assessment of Emergency Medicine Residents in Medical Toxicology

by Michael R. Christian, MD, Michelle J. Sergel, MD, Mark B. Mycyk, MD & Steven E. Aks, DO

Data are limited regarding the use of simulation as a tool for competency assessment.



Clockwise, from top left: Michael R. Christian, MD, MSMA member since 2012, is Assistant Professor of Emergency Medicine and Pediatrics, University of Missouri- Kansas City School of Medicine, Department of Emergency Medicine, Truman Medical Center, Medical Toxicologist, Division of Clinical Pharmacology and Medical Toxicology. Michelle J. Sergel, MD, Mark B. Mycyk, MD, and Steven E. Aks, DO, are with the John H. Stroger, Jr. Hospital in Chicago, Ill.
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Abstract

We compared high-fidelity medical simulation to short-answer written examination in the assessment of emergency medicine residents (EMR) on a month-long medical toxicology rotation. Knowledge-based assessment tools using cases of an aspirin overdose and a tricyclic antidepressant overdose were used to assess all consecutive rotating EMR (n=53). Assessment by simulation had similar accuracy and precision but higher satisfaction rates when compared to written examination. Incorporating simulation into the ABEM certifying examination warrants further study.

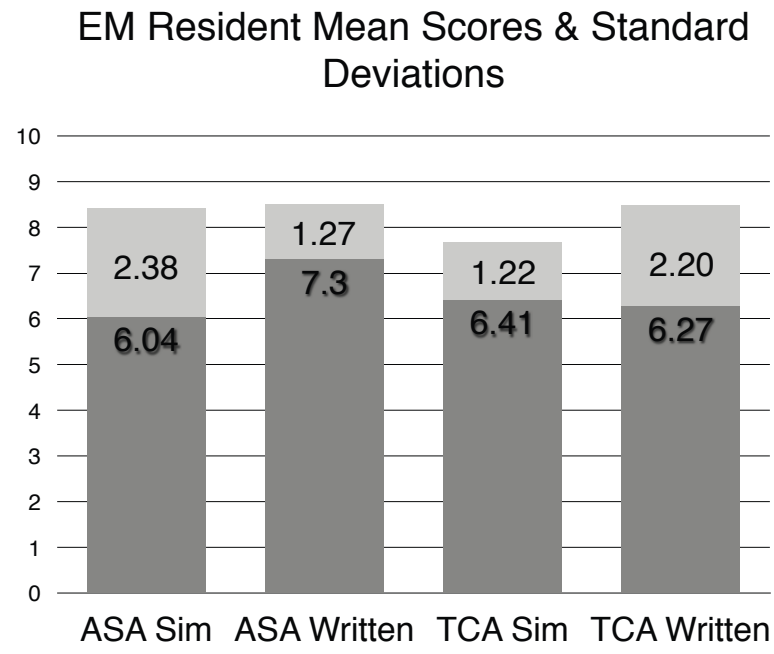
Introduction

Medical simulation is a popular and accepted teaching tool for post-graduate education. In addition, simulation is increasingly being used as an assessment tool particularly for procedures.[1,2,3] However, data are limited regarding the use of simulation as a tool for competency assessment. Some have advocated for the use of simulation in board certification and re-certification exams.[3,4,5]

Furthermore, simulation may have several advantages over traditional written tests in assessing procedural competency and certain American College of Graduate Medical Education (ACGME) core competencies (interpersonal & communication skills, professionalism, patient care, and systems-based practice). The next GME system, which started in July 2013, incorporates "milestones" into the traditional core competencies.[6] Since the types of procedures and complexity of simulation cases can be increased or decreased without much difficulty depending on the learner's level of training, simulation may lend itself to assessing these "milestones" more easily than traditional written tests for physicians-in-training. In a similar vein, a study by McGahie et al. demonstrated that standard examination tools like the USMLE Steps 1 and 2 are not correlated with reliable measures of medical students', residents', and fellows' clinical skill acquisition. Simulation may be a more accurate assessment tool, but more research is needed.[7]

Also, simulation evokes a physiologic response in physicians comparable to real-life clinical scenarios.[8] Despite these possible advantages, medical simulation is

Figure 1



much more expensive to proctor than written exams, and comparative research is warranted[9,10]. We sought to assess precision and accuracy of sim-based testing versus traditional written-based testing.

Methods

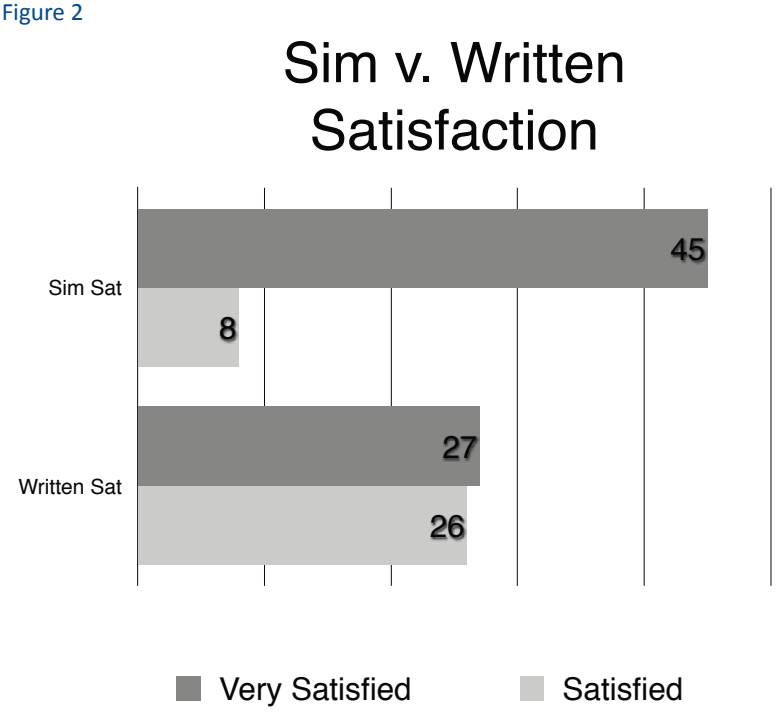
Knowledge-based assessment tools using sim and written examinations were developed, piloted, and revised by four physicians (authors) board-certified in Medical Toxicology and/or Emergency Medicine. These physicians were familiar with the Emergency Medicine core content requirements set forth by the American Board of Emergency Medicine (ABEM). From July 2011 to June 2012, all consecutive rotating EMR on a month-long Medical Toxicology rotation at an academic Emergency Medicine training program were eligible for participation in the study. Ten board-certified medical toxicologists as well as four fellows in training staffed the Medical Toxicology rotation. The rotation consists of daily patient rounds, daily didactics, and a weekly journal club. At any given time, approximately 20-25 medical students, pharmacy students, pediatric residents, emergency medicine residents, and pediatric emergency medicine fellows are on the service. However, only emergency medicine residents were assessed in this pilot study.

On odd months, EMR were assessed using a sim case of an aspirin (ASA) overdose patient and a written examination of a tricyclic antidepressant (TCA) overdose patient. On even months, testing modalities were switched (TCA sim and ASA written). The assessment tools each contained ten knowledge-based questions. For each toxin (ASA and TCA), the scenario, questions, and answers were exactly the same; only the assessment tool (sim versus written) varied. We specifically avoided the use of multiple-choice questions as an assessment modality as this would give a resident at least a 20% chance of guessing the correct answer (if five answer choices were given). Instead, we chose to compare two open-ended assessment modalities (sim versus written). At the end of the assessment, the EMR completed a survey. The content of the survey included demographic items, previous experience with simulation, and learner satisfaction. EMR were blinded to the purpose of the study. Scores were not used in the final rotation grade. Final scores were reported as 0 to 10 based upon the number of knowledge-based questions answered correctly (out of 10). The fourth author scored both the simulation and written tests to ensure consistency in grading. Data were analyzed using descriptive and inferential statistics. This study received IRB approval.

Results

From July 2011 to June 2012, 53 EMR [23 females, 30 males; PGY 3(38), 4(11), and 5(4)] from six different emergency medicine residencies were eligible for our study and all participated. All EMR were considered senior residents by their home institution. All residents who participated completed the study. Simple, descriptive statistics were used. Examination number, mean scores, and standard deviations were: ASA sim: N=26, M=6.04 SD=2.38; ASA written: N=27, M=7.30 SD=1.27; TCA sim: N=27, M=6.41 SD=1.22; and TCA written: N=26, M=6.27 SD=2.20 (see Figure 1). Although our study

Figure 2



was not powered to find a correlation between sim and written examinations, there was no statistically significant Spearman correlation between ASA sim and written ($\rho = 0.698$, $p = 0.742$) or between TCA sim and written ($\rho = -0.222$, $p = 0.276$). Both the written tests (51/53; 96%) and sim tests (53/53) were judged to be fair (as opposed to not fair) by EMR. On a three-point Likert scale (very satisfied, satisfied, and not satisfied), the sim tests had a higher satisfaction rate (45/53 very satisfied; 85%) than the written tests (27/53 very satisfied; 51%) (see Figure 2). Although only 6/53 EMR (11%) had been assessed using simulation previously, the majority of EMR (38/53; 72%) would prefer to see simulation incorporated into the American Board of Emergency Medicine (ABEM) certifying (oral) examination.

Discussion

We feel that our study has several important implications. In regards to graduate medical education, written examinations have many shortcomings in the assessment of future physicians. Specifically, it is very difficult, if not impossible, to assess some of the ACGME's core competencies (i.e., interpersonal & communication skills, professionalism, patient care, and systems-based practice) with a written examination. Medical simulation may be a better tool to assess some of these areas. In addition, medical simulation has a distinct advantage regarding patient safety in comparison to other methods of assessment like direct observation. The era of "see one, do one, teach one" is quickly ending in the wake of patient safety. In fact, some literature demonstrates that simulation-based education can have significant impact on patient outcomes (i.e., lowering the central line-associated bloodstream infection (CLABSI) rate at two participating hospitals).[11] Furthermore, some literature supports the use of simulation-based assessment tools in the assessment of residents in an Anesthesiology residency.[12] However, to our knowledge, no such data exist regarding residents training in Emergency Medicine and/or Medical Toxicology.

While medical simulation is certainly more expensive than proctoring a standard written test, it may be more cost effective than other commonly used methods of assessment like the so-called "standardized patient." These actor-patients are costly and difficult to standardize. There is certainly an opportunity for a comparative study between a medical simulation model and a standardized patient model. Currently, every allopathic medical student in the country is required to take the United States Medical Licensing Examination (USMLE) Step II Clinical Skills (CS) exam prior to receiving his or her medical license. There are only five testing centers in the U.S. and the exam is very costly. The use of a standardized medical simulation experience may lower costs overall and allow for a greater number of testing sites.

This study had several limitations. First, it was a small pilot study with only 53 participants. A larger sample size may have yielded different results. Similarly, we only compared two simulation scenarios (ASA and TCA) versus two written examinations (ASA and TCA) using 10 knowledge-based questions. We chose two of the most important topics in emergency toxicology: tricyclic antidepressant and salicylate poisoning. These

are low frequency, yet high morbidity events. These are two of the major learning objectives that will be relevant for patient care in Emergency Medicine. We estimated that two scenarios were adequate and feasible for an initial proof-of-concept study.

There is also uncontrolled variability in the EMR previous experiences in medical simulation as well as medical toxicology. In addition, a senior EM resident on July 1 is obviously not as experienced in emergency medicine or medical toxicology as a senior resident at the end of the same academic year. However, this inter-learner variability would be expected to progress in both study groups similarly throughout the year. While the residents were blinded to the purpose of the study and the cases were confidential, there is a possibility that some residents discussed the cases outside of the rotation. Similarly, all assessments used by the American Board of Emergency Medicine and other specialty certifying organizations have to deal with variability in training and experience. In addition, the scoring was performed by a single physician (fourth author), which could introduce some bias. However, we feel that this design was an overall strength in our study put in place to eliminate inter-rater reliability and potentially reducing bias on the whole.

In the future, it would be insightful to include more patient scenarios (sim versus written) among a larger pool of EMR. Similar results in simulation accuracy and precision as well as continued higher satisfaction, may justify the incorporation of medical simulation as an assessment tool as a trial in the ABEM certifying (oral) examination. As discussed previously, medical simulation may provide an avenue to assess procedural competency and certain American College of Graduate Medical Education (ACGME) core competencies (i.e., interpersonal and communication skills, professionalism, patient care, and systems-based practice) that cannot easily be assessed using the current ABEM certifying examination format. Other medical subspecialties might utilize medical simulation for similar reasons. Eventually, it would be ideal to quantify a real change in patient outcomes and/or patient satisfaction after an intervention with a simulation-based assessment tool versus a standard written examination. It should be pointed out, however, that simulation is merely a tool that can be used during assessment; simulation cannot replace direct faculty supervision during patient care.

Conclusions

In this pilot study, assessment by sim has similar accuracy (demonstrated by the similar mean scores) and precision (demonstrated by similar standard deviations) but higher satisfaction rates when compared to a written examination. Most participants felt simulation should be incorporated into the ABEM certifying (oral) examination.

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Disclosure

None reported. **MM**

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Nov. 3-4	44th Washington University Kilo Diabetes Symposium
Dec. 2	Congestive Heart Failure
Jan. 20	Hematology and ASH Abstract Review
Feb. 3	Breast Cancer Update
Feb. 3	Rheumatology Update and Highlights from ACR
Feb. 21-24	Annual Refresher Course and Update in General Surgery
March 23-24	10th Annual Sports Medicine Update
March 24	Nephrology Update
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