Missouri Medicine

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Gastroenterology & Hepatology



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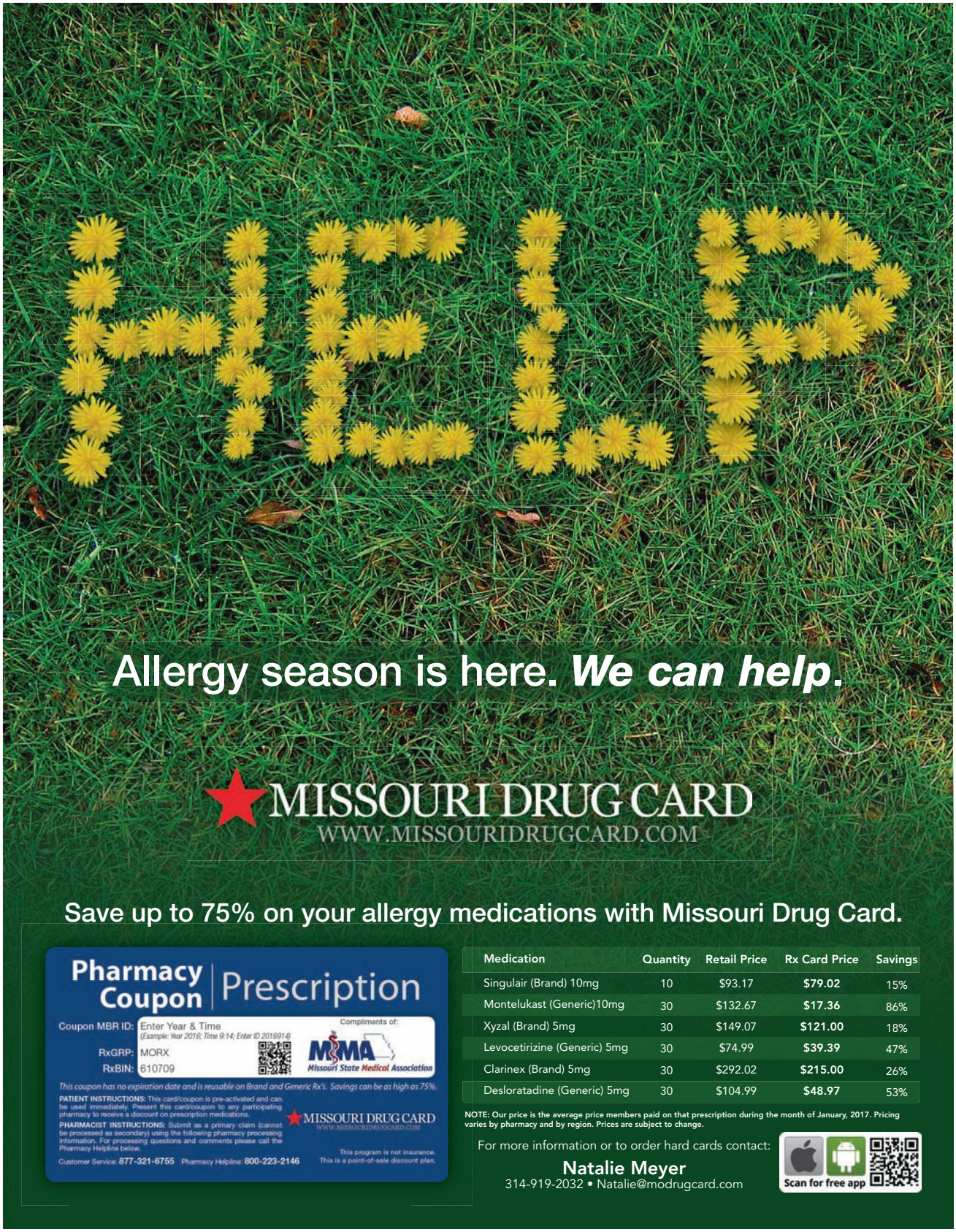
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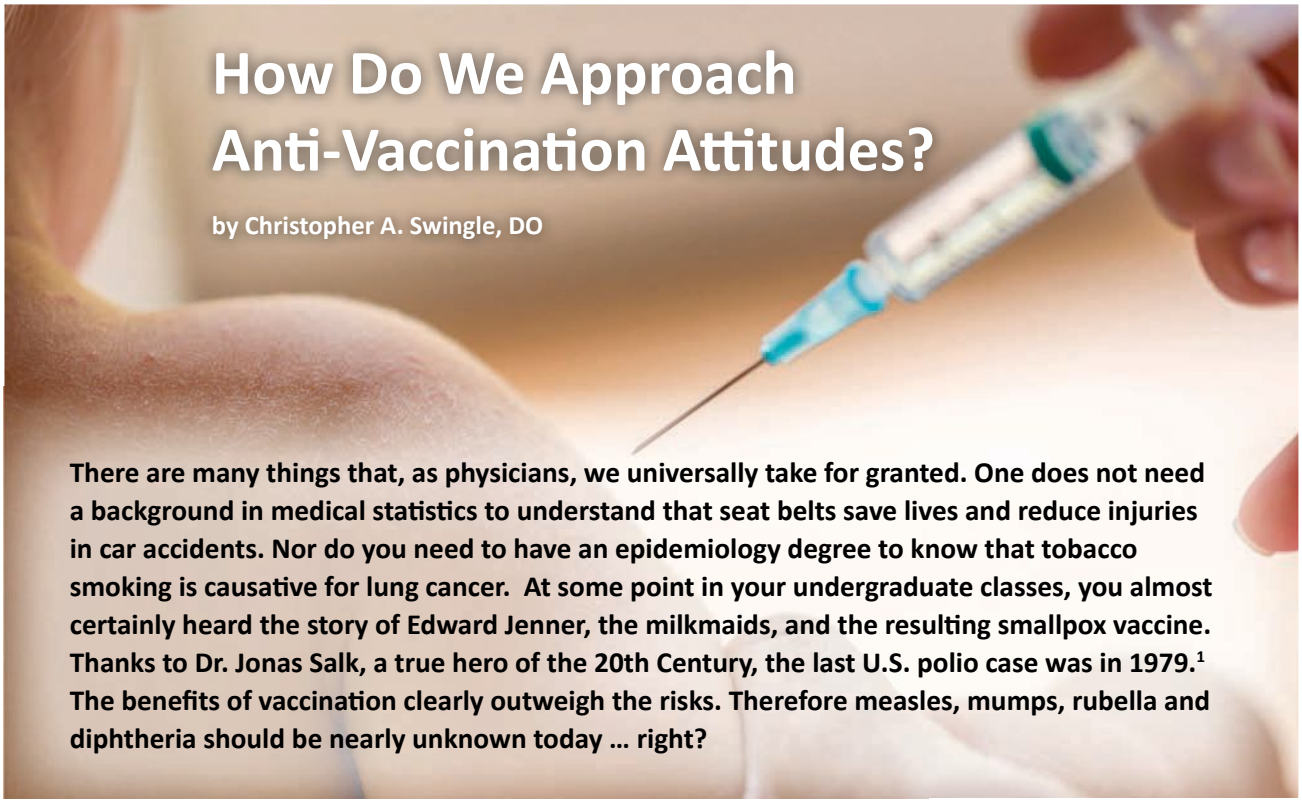
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How Do We Approach Anti-Vaccination Attitudes?

by Christopher A. Swingle, DO

There are many things that, as physicians, we universally take for granted. One does not need a background in medical statistics to understand that seat belts save lives and reduce injuries in car accidents. Nor do you need to have an epidemiology degree to know that tobacco smoking is causative for lung cancer. At some point in your undergraduate classes, you almost certainly heard the story of Edward Jenner, the milkmaids, and the resulting smallpox vaccine. Thanks to Dr. Jonas Salk, a true hero of the 20th Century, the last U.S. polio case was in 1979.[1] The benefits of vaccination clearly outweigh the risks. Therefore measles, mumps, rubella and diphtheria should be nearly unknown today … right?

Something else that we undoubtedly learned in our medical training is not found in a textbook, but is taught all the same. From the level of nations down to the individual, people do not necessarily share the same values. Between nations, this manifests as diplomatic disputes and war in the worst possible scenario. On the physician-patient level, it is the case of the physician convincing a diabetic who places greater value in the psychological comfort of fast food about the value of diet and exercise. We think that because the medical values we have spent years studying are second nature to us, logically they should be obvious to everybody. They are not.



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Anti-Vaccination Movement Is Long-Standing

Even in Edward Jenner's time, there was an anti-vaccination movement.[2] Sir William Osler got so fed up with the "anti-vaxxers" of 1910 that he dared them to expose themselves to smallpox and promised to personally pay for the resulting funeral expenses. He did not get any takers.[3] Historically, anti-vaccination sentiment gains momentum once the worst infectious diseases were no longer visible to the public. Now that there is a whole schedule of vaccinations, many of the most dreaded childhood infectious diseases have lost visibility. From this place of comfort and safety made possible by widespread vaccination, we now have to contend with a resurgent anti-vaccination movement.

Spend a few minutes on social media, or watch the feel-good daytime television shows ubiquitous in patients' hospital rooms. Wouldn't it be nice to have the same reach to millions that charismatic opportunists like Dr. Oz or Jenny McCarthy have? Could a few snarky pro-vaccination Facebook memes go viral and change minds our way for once? Until such time, physicians will have to leverage the physician-patient relationship in a smart and persuasive way.

To know how to intelligently respond, we need to examine where the fabrications are coming from, who

the consumers are, why they give it credence and what can be done to convince them otherwise.

According to a paper by Kata,[3] the origin of misinformation typically starts with valid scientific debate on the risks of vaccination. One would hope that debate would be based on honest data presented after a rigorous peer-review. Unfortunately, the fraudulent Lancet paper by Wakefield from 1998 (finally retracted by that journal in 2010 after 12 years of damage had already been done) calls even that assumption into question.[4] From there, the debate is spun to conform to the anti-vaccination agenda and then reaches the public, typically through social media.

Study Examines Common Traits of Anti-Vaccination Believers

One question that needs to be answered is, "What traits do anti-vaccination believers have in common?" Hornsey et al. tackled this question and found some commonalities while dispelling a few stereotypes.[5] Surprisingly, there seems to be no real correlation between vaccine attitudes and socioeconomic status or educational level. Much better predictors are a high level of conspiratorial thinking, a low tolerance to infringement on perceived personal freedom, aversion to needles or blood and religious issues. But most importantly, the consumers of misinformation are most commonly concerned parents.

A large part of why people buy into the anti-vaccination mindset is confirmation bias; when presented with evidence opposing existing beliefs, patients and parents will reject the information out of hand. A German study demonstrated that subjects will perceive increased risk to vaccination after only five to ten minutes of time on an anti-vaccination websites.[6] Additionally, a Canadian study suggested that the odds of parents perceiving vaccines as unsafe rose considerably for those who searched for vaccine safety information on the internet.[7] Herein lies the problem: From the skeptical point of view, these websites present valid questions. From our point of view they are absurd and dangerous, but providing evidence for an absence of risk is painfully difficult. How can you expect to find common ground in this scenario, much less be persuasive?

Frustratingly, direct pro-vaccination messages may not be simply unhelpful, but can potentially backfire. Nyhan et al. found that not only did none of their four approaches to directly educate concerned parents with CDC-sourced pro-vaccination materials help, but also further reinforced the exaggerated perception of risk.[8] The adversarial model that worked so well against the tobacco industry is unlikely to be helpful here. Moreover, nobody likes being lectured or talked down to, no matter how misguided their beliefs might be.

Education on the Consequences of Not Vaccinating

Horne et al. tried a different approach; instead of directly taking on vaccine misinformation, experimental parent groups were educated on the consequences of not vaccinating their children. They had success with the group that was shown pictures of children with mumps and rubella, along with a letter from a mother of a measles patient. Disappointingly, a second group that was educated on the nonexistence of a vaccine/autism link remained as unconvinced as ever.[9]

So we have evidence for an approach that potentially works for a select group of patients, but obviously much work remains to be done. On the individual level, I believe it has to come back to the doctor-patient relationship. Patients will continue to trust physicians who listen to their concerns. If we do not have that trust, we cannot reasonably hope to persuade on the real risks and benefits of vaccination. On the societal level, we need communicative physician leaders to engage the issue, not the activist. Rather than confrontationally going after anti-vaccination groups, physicians must clearly articulate a message on the consequences of being unvaccinated.

On a lighter note, if you need a break after reading this, look up ZDoggMD's clever House of Cards parody, "Magna Cum Measles" on YouTube.[10] While I cannot recommend his hilariously unorthodox approach to a skeptical mother as a "best practice," it is still a very funny three-minute skit on the subject of vaccination.

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PART 1

The 1918 Influenza in Missouri: Centennial Remembrance of the Crisis

by David S. McKinsey, MD, Joel P. McKinsey, MD & Maithe Enriquez, PhD

In September 1918, war-weary Missourians were bracing for the coming storm: not another extreme weather event, but the lethal influenza epidemic steamrolling through the country's eastern cities and military cantonments and bearing down on the Midwest. Tens of thousands of young people were dead; major cities were on the verge of collapse. Former Missourian Dr. Victor Vaughan, raised in rural Randolph County, headed the U.S. Army's Division of Communicable Diseases. In October 1918, Dr. Vaughan concluded, "If the epidemic continues its mathematical rate of acceleration, civilization could easily disappear from the face of the earth within a few weeks".[1]

This year marks the centennial anniversary of the 1918 Influenza pandemic. Although often overshadowed in our nation's collective memory by World War I, in fact influenza took more lives in a shorter time period in 1918-19 than any other event in human history.[2] Approximately 670,000 Americans succumbed to influenza in the U. S., more than the cumulative combat death toll of our military forces in World Wars I and II, the Korean conflict and the Viet Nam War.[3] Worldwide, 50-100 million died,[2, 4] a figure vastly exceeding the mortality tolls of other pandemics in the 20th and 21st centuries (Figure 1). This article, the first in a series, will address the origins and spread of the 1918 influenza, its clinical and pathological manifestations, the impact of the pandemic on Missouri's population, the responses of dedicated medical and nursing professionals in our state, and insights gained from new assessment of available epidemiologic data. The word influenza is rooted in the medieval Italian phrase influentia del freddo (influence of the cold), reflecting the centuries-old observation that annual epidemics occur in the winter months.[5] Interspersed lethal pandemics emerge at unpredictable intervals a few times each century. In the early twentieth century, physicians had not yet identified the cause of this generally mild and self-limiting illness, commonly known as the "grippe." Although the germ theory of disease had been well-established for a few decades some physicians still attributed influenza to miasmas (noxious vapors) rather than infection. The field of virology was in its infancy and the possibility that influenza was a viral illness had not yet been considered seriously. No known treatment or prevention for influenza existed, nor would any become available until long after the 1918 pandemic (Figure 2.)

In 1918 the country's attention was focused squarely on World War I, which led to the mobilization of more than four million American military recruits and the construction of 30 hastily built cantonments throughout the country, each of which housed up to 50,000 soldiers in overcrowded barracks.[6] Historians have concluded that the war effort was inextricably linked to the spread of the 1918 influenza in the United States and abroad.[6] The extremely high risk for epidemics among soldiers had been well-known for centuries.[7] During the war millions of young men, many of whom were immunologically naive to highly contagious infections, were dispersed around the country to military camps en route to battlefields in Europe, setting the stage for an explosive pandemic.

Although the 1918 pandemic is widely known as the "Spanish Influenza," a more appropriate name could be the "Kansas Flu."[8] The federal Sedition Act of 1918 prohibited the use of "disloyal, profane, scurrilous, or abusive language" about the U. S. government, in a heavy-handed attempt to improve morale during the war. Accordingly, little was published in the U.S. about influenza. However, in neutral Spain the uncensored press reported freely about the influenza pandemic, leading to the enduring misperception that the disease had begun there. In fact most historians



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believe that the first wave of 1918 "Spanish" influenza in the world began on March 4, 1918 at Camp Funston, Kansas, 120 miles west of the Missouri border.[1] During the following weeks thousands of soldiers developed influenza and 38 died.[9] (Figure 3) As soldiers from Camp Funston were transported to other cantonments throughout the country, influenza spread like wildfire.

Thousands of military personnel worldwide developed influenza in the spring and early summer of 1918, but little alarm was raised as the illness was deemed to be "everywhere of a mild form."[9] Barry has postulated that the trigger for the Camp Funston epidemic was a smaller outbreak in Western Kansas the previous year.[2, 9] However, an analysis of death certificates in St. Joseph, the third largest city in Missouri in the early twentieth century, suggests a trend of increasing influenza mortality in Missouri as early as 1915.[10] The pandemic therefore may have been heralded by mutating viruses not only in Kansas but also in Missouri and elsewhere, well in advance of the deadly 1918-19 season.

The second wave of the 1918 influenza pandemic struck with a fury in August. Simultaneous outbreaks were reported in Camp Devins, Massachusetts, (near Boston), France, and Sierra Leone. In contrast to typical seasonal flu, the 1918 influenza strain that reappeared in August was exceptionally virulent and often lethal, especially among young adults. The highest mortality rates were reported among persons between 20 and 40 years old, an age group generally unscathed by seasonal influenza.[4] A contemporaneous description from a physician at Camp Devins paints a chilling picture. "Victims develop the most viscious (sic) type of Pneumonia that has ever been seen. Two hours after admission they have the Mahogany spots over their cheekbones and a few hours later you can begin to see the Cyanosis extending from the ears and spreading all over the face."[11] Typical symptoms included fever above 105 degrees, delirium, lethargy, prostration, bleeding from the nose and ears, and hemoptysis "(resembling) tomato puree."[12] A feature of illness noted by many observers was "strikingly intense cyanosis."[13] The mortality rate was shockingly high: 757 previously robust young soldiers at Camp Devins died.[14] Several observers described seeing people who were healthy one day and dead within 24 hours.

Influenza Pandemic
Comparative Mortality

1918-9
U.S. 670,000 (0.6%)
Worldwide 50 Million (2.7%)

1957-8
U.S. 70,000 (0.03%)
Worldwide 2 Million (0.07%)

1968-9
U.S. 34,000 (0.02%)
Worldwide 1 Million (0.03%)

2009-10
U.S. 12,000 (0.004%)
Worldwide 284,000 (0.004%)

Figure 1. Influenza pandemic mortality, U.S. and worldwide, total (% of population).

The 1918 flu also was particularly prone to enabling aggressive secondary bacterial pneumonia, a common cause of death.[15] A biphasic illness pattern was noted in many cases: typical influenza was followed by transient improvement but subsequent abrupt deterioration after secondary bacterial infection was established. Pathologists noted "immediate exudation of dark bloody fluid" from the lungs of influenza victims.[13] The lungs appeared shapeless, blue, foamy, and edematous.[16] Features consistent with acute respiratory distress syndrome, an entity not formally described until decades after the pandemic, were noted in about half of autopsies.[17]

After influenza decimated Camp Devins and several other cantonments in September 1918, the disease quickly spread to eastern cities where public services and health care providers were nearly overwhelmed. The pandemic created widespread panic. A crossroads state, Missouri was an inevitable target. Historian Alfred Crosby's description was particularly applicable to our state: "Influenza moved across the United States in the same way as pioneers had, for it followed their trails, which had become railroads, and

Figure 2. Timeline of major events related to influenza

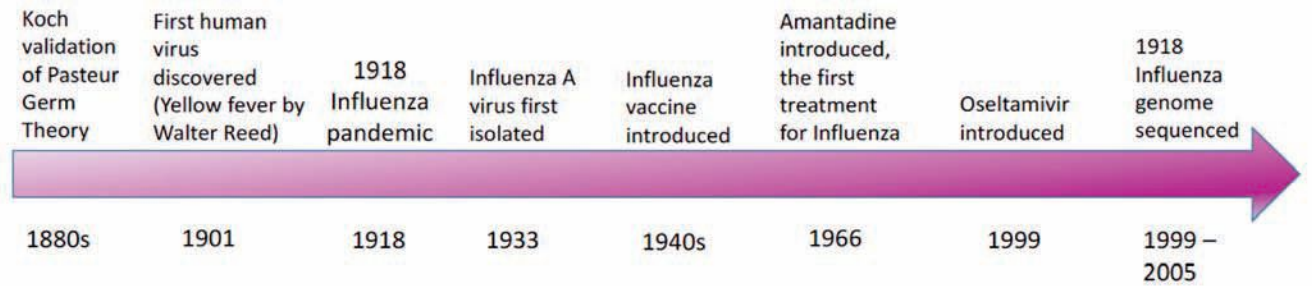




Figure 3. Camp Funston, Ks., emergency hospital during 1918 influenza epidemic.

propagated fastest in those localities most attractive to them – the confluences of rivers and trails."[18] In a few weeks the state's health care workers would address the worst medical crisis in the state's history, one which took a heavy toll and had a lasting impact.

In the 1910s, Missouri's population was almost 3.3 million, seventh highest among the 48 states. St. Louis, population 687,000, was the nation's fourth largest city and Kansas City, with 248,000 citizens, ranked twentieth. The state's third, fourth, and fifth largest cities, respectively, were St. Joseph, Springfield, and Joplin. About half (49%) of the state's population resided in rural areas. Travelers primarily relied on a train system with more than 8,000 miles of track, twice today's figure. Although past their prime, riverboats plied the Osage River, which was still navigable a decade before the construction of Bagnell Dam created the Lake of the Ozarks, as well as the Mississippi and Missouri Rivers. Cross-state driving was challenging. Although each county was served by at least one highway, all of the highways were unpaved. Thus several routes existed for influenza's introduction to Missouri and its rapid spread throughout the state.

In Missouri, as in other states, the first cases of influenza probably began at a local military camp when infected soldiers arrived from cantonments in other parts of the country. The disease then spread quickly to the civilian population. On September 27, cases were reported at two Army motor schools in Kansas City; on October 4, 1918, influenza exploded at Missouri's large military base, Jefferson Barracks, near St. Louis, where 500 cases were reported among 6,000 soldiers. Simultaneously cases were reported in southwestern Missouri, possibly among soldiers returning home from training at cantonments in neighboring states. As the epidemic spread during the first weeks of October, physicians, nurses, hospitals, and health departments throughout Missouri struggled to cope with an unprecedented burden of disease, while handicapped by a substantially reduced work force: fully half of the state's physicians were away, serving in the military.

Missouri's physicians had few therapeutic options for their acutely ill patients with influenza. The primary goals of treatment were pain alleviation, cough control, and either stimulation or reduction of heart rate depending on the situation. The pharmaceutical armamentarium was limited. Quinine, first introduced in the U. S. in Arrow Rock, MO in the 1800s for treatment of malaria, was now given as an influenza preventative, without benefit. Other available medications included aspirin, morphine, codeine, heroin, atropine, digitalis, strychnine, and epinephrine. Physicians at the time correctly concluded that "no especial measure was of avail."[13] Aside from providing symptomatic treatment, probably the most useful functions of the physician were to advise bedrest and to monitor for signs of bacterial pneumonia, which connoted a worsened prognosis.[19]

Actually, by far the most important need of 1918 influenza patients was for nursing care. "Nursing is nine tenths, just the same," said the nurse in Katherine Anne Porter's "Pale Horse, Pale Rider," referring to the totality of a patient's care.[20] Porter, who almost died from influenza, probably was underestimating. However, in 1918 nurses were in even shorter supply than physicians: there were one-quarter as many trained nurses as doctors. The American Red Cross (ARC), founded by Clara Barton in 1882, stepped into the void. The Red Cross not only had full responsibility for supplying nurses for the U.S. Army, but also was tasked with identifying civilian nurses to battle the epidemic at home.[21] Many Missouri nurses became ill while caring for their patients, and those who remained on the job had staggering workloads of 30-40 inpatients per day.[22]

Table 1
Missouri All Cause Mortality Rate Analysis by Region (excluding St. Louis and Kansas City)
1915 and 1918, Missouri counties (n=112)

Region State of Missouri	*Number of counties*	***Pop. density mean (sd)*	*1915 mortality Mean (sd)*	*1918 mortality mean (sd)*	*% increase mortality from 1915 to 1918*
Southeast	13	33.7 (14.1)	11.8 (3.9)	15.1 (6.04)	28%
East	10	35.6 (17.2)	10.9 (1.7)	13.7 (1.9)	26%
West	12	37.2 (9.1)	11.2 (2.0)	13.7 (3.2)	22%
Northeast	16	34.3 (12.1)	9.5 (1.4)	12.6 (2.1)	32%
Central	13	31.5 (10.2)	10.2 (1.9)	12.5 (3.4)	22%
Northwest	15	32.5 (4.1)	10.3 (1.8)	11.7 (2.2)	13.5%
Southwest	18	35.1 (19.2)	9.3 (2.1)	11.4 (4.2)	23%
South Central	6	20.5 (2.6)	9.3 (1.9)	10.5 (1.7)	13%
South	9	17.8 (5.5)	7.9 (1.4)	9.4 (2.5)	19%

**Region based on current Missouri State Highway Patrol definition*
***Population density = people per square mile in 1910*

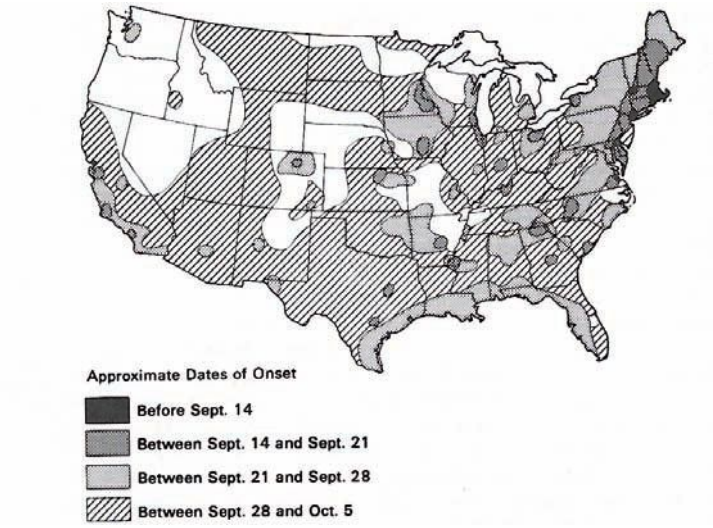


Figure 4. Approximate dates of onset.

Missouri's influenza and pneumonia mortality rate in 1918, 476.6 per 100,000 population, ranked 22nd among in the 30 states for which data are available.[23] This figure more than doubled from the prior year.[24] In 1918 detailed disease surveillance data were maintained for the state's two largest cities, St. Louis and Kansas City, but not in other areas of the state. The mortality ratio in these two cities has been reported to be 1.32 times higher than in Missouri's rural areas.[24] However, "rural" areas included cities of up to 100,000 population.[24]

We conducted a more detailed analysis of the geographic differences of 1918 influenza on the state's population. The annual all-cause mortality rates of Missouri counties (n=112) were compared to baseline figures from 1915 using data from the U. S. Bureau of the Census (Table 1).[23] Data from St. Louis City and County (administratively distinct entities) and Jackson County, each of which had much higher death rates than the remainder of the state, were omitted from our analysis. Counties were grouped into nine regions, as defined by the Missouri State Highway Patrol currently. The mean statewide mortality in 1918 per 1,000 population was 12.4 (range 5.1-29.4), up from 10.1 (range 5.1-19.9) in 1915. In each of the state's regions the mortality rate in 1918 was significantly higher than that in 1915 (p= .000). The three counties with highest mortality rates were Dunklin (29.1), Vernon (23.1), and Butler (23); the lowest rates were identified in Dallas (5.1), Douglas (6.1), and McDonald (6.2) counties. The southeastern region of Missouri had the highest mortality rate (15.1); the two lowest rates were seen in the south (9.4) and south central (10.5) regions, the least populated areas in the state. A 5.7-fold mortality difference was noted between the state's highest and lowest ranked counties. Thus, although influenza in 1918 significantly increased mortality in every region of the state, there was an uneven impact on Missouri's population.

To some extent Missouri was fortunate to be struck by influenza's second wave at a later stage than the eastern seaboard, particularly in rural areas of the state (Figure 4). As a general rule influenza cases were less severe in the later weeks of the epidemic's second wave than at the beginning.[25] This factor may have contributed to Missouri's disproportionately lower mortality than other highly populated states. Social determinants of health, such as poverty, may have accounted in part for the higher death rate in southeastern Missouri.

Contemporaneous accounts described the impact of influenza throughout the state. At the University of Missouri, Dr. Dan Stine recorded 1,020 student cases of influenza between September 26 and December 6. He "saw one patient die within 18 hours of this disease and 12 hours after being put to bed."[26] The volume of influenza cases was so high in Columbia that patients were admitted not only to Parker Hospital but also to the Athens Hotel, Welch Military Academy, and a women's dormitory at the University. In Van Buren, members of several families were all are sick in bed at the same time and "both local doctors (were) on the go both day and night."[27] Dr. William E. Kitchell of St. Clair, the county health officer, was so busy that he didn't change clothes for three straight days and

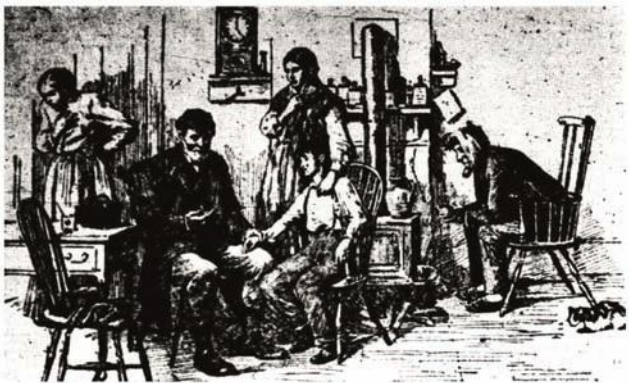


Figure 5. "We've got that durned influenzy agin" by A.B. Frost, *Kansas City Star,* November 27, 1918

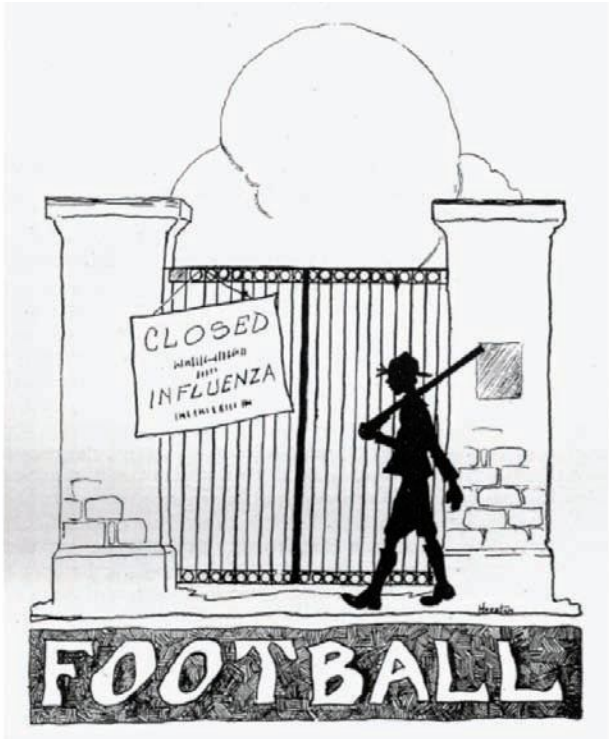


Figure 6. University of Missouri yearbook The Savitar, 1919

nights.[28] Private Charles Hill died from influenza while fighting in France. His commanding officer informed Private Hill's mother of Dunnegan, Mo., that "it came so fast and with such little warning that the best medical care could not save him."[29]

Famous Missourians were among those afflicted with the 1918 influenza. General John J. Pershing, of Laclede Mo., was commander of the American Expeditionary Force in World War I. He developed severe influenza in late October and became encephalopathic, before he recovered fully. U.S. Representative Champ Clark, from Louisiana, Mo., the only Missourian to serve as U.S. Speaker of the House of Representatives, was confined to bed with influenza, necessitating a several-week recess of the U.S. Congress. Clark recovered but two of his fellow Missouri congressmen, Representatives Jacob Meeker and William Borlan, did not. Meeker visited Jefferson Barracks on October 10 and seven days later was dead from influenza, likely acquired at the base. Borlan, co-founder and former Dean of Kansas City School of Law (predecessor of the University of Missouri-Kansas City law school), died from influenza while touring army camps in France. Captain Harry Truman, writing to his fiancée Bess Wallace in Independence in early 1919 from Europe, expressed relief at her recovery from influenza. Walt Disney lived in Marceline, Mo., (the model for Main Street USA at Disney World) from 1906-11 and in Kansas City from 1911-17. He enlisted in the Red Cross Ambulance Corps in Chicago in September 1918, and developed influenza while in training. The resultant convalescence period delayed his departure to Europe until after conclusion of the war's bloodiest fighting.[30] Thus, arguably influenza may have saved Mr. Disney's life.

Missouri's schools and universities were substantially impacted by influenza. Each of the state's three medical schools (the American School of Osteopathy, now known as A.T. Still University; Saint Louis University; and Washington University) graduated their classes early, to bolster the understaffed health care workforce. Washington University students received their degrees in absentia in Europe. Public school systems across the state cancelled classes for weeks at a time, sometimes on multiple occasions, leaving parents to care for restless children in their quarantined homes (Figure 5.) The University of Missouri was quarantined twice, and the Mizzou Tigers, under Coach John F. Miller, cancelled the entire 1918 football season (Figure 6).

After the 1918 influenza pandemic receded, Missourians continued to carry a heavy burden. Some survivors developed von Economo disease (post-encephalitic Parkinson Disease.)[31] Thousands of families lost loved ones; countless children were orphaned. Despite, or perhaps because of, the trauma of these grievous experiences, in the coming decades most survivors preferred to avoid the subject. Famous authors of the era, including former Kansas Citian Ernest Hemingway, a *Kansas City Star* reporter in 1917 and 1918, did not discuss influenza in their works. This dearth of recorded material may have contributed to the general lack of recognition by subsequent generations of the catastrophic impact of 1918 influenza.

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The next article in this series will compare the well-documented experiences with 1918 influenza in Missouri's two largest urban areas, St. Louis and Kansas City, including important public health lessons that still resonate after a century. In addition the impact of influenza on Jefferson Barracks and Base Hospital 21, a World War 1 medical center in France staffed by Missourians, will be addressed.

Acknowledgment

The authors dedicate this manuscript to Ladene Stark Smith, our great Aunt, who succumbed to influenza in early 1919 at age 19 shortly after moving from Missouri to an adjacent state.

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MM



Prescription Opioid Misuse and Overuse in the U.S.

by David A. Fleming, MD

Better science, better training, improved health care access, improving public awareness, and policies aimed at alleviating social contributions to poor health are all important in addressing the opioid epidemic

A recent report by the U.S. Senate Homeland Security and Governmental Affairs Committee offered results of an investigation into the aggressive efforts of opioid manufacturers and distributors to boost sales.[1] This report describes the efforts of at least one drug manufacturer to boost approvals for highly addictive controlled substances, including for inappropriate and off-label uses. It also details an audio recording in which a sales representative misidentifies herself and attempts to circumvent the required prior authorization process. These are serious and concerning allegations as to how some in the pharmaceutical industry systematically and aggressively pressure employees and the medical system to increase sales and use of their products. These events are particularly egregious because the products in question are opioids that when distributed inappropriately place the public at risk.

Many in our society use opioids but some are more negatively impacted than others when using them. The recently published 2015 National Survey on Drug Use and Health (NSDUH) revealed that an estimated 38% of U.S. adults (92 million) use prescription opioids, among which nearly 5% (11.5 million) misuse them; nearly 1% (2 million) report a prescription opioid use disorder (dependence and abuse).[2]



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There are two findings of particular concern from this survey, the first being that of those misusing opioids, 60% reported doing so without having a prescription and 41% obtained them from friends or relatives; second, that misuse and use disorders were most commonly reported in adults who were uninsured, unemployed, had low income, or had behavioral health problems.

The opioid epidemic in the U.S. has become a national emergency and deemed one of the most consequential preventable public health threats facing the nation.[3] Opioids are heavily prescribed and overused, all too often with deadly consequences. Opioid overdose deaths increased 156% from 2010 (21,088) to 2015 (33,091); in teenagers overdose death rates increased 19% from 2014 (649) to 2015 (772), more than double the rate increase since 1999. Aggravating the situation is the availability of highly potent opioids such as fentanyl that may be produced and obtained illegally and are potentially lethal through skin absorption, inhalation, incorrect dosing, or lacing with other drugs.[4]

Paradoxically, in the face of this shocking data, opioid prescribing has actually gone down in recent years. The US Centers for Disease Control and Prevention (CDC) recently reported that between 2006 and 2015 opioid prescribing in the U.S. peaked in 2010 and then decreased through 2015.[5] Prescribing rates increased from 72 to 81 prescriptions per 100 persons then declined to 71 per 100 persons by 2015 (a 13% decline). However, personal prescription use in the U.D. in 2015 was still 3 times higher than in 1999 and nearly 4 times higher than in Europe. Of particular concern is that in spite of observed reductions in opioid prescribing opioid-involved overdose death rates continue to increase.

Several factors contribute to the overuse and dangerous misuse of opioids. The question is, who is accountable and what can be done to stem the tide of inappropriate opioid use? Certainly, physicians must assume substantive responsibility because they are doing the prescribing. Several major professional societies, including the American

College of Physicians, the American Academy of Family Practice, and the American Medical Association have developed guidelines and introduced programs to help educate physicians about opioid prescribing and addiction. Yet many patients are still not being treated effectively or appropriately. A recent study found that 40% of those with a heroin overdose and 60% of those with a prescription opioid overdose filled a prescription within six months following their overdose and often for the same medication with which they previously overdosed. At the same time, medication assisted treatment following opioid overdose increased by only 3.6%.[6]

In the face of this opioid crisis pharmaceutical companies are culpable and must also assume responsibility because they develop and often aggressively market substances that are known to be addictive and potentially deadly. Marketing strategies also attempt to influence physician-prescribing behavior and boost sales of their product. Pharma spends over $20 billion a year on marketing, most of which goes to doctors as gifts.[7] A survey of doctors in 2003 and 2004 revealed that nearly 95% of American doctors receive free food, beverages, drug samples, sports tickets, and other benefits from drug companies despite voluntary reporting guidelines set in 2002.[8] Most of these relationships (83%) involved receiving free food while 78% involved giving free drug samples. About one-quarter received full or partial reimbursement for continuing education, while 18% were paid consultant fees. Cardiologists are the most likely to receive direct payments while anesthesiologists received the most payment from the pharmaceutical industry.

In an eighteenth month study of the Centers for Medicare and Medicaid Services data identifying pharmaceutical industry payments (2013-2015) to physicians related to the use of an opioid, 1 in 12 physicians (over 68,000) received payment (median=$50; range=$16-$151).[9] The top 1% received 82% of all payments, mostly as speaking fees or honoraria. The data is compelling that pharmaceutical pandering to physicians affects prescribing behavior, even when offering small gifts. This has led to legislative efforts in several states and the federal government, as well as stepped up efforts at self-regulation by the pharmaceutical industry and medical professional groups, to limit the influence of the pharmaceutical industry.[10] Even free drug samples are viewed as suspect because when then given to a patient the doctor must then complete the course of treatment by giving a prescription for the same medication. Some have argued that the problem isn't with the pharmaceutical industry but with the profession itself for not having the discipline or training to fend off these influences.7

The CDC contends that the epidemic of opioid misuse, overdose, and death is a multifaceted crisis that requires partnership across sectors to respond with effective health care and public safety strategies. Findings of the recent NSDUH survey underscore the urgent need for more effective approaches to pain treatment that include better training of physicians in how to prescribe, when to treat, better access to evidence based and effective non pharmacologic modalities of treatment, and development of better non addictive drugs to treat pain. Enhancing general availability and access to proven and safe pain treatment for all sectors of society may help decrease opioid misuse. Changing prescribing patterns that leave people with unused opioids available for misuse by others could also help.

Better science, better training, improved health care access, improving public awareness, and policies aimed at alleviating social contributions to poor health are all important in addressing the opioid epidemic but there is an equally pressing need to reign in marketing forces that unduly and sometimes illegally influence the prescribing behavior of physicians.

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MM

Why Marijuana Will Not Fix the Opioid Epidemic

by Kenneth Finn, MD

Currently, there is no widely available or accepted medical literature showing any benefit for pain with dispensary cannabis in common pain conditions.



Marijuana has been used for reported medical purposes for thousands of years when the plant at that time had THC content of 0.5-3%. Currently, the most common reported medical use is for pain. As of this writing there are 30 states and the District of Columbia have some form of legalized marijuana, with eight states having legalized for recreational use.

The United States is currently in the grips of an opioid epidemic which has been growing over the last 20 years and began with "pain" being termed the "5th vital sign." At the time, it was reported that people in pain did not become addicted to opioids, and the number of opioid prescriptions started to increase over time, followed by an increase in opioid overdose deaths.[1]

There has been a lot of discussion about how the use of cannabis will help curb the opioid epidemic.[2] It has been reported that medical cannabis laws are associated with significantly lower opioid overdose mortality rates, and others have suggested that legalization may result in less opioid overdose deaths.[3] Other studies have reported that medical marijuana laws were associated with a decrease in Medicare prescriptions, saving millions of dollars.[4] The same authors followed up with another report suggesting that medical cannabis laws are associated with significant reductions in opioid prescribing in the Medicare Part D population.[5] Cost savings in this day and age of health care is very important, but it was noted that "the researchers themselves cannot say if people switched from opioid prescriptions to using a medical marijuana product." It is difficult to translate population-level analyses to individual marijuana-opioid substitutions, and this patient population is a rather small percentage of people who may be using opioids and/or medical marijuana. In 2017 Colorado had a record number of opioid overdose deaths from any opioid, including heroin and Colorado has had a medical marijuana program since 2001.[6]

In the face of the opioid crisis, the medical providers should utilize other ways for people to avoid the use of opioids. Treatments such as physical therapy, acupuncture, chiropractic, massage, and cognitive-behavioral therapies are some of the standard treatments in the management of people with pain. Other naturopathic remedies have been suggested and tried but not proven.[7]

There is some evidence that there are components of the marijuana plant which may have therapeutic medical value.[8] Cannabinoid and opioid receptors belong to the rhodopsin subfamily of G-protein-coupled receptors and are synergistic.[9] Both, are localized primarily at the presynaptic terminals and when activated, reduce cellular levels of cyclic adenosine monophosphate (cAMP) by inhibition of adenylyl cyclase, which effects neurotransmission. Receptor activation of both also modifies the permeability of sodium, potassium, and calcium channels and receptors of both systems coexist in the central nervous system, with overlapping distribution in the brain, brainstem, and spinal cord.[10] Both receptors co-localize on GABA-ergic neurons with potential coupling to second messenger systems, and receptor stimulation can suppress inhibition, suppress excitation, as well as inhibit the release of several neurotransmitters, including L-glutamate, GABA, norepinephrine, serotonin, dopamine, and acetylcholine, therefore modulating pain pathways and potentially provide antinociception. Opioids and cannabinoids



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share pharmacologic profiles and both can cause sedation, hypotension, hypothermia, decreased intestinal motility, drug-reward enforcement, and antinociception.

There are several reasons as to why any reported benefit will be outstripped by lack of benefit and increased risk of harm, and why cannabis is contributing to ongoing opioid use, and subsequently, the opioid epidemic. There is evidence in animal models showing adolescent rats exposed to THC will develop enhanced heroin self administration as adults[11] which may be due to activation of mesolimbic transmission of dopamine by a common mu opioid receptor mechanism.[11,12] More than 90% of heroin users report a prior history of marijuana use compared to a prior history of painkiller use (47%).[13] Prospective twin studies demonstrated that early cannabis use was associated with an increased risk of other drug abuse.[14] This particular study was conducted when the THC content was much lower than todays products which can reach 95% THC.

The currently accepted body of evidence supporting use of cannabis in pain consists of 28 studies comprised of 63 reports and 2,454 patients.[15] Additional articles relying on this primary paper misleading stating that "there is substantial evidence that cannabis is an effective treatment for chronic pain in adults."[16] Both articles noted that products typically studied are not available in the United States (nabiximols, Sativex) or were with available synthetic agents (dronabinol, nabilone), and were studied in less common pain conditions: neuropathic and cancer pain. Currently there is no widely available or accepted medical literature showing any benefit for pain with dispensary cannabis in common pain conditions.[17]



Dispensary cannabis is a generic substance containing multiple components which may have physiologic activity in the body. The College of Family Physicians of Canada outlined potential prescribing guidelines of medical cannabinoids in primary care.[18] They strongly recommended against use for acute pain, headache, osteoarthritis, and back pain, and also discouraged smoking.

There is currently a large and growing body of evidence showing that cannabis use increases, rather than decreases non-medical prescription opioid use and opioid use disorder, based on followup of more than 33,000 people.[19] Concurrent use of cannabis and opioids by patients with chronic pain appears to indicate a higher risk of opioid misuse.[20] Closer monitoring for opioid-related aberrant behaviors is indicated in this group of patients and it suggests that cannabis use is a predictor of aberrant drug behaviors in patients receiving chronic opioid therapy.

Inhaled cannabis in patients with chronic low back pain does not reduce overall opioid use, and those patients are more likely to meet the criteria for substance abuse disorders, and are more likely to be non-adherent with their prescription opioids.[21] It has been found that patients with chronic pain participating in an interdisciplinary pain rehabilitation program using cannabis may be at higher risk for substance related negative outcomes, and were more likely to report a past history of illicit substance, alcohol, and tobacco use.[22] A more recent study of 57,000 people showed that medical marijuana users are more likely to use prescription drugs medically and non-medically, and included pain relievers, stimulants, tranquilizers, and sedatives.[23] There is also evidence that state medical marijuana laws lead to the probability people will make Social Security Disability claims.[24]

There is sufficient and expanding evidence demonstrating that medical marijuana use will not curb the opioid epidemic. There is further evidence that marijuana is a companion drug rather than substitution drug and that marijuana use may be contributing to the opioid epidemic rather than improving it. Although there are patients who have successfully weaned off of their opioids and use marijuana instead, the evidence that marijuana will replace opioids is simply not there. Medical provider and patient awareness, utilization of prescription drug monitoring programs, widespread availability and use of naloxone, and increasing coverage for atypical opioids and abuse deterrent formulations are only some of the other factors which hopefully be contributing to any impact on the opioid crisis. Education and prevention efforts as well as medication assisted therapies will be additional benefits to impact the opioid epidemic. Physicians should continue to monitor their patients closely, perform random drug testing to detect opioid misuse or aberrant behavior, and intervene early with alternative therapies when possible. Marijuana alone is certainly not the answer.

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Disclosure

None reported. **MM**

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Toxic Work Environment

by Charles W. Van Way, III, MD

If we do not find ways to make out work environment more functional and less frustrating, and if we cannot push our health care organizations into promoting change, we will be in a toxic work environment for a long time to come.

At the 2018 MSMA Annual Meeting, I had the great privilege of participating in a session on physician burnout, for the Missouri Psychiatric Association. The main speaker was Dr. C. Robert Cloninger, professor of psychiatry and director of the Center for Well-Being at Washington University. His presentation was much more complex and sophisticated than mine, resting on his extensive work on the psychobiological theory of personality.[1] But we agreed on the central point of the problem. Since Dr. Cloninger made the point much better than I did, let me paraphrase his argument. Physicians are people who have made it through rigorous selection and training processes, and are resilient and adaptable, as well as compulsive and highly conscientious. If this group of people are frustrated with their working environment, a reasonable conclusion is that the working environment itself is flawed. We are, as a group, being subjected to a toxic work environment.

A recent commentary on the website of WBUR, Boston's public radio station, focused the debate more clearly on Electronic Health Records.[2] Three eminent Boston physicians engage in harsh criticism of the use of the EHR, saying it forces physicians to relate as much to the computer as to the patient, and robs patient encounters of the time needed for the physician to listen to the patient. They point out that the current EHR systems force large amounts of unneeded work on physicians, offload most of the work involved in hospital billing onto physicians (and nurses), and come between physicians and patients. EHRs, in short, have failed in their promise to make health care simpler and more cost-effective. They have, in fact, made it more complicated, more expensive, and more frustrating to both doctors and patients.

And the economics of the whole system is just nuts. Consider. Physicians and nurses are the most highly paid people in hospitals.[3] So, we require them to spend up to half their working time shoveling data into computers. Besides drastically lowering their actual productivity, this forces them to eliminate parts of their former activities. Like, for example, sitting down and actually talking with patients. As a result, we need nurses and physicians in much greater numbers, and they are working far less efficiently, with less patient contact. Data entry can certainly be productive work, but not for physicians and nurses.

So … why are EHRs so difficult to use? Given that we all need to document our findings and our procedures, why have we made it so difficult? Probably the best answer comes from the observation that those using the systems are not those purchasing them. Hospital administrators are properly concerned with such things as billing, operations, and inventory. But while hospitals often solicit opinions from doctors and nurses, they don't really take their needs into account. The EHR companies are focused on managing data, and the interaction with the "users" is of relatively small importance.[4] Many physicians and computer



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scientists have worked out better ways of interacting with EHRs, but they don't run the computer companies, nor do they have much influence within health care organizations.

The Boston physicians noted that they are organizing town meetings, and other such activities, to try to improve the EHR. Whether this sort of "grass roots" pressure will be effective is anybody's guess. Personally, I'm not hopeful. There is a great deal of inertia to overcome. EHR systems are very expensive, and there is a very large installed base. It is difficult to make even small changes in existing systems. Government regulations have the effect of freezing existing systems. Significant changes may require Congressional action and/or regulatory reform. Any objective observer would realize that the whole regulatory framework for EHRs is ineffective, and should be scrapped. The AMA, after a great deal of work and much lobbying, succeeded only in softening the terms of MACRA, which is now called MIPS. (Don't bother to remember those. They'll be different next year.) So, improving EHRs is going to take a lot of work, much political capital, and a long time.

But our toxic work environment isn't limited to EHRs, frustrating as they may be. Let us consider piece work. Now, piece work is the practice of paying the worker for each item produced. It was the common method of paying industrial workers at the end of the 19th century. But in industry after industry, it was abandoned during the first half of the 20th century, because of union pressure, technological change, and the increasing need of companies to obtain a stable work force. For a case history, see the reference below.[5] Of course, it still exists for physician practices. More than that, modern management fads such as "pay for productivity" and "incentive payments" have tried to move piece work from private practice into organizations for knowledge workers such as physicians.

Piece work is not especially conducive to either good medical care or a healthy working environment. Shanafelt, et al. reported on the American College of Surgeons study of 7,900 general surgeons.[6] They found that compensation based only on productivity was significantly associated with burnout symptoms (odds ratio, 1.37:1). Piece work is superficially attractive to managers, insurers, and government. For one thing, it makes it easier to cut pay. There has been a steady erosion in physician reimbursement for standard services over the last 30 years. Since there are more services now, with new ones popping up every year, cutting our pay has not resulted in lower costs. A hospitalization which required one or two physicians in 1960 might require ten consultations today. Personally, I believe the team approach provides better care. But it has the entirely coincidental side effect of increasing overall physician reimbursement.

As most of us realize, painfully, our work environment has other toxicities. With the ever-increasing role of regulation in medicine, we are all subjected to multiple bureaucratic harassments. Some of these are unnecessary, perhaps even most of them. Do we need quality measures? Sure. But why aren't they any better? Does an internist control his or her patients so closely that the average hemoglobin A1c level have any meaning? What about the average blood pressure? These aren't quality measures, except in the negative sense that they indicate physicians who are willing to care for difficult patients.

Some are self-inflicted. For example, we awarded power to specialty boards, who then approved re-certification examinations, and maintenance of certification. We are not doing nearly enough to take back that power. Why should a cardiac sub-specialist, for example, have to take three exams every ten years, and engage in multiple MOC activities? And yet, these particular ills are inflicted on the profession by itself.

A great deal more can be said about the working environment for physicians today. Unfortunately, most of it is negative. Perhaps some of it is not avoidable. But the EMR isn't going to get better without a lot of agitation by physicians. Re-certification and MOC aren't going to improve, unless we reform the specialty boards. That won't be pleasant. The boards have entrenched power, and money, and strongly resist any changes. Government regulation will continue to be intrusive and will get worse if we don't start pushing back. If we do not find ways to make out work environment more functional and less frustrating, and if we cannot push our health care organizations into promoting change, we will be in a toxic work environment for a long time to come.

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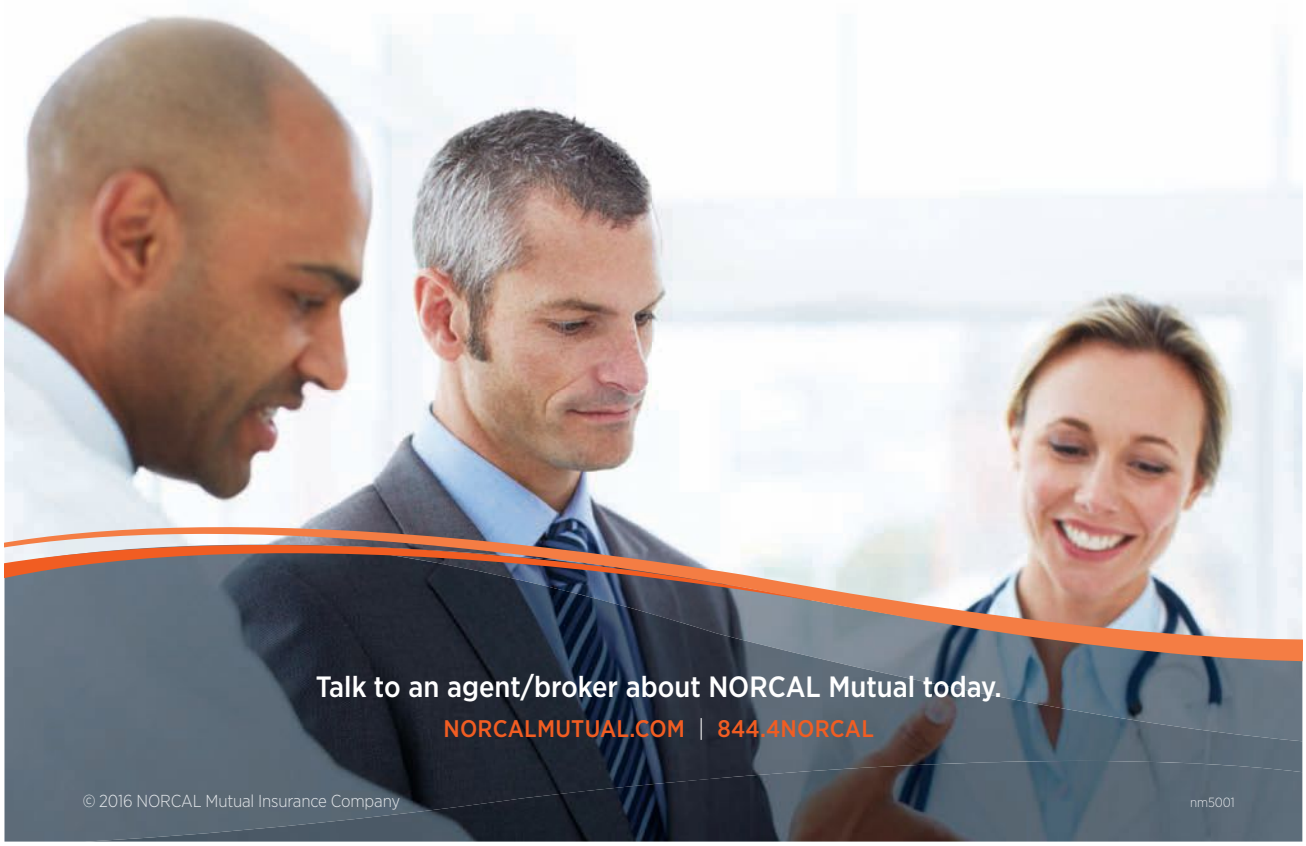
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Coffee Is Not a Carcinogen

by James J. DiNicolantonio, PharmD & James H. O'Keefe, MD



The data in humans on coffee consumption indicates that coffee may even have a protective effect on numerous types of cancer, including colorectal, liver, and breast cancers.

Coffee is the second most common beverage consumed in the United States.[1] Recently, a California judge ruled (though the decision is not yet final) that coffee must carry a cancer warning because it contains acrylamide—a chemical compound created during the roasting process.

While acrylamide is considered a "probable carcinogen," probable is certainly not definitive. In fact, one recent review on coffee and cancer risk noted, "… epidemiological studies and retrospective re-analyses of data published so far failed to provide sufficient evidence that dietary acrylamide increases the risk of any type of cancer in humans, including kidney, large bowel, bladder, oral cavity, breast, and ovarian cancer."[2] Moreover, the evidence upon which acrylamide is considered a probable carcinogen is based on studies in rodents that "were dosed at rates 1,000 to 10,000 times higher than what humans consume in food."[3] In other words, there is no sound evidence that acrylamide, especially in the trace doses found in a cup of coffee, would cause cancer in humans. Coffee is a complex brew containing hundreds of biologically active compounds and one of its parts is not the sum of its parts. So, coffee needs to be looked at as a whole not just one of its constituents.

Thus, it appears that the cancer warning to be placed on coffee is based solely on animal data that used much higher doses than what humans would ever get from consuming coffee. Adding insult to injury, the data in humans on coffee consumption indicates that coffee may even have a protective effect on numerous types of cancer, including colorectal, liver, and breast cancers.[2]

When deciding whether a food or beverage increases the risk of cancer (or any outcome for that matter) one must look at the entire food or beverage matrix not just a single constituent. In order for there to be any sound scientific justification for the vilification of coffee as a carcinogen there would need to be studies in animals showing that consuming coffee at doses relevant to human consumption increases the risk of cancer. We are unaware that any such data exists in animals let alone humans. Thus, it is undoubtedly premature for coffee to hold a cancer warning label.





James J. DiNicolantonio, PharmD, (left), and James H. O'Keefe, MD, (right), MSMA member since 2003, are at Saint Luke's Mid America Heart Institute, Kansas City, Mo.
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The international Agency for Research on Cancer (IARC)—a branch of the World Health Organization (WHO), recently classified the consumption of beverages hotter than 149 degrees Fahrenheit or 65 degrees Celsius a probable carcinogen.[4] Hot coffee is usually served at approximately 65 degrees Celsius, therefore it should be allowed to cool to less than scalding temperatures before drinking. Even so, the IARC after scrutinizing all of the relevant scientific data recently concluded that coffee is associated with lower risks for liver cancer and endometrial cancer, and is unlikely to cause breast cancer, prostate cancer, or pancreatic cancer.[4]

Importantly, massive prospective epidemiological studies consistently report inverse associations between coffee consumption and all-cause mortality as well as cardiovascular mortality.[1] Furthermore, long-term coffee consumption is linked with reduced risks for coronary heart disease, congestive heart failure, stroke and type 2 diabetes.[1] Habitual coffee intake also is associated with lower risks of Parkinson's disease, depression, and liver disease.[1] The dose of coffee associated with the most impressive health benefits is approximately 3 cups daily. Thus, for health, wellbeing and longevity, black unsweetened coffee appears to be one of the most beneficial components of the American diet.

It is possible that one day coffee may indeed hold a label, but that label may in fact be for a claim for its ability to reduce the risk of cancer not cause it. As one article put it, "Is it time to write a prescription for coffee?"[5] It just might be, however, a cancer warning label (if indeed placed on coffee) will certainly decrease the number of those "prescriptions" written.

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MSMA Members in the News

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



Kathy Perryman, MD, FAAP, MSMA member since 1989, is the new *Missouri Medicine* Board member for Anesthesiology. She is the Secretary/ Treasurer of Medical Staff and Associate Professor of Pediatric Anesthesiology at the University of Missouri - Kansas City School of Medicine. She replaces Jim Gibbons, MD, in that position.

The Kansas City Ophthalmology & Otolaryngology Society presented its annual Hal Foster Lifetime Achievement Awards. Receiving the award for otolaryngology was Bradley S. Thedinger, MD, of the Otologic Center. Co-recipients of the award for ophthalmology were Carl V. Migliazzo, MD, recently retired from the Kansas City Eye Clinic, and Charles M. Lederer, MD, of Associated Ophthalmologists of Kansas City. The Hal Foster Award was developed in 1991 and is presented to members of the Society who have demonstrated exemplary dedication and service to the Society and the local medical community. See photos, right.





Displaying their awards are above, Charles M. Lederer, MD, middle left, with his wife Marilyn, and Carl V. Migliazzo, MD, with his wife Beth. Bradley S. Thedinger, MD, right, accepts the award from Robert D. Cullen, MD.



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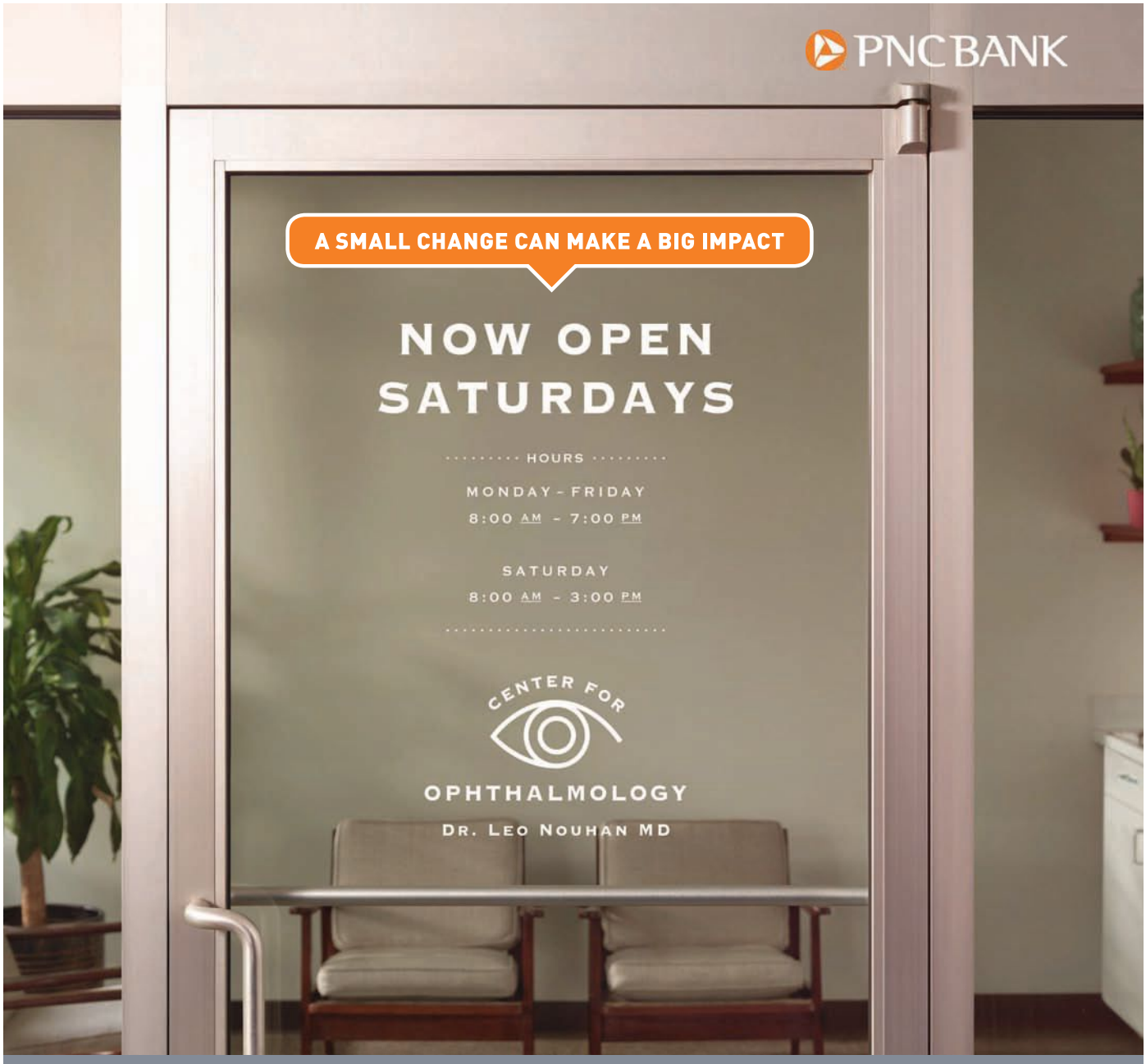
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The Case for Organized Medicine: Why You Should Get Involved

by Albert Hsu, MD

As a busy physician, you might wonder what organized medicine can do for you. This is why I think you should get involved.

1. Medicine can be better. It should be better. For our patients. For you. For all involved. We chose medicine to care for patients, but much of our clinical day is spent struggling with insurance companies, worrying about liability concerns, and drowning under ever-increasing clerical duties. Ethically, we cannot abandon our patients to go on strike, while anti-trust law hamstrings our ability to effectively negotiate with payers. If you have an issue or concern, and especially if you're not being heard, I encourage you to bring it up at your specialty, local, state, or national meetings.

2. It's wonderful to know that you're not alone in contending with the frustrations in medical practice today. Many like-minded colleagues attend our regular meetings, and some of my best friends are those whom I have met through organized medicine.

3. We are more powerful when we speak with a united voice to advocate for our profession, which allows us to achieve our twin missions of protecting public health and defending the practice of medicine.

My name is Albert Hsu, and I am the current Chair of the MSMA-Young Physician Section. As a reproductive endocrinologist at University of Missouri Health Care, I see patients in my clinical practice and am involved in research on endometriosis (a common cause of both pain and infertility). My wife, Tracy, and I both are in medicine, and we have four children who keep us busy with soccer, baseball, crew, and Ultimate Frisbee. My previous practice was at Dartmouth-Hitchcock Medical Center in New Hampshire, and I had served on the New Hampshire Medical Society's Leadership Council for the past three years.



Albert Hsu, MD, MSMA member since 2017 and Chair of the MSMA Young Physician Section, is a Reproductive Endocrinologist at the Missouri Center for Reproductive Medicine and Fertility in Columbia, Mo.
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Before coming to Missouri, I had the opportunity to participate in several advocacy efforts that led to real change. Memorable examples include campaigns to:

- ban smoking in bars and restaurants in New York City, arguing that workers should not have to choose between their health and their employment. Our successful lobbying efforts on the city and state level in 2002 helped encourage other states (and countries) to pass similar laws;

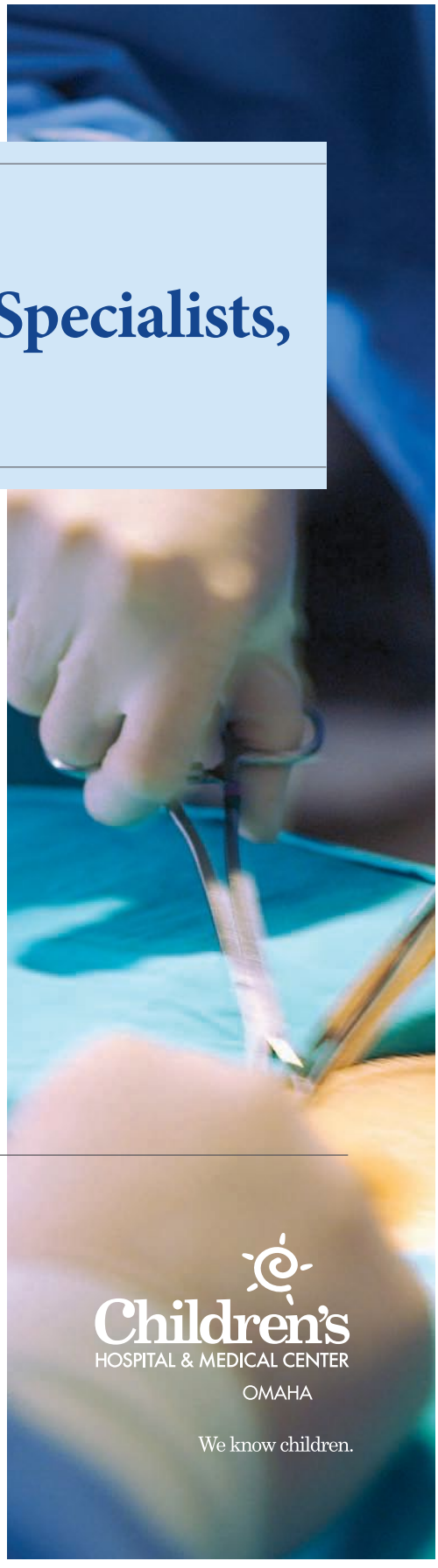
- encourage Medicaid in Massachusetts to cover medications to prevent preterm labor in women with histories of preterm deliveries. Medicaid was unwilling to pay for a $100 weekly injection for these patients. This penny-wise policy was rather shortsighted, however, and taxpayers were paying for it, as those weekly injections could have saved hundreds of thousands of dollars in additional NICU costs;

- lobby against mid-year and retroactive tuition increases at the public medical schools in New York State. My friends and I passed an "emergency" resolution on this issue in the AMA House of Delegates, and a few years afterwards, students at public medical schools in California won a court case and received some reimbursement for similarly inappropriately-timed tuition increases at their medical schools.

Despite the ongoing and exciting revolutions in biology and medicine today, we also are in a time of severe austerity, in which we must fight merely to preserve funding for clinical care, for medical education and research, and for public health initiatives. While I believe in the effectiveness of advocacy and organized medicine, most of us lack the time or patience to go marching in the streets – or lobby in Jefferson City or Washington DC. However, there are things that you can do without leaving your town, such as calling state and national representatives, meeting with local legislators, giving to a political action committee, and attending meetings of your specialty, local, state, and national medical societies.

In organized medicine, we don't have permanent "friends" – just permanent interests. We work closely with both Republicans and Democrats to advance solutions to issues that are important to us, such as with Republicans on liability reform and with Democrats on preventing abuses by the health insurance industry. Medicine has "friends" in both parties, but we also have politicians of all stripes who view us as the problem, and not the solution. When protecting our patients and our profession, we are most effective when we speak with a unified voice.

I look forward to meeting you at an MSMA or AMA event! **MM**



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by Kevin E. Behrns, MD

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I am privileged to write on behalf of the faculty, students, and staff at Saint Louis University School of Medicine (SLUSOM) to provide an update on the activities in the oldest school of medicine west of the Mississippi River. Using our historic accomplishments as a foundation, our faculty, students, and staff have been busy transforming our school. Since my arrival in January 2017, we have engaged in a disciplined process called Transformative Excellence in Academic Medicine or TEAM. Through this process we seek to establish a culture of excellence and accountability that will lead to quality and growth in everything we do. Our aspirational goals include setting the standard for delivery of high-value care in an academic setting, becoming a desired destination for faculty, students, and staff who are empowered to make change, and achieving leading financial results that permit reinvestment in our mission. To provide focus to our TEAM initiatives we are concentrating our work in six areas: (1) delivery of high-value care, (2) patient access, (3) research and education, (4) integration of our missions, (5) supportive infrastructure, and (6) strategic direction. As we move forward with project TEAM, we are contemplating carefully the dynamic healthcare landscape and anticipating a future of medicine in which clinical care delivery, team-based research programs, and inter-professional education look vastly different than they do today. In the following paragraphs, I will share highlights of the good work our faculty, students, and staff are performing in the clinical, research, and education missions.

Our clinical mission is dominated by our continual improvement in the delivery of high-value care. In our practice, SLUCare, a dedicated unit, led by Ali Kosydor and Beth Page, seeks first to improve patient access because without access we cannot deliver high-quality care. As a result of their efforts and many others we have experienced six (6) percent year-over-year growth in arrived patients. Importantly, the quality of care delivered has improved markedly, and our rate of improvement with some outcome measures, such as smoking counseling and cessation, is the greatest in the nation (Figure 1). In addition, our quality team is working hand-in-hand with our population health team to address patients with uncontrolled diabetes mellitus. In one example, they worked diligently with a patient in their home to decrease the hemoglobin A1C from 16% to less than 6% and sustain this improvement over nine months through diet control and exercise. This example of meeting patients where they live exemplifies the personalized, quality care our teams are providing.

Our partners in the delivery of clinical care, SSM-STL, are likewise working assiduously to offer high-value care at our three academic hospitals: Saint Louis University Hospital, Cardinal Glennon Childrens' Hospital, and St. Mary's Hospital. Furthermore, leaders across Saint Louis University and SSM are working to develop an integrated delivery network across the St. Louis region so our patients receive the correct care, at the appropriate time, and in a convenient location. Collectively, we seek to put the patient first in our decision-making processes. As part of this decision-making process, a $550 million investment in

facilities is being made by SSM on Grand Avenue (Figure 2). We are excited about the new facilities, which are rapidly becoming a reality as steel girders are now visible above the ground. The new 316-bed hospital will offer state-of-the-art facilities for our patients and is uniquely designed to accommodate teaching rounds for faculty, students, residents, and staff. In addition, the adjacent ambulatory care center will offer patients quick and convenient access to our physicians and staff. These two healthcare facilities will be the nucleus of greater community investment in midtown St. Louis, where a billion dollars of construction will reshape the community. This opportunity for redevelopment of midtown St. Louis is led by the 353-redevelopment project that the city of St. Louis granted to Saint Louis University. Clearly, the next several years will be highlighted by construction of facilities that will improve the health of our community.

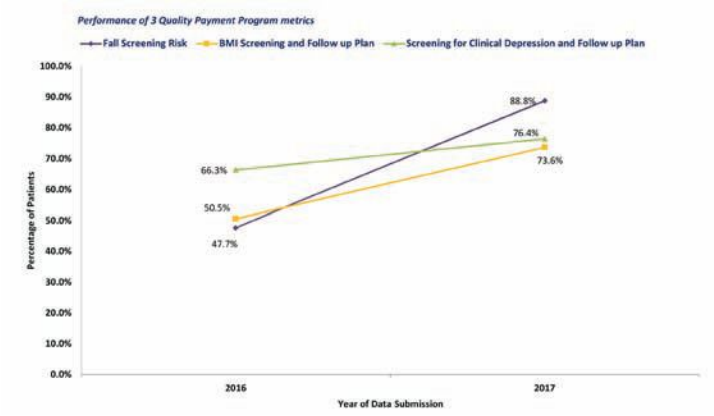


Figure 1. SLUCare quality data demonstrating year-over-year marked improvement in outcome measures.



Figure 2. Rendering of the new SSM-Saint Louis University Hospital and ambulatory care center, which are under construction and set to open in September 2020.

We are proud of the clinical care we deliver, but we seek to enhance that care by offering research opportunities for the patients. As I write this article, we are in the midst of one of the worst flu seasons in recent history. With a vaccine that was 36% or less effective, we have plenty of opportunity to improve preventive vaccines and our Saint Louis University Vaccine Center is poised to improve the flu vaccine. The Vaccine Center, led by Dr. Dan Hoft, is one of nine federally-funded vaccine centers and a research treasure for our School. Importantly, the Vaccine Center will soon add an important resource to conduct human clinical trials as we are completing construction of a human vaccine trial unit. This physical space will allow the conduct of clinical trials that seek to improve the effectiveness of a universal flu vaccine, a top priority for the National Institutes of Allergy and Infectious Diseases. Our Vaccine Center and the human clinical trials unit will make major contributions to achieving a more effective universal flu vaccine.

When we think about recent major contributions to eradication of disease, the Saint Louis University Liver Center played an integral role in curing hepatitis C. Through basic science research and clinical trials led by Drs. Bruce Bacon, Adrian Di Bisceglie, and team, hepatitis C has essentially been cured pharmacologically. This team of investigators, however, has pivoted their focus to non-alcoholic steatohepatitis (NASH) or fatty liver disease. We are currently adding liver scientists to our team and seek to make major contributions to alleviating the effects of NASH.

Nationally, treatment of sepsis is a major focus of the Center for Medicare and Medicaid Services because of the high mortality and morbidity coupled with the excessive cost of treatment. At SLUSOM, we are fortunate to have excellent scientists who are uncovering the basic mechanisms by which sepsis creates its deleterious effects. Drs. David Ford and Jane McHowat have recently published high-impact research papers in the Journal of Clinical Investigation and Journal of Lipid Research detailing their work on the role of 2-chlorofatty acids as potential biomarkers in sepsis (Figure 3). Their efforts to engage multiple investigators at SLUSOM and across the country will lead to the creation of an integrated team of scientists that will have a major impact on the care of septic patients.

Sadly, the opioid epidemic and crisis has crippled many patients and families in the United States and our region, in



Figure 3. SLU faculty members, Drs. David Ford, PhD, and Jane McHowat, PhD, collaborate on a project examining the role of lipids in sepsis. The work has led to several high-impact publications.

particular. The federal government has recently recognized this crisis and will increase funding for many programs that will address addiction from a variety of viewpoints. SLUSOM is also playing a role in this nationwide approach by developing non-narcotic pharmacologic alternatives to treat chronic pain. Dr. Daniela Salvemini is well-funded and has published extensively in this field and identified several non-narcotic compounds that can alleviate pain in experimental models. Because of the national crisis, we seek to increase our presence in this tragic crisis and to incorporate our basic science efforts into a comprehensive program that will examine and treat opioid abuse.

Finally, I would like to address developments in our educational programs. In February 2017, we received the unwelcome news from the Liaison Committee on Medical Education (LCME) that our accreditation status would be "accredited with probation." This designation mandated notification to our students and potential students and caused a great deal of anxiety among our faculty, students, staff and alumni. I am proud to say, however, that we quickly assembled a steering committee and two working groups to address the citations. Our faculty, students, and staff diligently got to work assessing our citations, developing a gap analysis, and writing an action plan, which was approved by the LCME. Though the initial news of probation was upsetting, the dedicated work of many individuals, working in teams, has been a galvanizing effort across SLUSOM. We look forward to our June 2018 site survey visit to demonstrate the numerous advances in our medical education program. Throughout this process, we sought not only to rectify our deficiencies but to create changes that would make us a leading medical education program. As we continue to remodel our medical education program, we will seek to become a leading medical school.

Our SLUSOM sponsored graduate medical education program (GME) was reviewed in January of 2018 and received a status of continued accreditation, the highest status designated. We are delighted that our GME programs are in good standing, but here too, we will strive for continuous improvement. Our residents and fellows work hard to deliver the highest-quality care, and we will work relentlessly to offer the best training programs available.

In conclusion, SLUSOM is undergoing transformative change to deliver high-quality care that is research inspired and follows our Jesuit tradition of treating the entire patient. Through clear definition and adherence to our mission and values, we will make valuable contributions to the care of the people of St. Louis and across Missouri. We welcome your engagement in our journey to transform healthcare.

MM

Feature Series Overview

by Brent A. Neuschwander-Tetri, MD

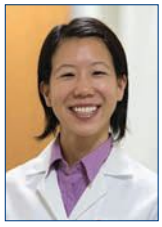
This issue of *Missouri Medicine* features seven reviews by members of the Division of Gastroenterology and Hepatology in the Department of Internal Medicine at Saint Louis University School of Medicine. Under the leadership of the late Dr. Coy Fitch, the Department of Medicine was revamped into an academically productive group of outstanding clinician investigators beginning in the late 1980s. This included the recruitment of renowned and promising hepatologists and gastroenterologists from across the country that included Drs. Bruce Bacon, Adrian Di Bisceglie, Charlene Prather, and we built further upon that over time to have national and international recognitions for our contributions in liver, GI, and pancreatic disease.

The seven reviews in this issue reflect the work by some of our outstanding fellows under the guidance of our junior faculty members who have established themselves regionally for their expertise in the areas that they have chosen to cover. We hope that you find these concise reviews helpful in your practice as they provide practical advice on common and challenging areas of gastroenterology and hepatology. **MM**

Dysphagia

by Prianka Chilukuri, MD, Florence Odufalu, MD & Christine Hachem, MD

Evaluation and management of the patient with dysphagia requires a structured assessment to identify functional, neurologic, inflammatory, and malignant causes.







Prianka Chilukuri, MD, (bottom left), and Florence-Damilola Odufalu, MD, (bottom right), are Fellows, and Christine Hachem, MD, (top) is an Associate Professor of Internal Medicine in the Division of Gastroenterology and Hepatology, Saint Louis University School of Medicine, St. Louis, Mo.
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Abstract

A complaint of dysphagia suggests difficulty in swallowing and is characterized based on the symptoms and location of pathology. Oropharyngeal dysphagia is typically due to difficulty initiating a swallow and is generally due to structural, anatomic or neuromuscular abnormalities. Esophageal dysphagia arises after the swallow and causes include intrinsic structural pathology, extrinsic compression, or disruption in normal motility. Etiologies, methods of evaluation, and management options of dysphagia are reviewed here.

Introduction

Dysphagia is defined as an abnormal delay in the movement of a food bolus from the oropharynx to the stomach.[1] Patients often report difficulty swallowing.[2] Dysphagia is a common symptom in the general population, however, dysphagia always represents a pathologic process. Swallowing encompasses three phases: oral (preparatory) phase, oropharyngeal (transfer) phase, and the esophageal phase. Often, dysphagia involves overlap of both the oropharyngeal and esophageal phases. Specific etiologies will be discussed here.

Epidemiology

Few population-based studies are available on the prevalence of dysphagia in the community.[3] There are several structural, socioeconomic, age, and sex factors that affect the incidence of dysphagia.[4, 5] Based on limited data, the prevalence of dysphagia in the general population is estimated around 20%, and it is estimated to affect up to 50% to 66% of people over 60 years of age.[6] Dysphagia is more prevalent in women than men across all age groups.[3] Older populations, patients with a history of stroke, Alzheimer's disease, or amyotrophic lateral sclerosis are more likely to report dysphagia.[7] In younger populations, dysphagia is often associated with an underlying systemic illness, such as autoimmune diseases, gastroesophageal reflux disease (GERD), or eosinophilic esophagitis. Despite this high prevalence, only half of patients with dysphagia will report their symptoms to clinicians.[7] Dysphagia is an alarm symptom and is not a part of normal aging. Any new reports of dysphagia should prompt a systematic approach to aid in diagnosis and treatment.

History & Clinical Approach to Dysphagia

Patient-provided history often helps to differentiate oropharyngeal versus esophageal dysphagia. The normal swallow mechanism involves easy passage of a food bolus from the oropharynx to the esophagus. Symptoms of oropharyngeal dysphagia generally arise within seconds after swallowing, and patients often report drooling, coughing, nasal regurgitation, aspiration, or choking. Clinicians can use the following questions to help determine the origin of symptoms.

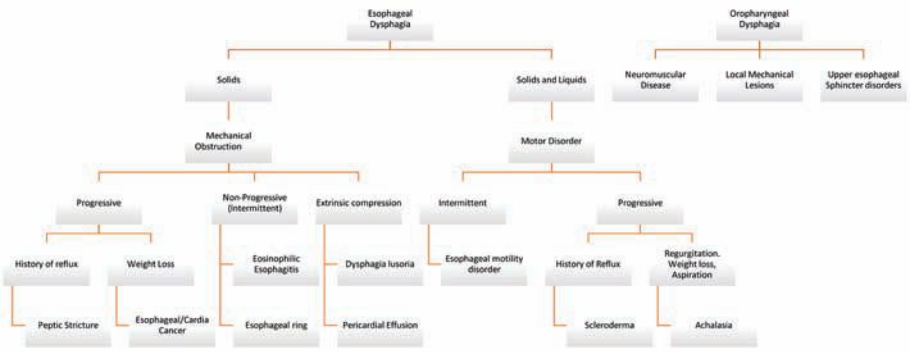


Figure 1. Differential diagnosis of common presentations of dysphagia.

1. Does it take longer than one second to pass food from the mouth to the esophagus?
2. What type of food or liquids cause symptoms?
3. Are symptoms intermittent or progressive?
4. Is there heartburn?

Patients with oropharyngeal dysphagia often recount experiences of delayed food bolus passage. Patients with esophageal dysphagia, on the other hand, will often recount the sensation of food "stuck in throat or chest" after swallowing. Patients may point to a specific region in the chest, however, this is often unreliable at pinpointing the actual location of the problem. Patients often localize pathology occurring in the distal esophagus as discomfort by their sternal notch.Dysphagia should be approached systematically as outlined in Figure 1. Given the complexity and multiple etiologies of dysphagia, it is important to differentiate the level of pathology early in the evaluation, as the differential diagnosis, work up, and management can be markedly different.

Oropharyngeal Dysphagia

The oropharyngeal phase of swallowing involves transferring a food bolus posteriorly to the epiglottis and then to the upper esophageal sphincter. The oropharynx comprises of the tongue, epiglottis, palatine tonsils, hard palate and soft palate. Anatomic abnormalities at any of these structures, such as upper esophageal sphincter (UES) dysfunction, can lead to oropharyngeal dysphagia. Structural causes include head and neck malignancy, infections of the pharynx, vertebral osteophytes, prior head and neck radiation, proximal esophageal webs, thyromegaly, or Zenker's diverticulum. Neuromuscular abnormalities are often the most common causes of oropharyngeal disorders. Cranial nerve injury, cortical, or supranuclear lesions after cerebral vascular accidents are common etiologies that lead to dysfunction in the oropharyngeal phase of swallowing.[2]

Patients presenting with symptoms of oral stasis of food, inability to form a food bolus in the mouth, coughing, or aspiration pneumonia should undergo further evaluation of oropharyngeal dysphagia. Furthermore, "silent aspiration," which is, aspiration without cough or other outward signs of aspiration, can be the presentation of dysphagia in patients after a cerebral vascular accident.

Esophageal Dysphagia

Esophageal dysphagia can occur due to structural abnormalities or dysmotility. On initial presentation, esophageal dysphagia should be approached methodically with critical attention to patient-provided history. Mechanical or obstructive esophageal disorders are the most common causes of esophageal dysphagia, and patients generally present with dysphagia to solids alone with potential progression to include liquids.[6] Mechanical obstruction can manifest with symptoms of intermittent dysphagia or progressive symptoms. In contrast, patient-reported symptoms of dysphagia with both solids and liquids most likely point to an underlying motility disorder.

Intermittent (Non-Progressive) Dysphagia

Patients will often present with a history of difficulty swallowing solids. In some clinical scenarios, symptoms may manifest with food bolus impaction. In younger patients with non-progressive dysphagia, eosinophilic esophagitis (EoE) should be considered. The exact etiology of EoE remains unknown, but it is thought to be related to esophageal reflux or atopy. EoE is diagnosed based on characteristic endoscopic findings and histologic evidence of mucosal eosinophilia.(Figure 2). However, several patients can present with a grossly normal-appearing esophagus, therefore, it is important to maintain a high level of suspicion regardless of endoscopic findings. Alternatively, esophageal webs and Schatzki rings can cause non-progressive dysphagia that can occur across all age groups. A Schatzki ring is a thin mucosal structure often found near the gastroesophageal junction.[2] It manifests with symptoms of food bolus impaction, food regurgitation and often occurs after rushed meals.[2]

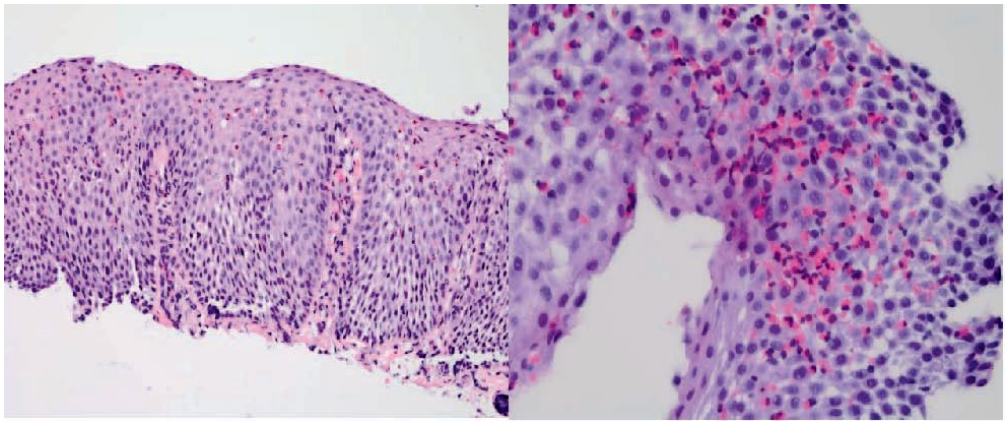


Figure 2. Photomicrograph of an esophageal biopsy obtained during routine upper endoscopy shows squamous mucosa with increased intraepithelial eosinophils, basal hyperplasia, and elongation of papillae. Photo credit: Paul Friedman, MD, Department of Pathology, Saint Louis University School of Medicine.

Progressive Dysphagia

In contrast to intermittent or non-progressive dysphagia, progressive solid food dysphagia is worrisome for an esophageal stricture or carcinoma within the esophageal lumen. Peptic strictures are benign esophageal strictures that develop in patients with long-standing GERD and may present similarly to esophageal carcinoma. Weight loss is not common in patients with peptic strictures, as they often will modify their diet to more tolerable formulations.[8] With long-standing peptic strictures and GERD, the risk of developing malignancy is increased. In patients with rapidly progressive dysphagia, weight loss, and anorexia, esophageal squamous cell carcinoma or adenocarcinoma should be considered until proven otherwise. Esophageal adenocarcinoma is a growing health concern that is expected to increase in incidence over the next 10 years.[9] Patients may or may not have a history of heartburn, and heartburn may have occurred in the past but not the present. Esophageal adenocarcinoma can occur anywhere in the esophageal lumen or at the gastric cardia. Gastric cardia lesions can also present with progressive dysphagia or give an achalasia like picture called pseudoachalasia.

Extrinsic Dysphagia

Based on location, the esophagus is subject to external compression by surrounding structures within the mediastinum.[1] Diseases that lead to altered cardiac anatomy can progress to external compression of the esophagus. They may lead to hemodynamic compromise and luminal narrowing. Dysphagia lusoria is a term that refers to any congenital vascular abnormality leading to esophageal compression and the development of intermittent or persistent dysphagia symptoms. Anatomically, dysphagia lusoria typically refers to an aberrant right subclavian artery arising from the left side of the aortic arch, a double aortic arch, or a right aortic arch with left ligamentum arteriosum. Rarely, any clinical entity contributing to left atrial enlargement can lead to esophageal compression based on anatomic positioning.[10] An enlarged thyroid, mediastinal masses or other mediastinal abnormalities may present similarly. Clinical clues suggestive of extrinsic compression from vascular or cardiac etiologies include respiratory distress, hypotension, and atypical chest pain.

Dysmotility

A report of dysphagia to liquids or a combination of solids and liquids should prompt concern for an abnormality in esophageal motility. The major motility disorders are broken down into achalasia, diffuse esophageal spasm, hypertensive esophagus, and ineffective esophageal motility.[11] Achalasia is the most commonly recognized disease within this category and is characterized by insufficient lower esophageal sphincter relaxation and esophageal aperistalsis. This disease occurs as a result of degeneration of myenteric plexus ganglion cells, which leads to an imbalance between excitatory and inhibitory neurons with resulting sustained lower esophageal sphincter contraction. The trigger for this overall process, however, often remains unclear with the exception of Chagas disease.[12] Diffuse esophageal spasm is characterized by normal peristalsis with sporadic simultaneous contractions and generally presents as intermittent dysphagia with or without chest pain. Patients with a hypercontractile esophagus may also present with chest pain due to elevated esophageal and lower sphincter pressures. At the other end of the spectrum, motility tracings that demonstrate low amplitude pressures or failed peristalsis are considered ineffective esophageal motility.[11, 13] Secondary causes of dysmotility include connective tissue disorders, parasitic infection, neurodegenerative diseases, pseudo-obstruction related to malignancy, or general aging.

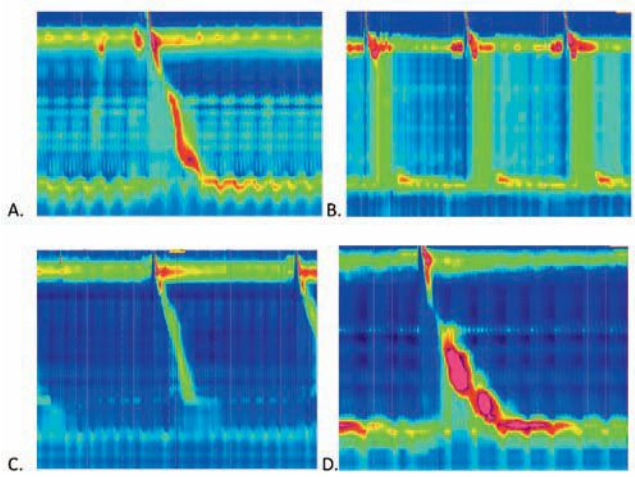


Figure 3. High resolution manometry images demonstrate the pressures along the length of the esophagus (vertical axis) over time (horizonal axis) after swallows in the setting of common abnormalities. A. Normal esophageal manometry with normal progression of the pressure wave over time; B. Manometry in achalasia type II (classic achalasia) shows a lack of a normal peristaltic pressure wave; C. Manometry demonstrating weak lower esophageal sphincter (LES) tone that predisposes to GERD; D. Manometry demonstrating esophagogastric junction outflow obstruction (EGJOO) due to abnormally high pressures. Photo credit: Charlene Prather, MD, Division of Gastroenterology and Hepatology, Saint Louis University School of Medicine.

Diagnostics

Recommended diagnostic approaches to evaluate dysphagia can vary and are generally guided by the patient's reported symptoms and risk factors. The first line of diagnostic evaluation is centered around obtaining a detailed clinical history and physical exam (Figure 1). Investigative questions that characterize swallow initiation, postnasal regurgitation, deglutitive coughing, and resolution with repetitive swallowing have been shown to distinguish oropharyngeal and esophageal dysphagia with 80% accuracy.[14] Specific features including chronicity, frequency, aggravating factors, and severity can help determine which additional diagnostic tools should be pursued. Evaluation of the oropharynx, neck and dentition may provide helpful clues. The main diagnostic tests to evaluate dysphagia include modified barium swallow, barium esophagram, endoscopy, and manometry.[1]

Barium esophagraphy is often utilized as the initial diagnostic test if there are clinical features that raise concern for complications related to blind endoscopic intubation. This can be applicable to patients at risk for laryngeal or esophageal malignancy, Zenker's diverticulum, or a stricture related to radiation or caustic injury.[15] The barium esophagram can also be helpful after an unrevealing endoscopy if there is clinical suspicion for morphologic abnormalities or dysmotility. If symptoms persist despite normal endoscopic and manometric evaluation, radiographic evaluation with ingestion of barium-coated foods or tablets can help identify subtle luminal narrowing or functional dysphagia.[16] History that is suggestive of oropharyngeal dysphagia should prompt evaluation with a modified barium swallow, which can provide diagnostic information to help guide lifestyle modifications to alleviate symptoms and decrease aspiration risk.[15]

Endoscopy offers the dual benefits of providing both diagnostic information and a route of therapeutic intervention. It is especially valuable when symptoms are suggestive of an anatomic abnormality and if there is concern for a malignant or premalignant condition. This twofold application has also demonstrated a significant cost benefit when used as the initial diagnostic tool as barium swallow generally prompts follow-up testing or intervention.[17] Evaluation of the utility of endoscopy in dysphagia workup demonstrated diagnostic value in 54% of cases with superior outcomes in males older than 40 years with associated heartburn, odynophagia, or weight loss.[18]

Manometry is employed if dysmotility is suspected, as it provides insight into esophageal peristalsis and sphincter function (Figure 3). Manometry helps differentiate between subsets of motility disorders and can help predict response to endoscopic and surgical interventions.[19] The development of high-resolution manometry led to the creation of *The Chicago Classification*, an algorithmic format to diagnose motility-related pathology.[13, 20]

Therapeutics

Management of esophageal dysphagia is targeted to treat the underlying etiology. Mechanical obstruction due to intraluminal rings, webs, and benign strictures can be endoscopically dilated using a mechanical or balloon dilation. Bougie dilator is considered to be more effective and associated with less risks, as it provides both radial and axial forces and decreases the degree of force applied within the lumen. Balloon dilators, on the other hand, exert an isolated radial force, which allows for less dilation pressure but can be associated with higher perforation risk. Concurrent acid suppression therapy is frequently recommended with dilation to reduce stricture recurrence after successful dilation. Esophageal stents and intralesional steroids may be considered in refractory cases of benign strictures to help maintain lumen patency but are usually reserved for malignant strictures. Obstruction secondary to intraluminal masses, diverticula, and extrinsic compression may require surgical intervention.[21]

Dysphagia due to abnormal motility requires therapeutic approaches that target esophageal kinetics and pressure. Achalasia therapy focuses on reduction of the pressure created by the lower esophageal sphincter. The most effective nonsurgical intervention to date has been pneumatic dilation, which involves balloon dilation across the lower sphincter in an attempt to tear the muscle fibers in a controlled manner. A surgical myotomy may be performed laparoscopically and involves an anterior myotomy across the lower esophageal sphincter with success rates reported to range from 80 to 100%.[11, 22] More recently, peroral endoscopic myotomy (POEM) has become an emerging technique for nonsurgical candidates, however, availability of this procedure currently remains limited to specialized centers.[23] Botulinum injection and oral smooth muscle relaxants are less effective and are generally reserved for patients considered poor candidates for dilation or surgical intervention.[11, 22] Distal esophageal spasm and hypercontractile esophagus management involves systemic therapy with oral smooth muscle relaxants and neuromodulatory agents.[19]

Functional dysphagia management can be challenging and involves elimination of motility-altering medications, a trial of high dose acid suppression, consideration for empiric bougie dilation, trials of neuromodulatory medications, and reassurance with simple lifestyle measures.[6] The use of acid suppression stems from a variety of trials that have demonstrated an association of dysphagia with esophagitis severity, degree of gastric acidity, as well as reported improvement with empiric proton pump inhibitor therapy even in the absence of endoscopic pathology.[24-26] Empiric bougie dilation and antidepressant use do not have significant data to support their use, but each can be considered after weighing the potential risks and benefits.[6, 27] Conservative measures include eating in an upright position, avoiding exacerbating foods, thorough mastication, and alternating solid and liquid ingestion.[24]

Conclusion

An initial description of dysphagia offers an expansive list of potential etiologies, however, an organized approach to evaluation by means of thorough clinical history and use of modern diagnostic techniques can help determine underlying pathology and direct therapeutic options in a targeted manner.

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Disclosure

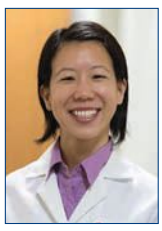
None reported. **MM**

Barrett's Esophagus

by Daniel E. Bujanda, MD & Christine Hachem, MD

Chronic reflux esophagitis leads to the development of Barrett's esophagus; who and when to conduct surveillance for adenocarcinoma in patients with Barrett's remains controversial.





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Abstract

The prevalence of Barrett's esophagus is increasing in the United States and is a major risk factor for esophageal adenocarcinoma. This review serves to help primary care physicians and family practitioners better understand who should be screened for Barrett's esophagus, know the appropriate surveillance intervals for repeat endoscopy, and understand therapeutic options for the management of Barrett's esophagus.

Introduction

Gastroesophageal reflux disease (GERD) is highly prevalent in the United States and complaints related to gastroesophageal reflux disease constitute a large proportion of the primary care physicians' practice.[1] However, only a small proportion of patients with GERD are at risk of developing Barrett's esophagus (BE).[2] Barrett's esophagus is a pre-malignant condition that places patients at risk for esophageal adenocarcinoma (EAC).[3] Within the last decade, our understanding of the pathogenesis of Barrett's esophagus has increased substantially, with improved risk stratification to identify patients who are at risk for progression to esophageal adenocarcinoma. Equally impressive is the ever-expanding endoscopic armamentarium to treat dysplastic lesions, obviating the need for more invasive therapies such as esophagectomy. Discerning which patients should be referred for BE screening and surveillance will enable optimization of treatment regimens for Barrett's esophagus.

Definition of Barrett's

Barrett's esophagus occurs when the normal squamous epithelium of the distal esophagus changes to columnar-lined intestinal type cells, a transition known as intestinal metaplasia. Its importance lies in that it is the only known precursor to esophageal adenocarcinoma.[4] The transition occurs when the esophagus is repeatedly exposed to gastric acid, which in turn causes mucosal inflammation. When intestinal metaplasia occurs, the normal esophageal mucosa will take on a salmon colored appearance when viewed endoscopically (Figure 1: Panel A and B). When this is seen and is greater than one centimeter in length, endoscopic biopsies should be obtained to determine if goblet cells or dysplasia are seen on histological review. The diagnostic criteria for Barrett's esophagus that goblet cells are present is controversial, but is the accepted practice in the United States.[4] Patients with intestinal metaplasia less than one centimeter in length do not have an increased risk for further complications. Unfortunately, there is a great deal of inter-observer variability in the histologic interpretation of dysplasia and the diagnosis should be confirmed by two pathologists, one of whom has extensive experience in the interpretation of Barrett's-associated neoplasia.[2]

Risk Factors

Although gastroesophageal reflux disease is highly prevalent in the United States, only 10-15% of patients with gastroesophageal reflux disease will develop Barrett's esophagus and up to 50% of subjects with Barrett's or esophageal adenocarcinoma will

Table 1. Risk Factors for Barrett's Esophagus

Risk Factors for Barrett's Esophagus
Caucasian race
Male
Age > 50
Central obesity (waist circumference >102 cm)
History of GERD
Smoking history
Family history of Barrett's esophagus
Esophageal adenocarcinoma in a first-degree relative

report no history of gastroesophageal reflux symptoms.[2] Overall, Barrett's esophagus affects 2-7% of adults in western countries.[4] Shown in Table 1 are the known risk factors for Barrett's esophagus and esophageal adenocarcinoma.[2]

Current guidelines by the American College of Gastroenterology recommend screening only men with frequent gastroesophageal reflux disease (at least weekly symptoms or symptoms that have persisted more than five years) and two or more of the known risk factors. Routine screening of women is not recommended except those with multiple risk factors and a documented family history of Barrett's esophagus or esophageal adenocarcinoma in a first-degree relative.

Natural History

The incidence of esophageal adenocarcinoma has increased substantially over the past four decades with an estimated incidence of 2.8 cases per 100,000 in the United States.[3] Esophageal adenocarcinoma in Barrett's esophagus develops through a progressive sequence of histologic and molecular events that begin with metaplasia and then progresses through various stages of dysplasia before development of adenocarcinoma.[4] The specific cell type at the squamocolumnar junction responsible for the development of Barrett's was recently described.[5] Dysplasia is defined as neoplastic epithelium that is confined to the basement membrane and the use of the descriptors low grade or high grade is based upon the severity of architectural distortion seen histologically. Advancing age, increasing Barrett's segment length, and endoscopic irregularities of the mucosa (e.g. nodules, ulcers) are risk factors for dysplasia. The risk of esophageal adenocarcinoma is proportional to the degree of dysplasia and survival in esophageal adenocarcinoma is stage dependent.[6] Malignant progression in patients with non-dysplastic Barrett's is low with an annual incidence of 0.33% per year,[2] however, Barrett's esophagus with high grade dysplasia has an annual incidence rate of 7% for developing EAC.[7] Unfortunately, more than 90% of diagnosed esophageal adenocarcinoma cases occur in patients without a prior history of Barrett's esophagus.[2] Nevertheless, given the low five year survival rates of patients with esophageal adenocarcinoma, screening and surveillance strategies have been proposed to decrease rates of EAC.

Therefore, the best hope for survival in esophageal adenocarcinoma remains endoscopic screening and surveillance of Barrett's esophagus patients to detect dysplasia and esophageal adenocarcinoma at an early stage where potentially curable interventions exist.[2] Patients with esophageal adenocarcinoma detected in a surveillance program have their cancers detected at an earlier stage with markedly improved five-year survival compared with similar patients not undergoing routine surveillance.[6] However, only 7% of patients with Barrett's esophagus die of esophageal adenocarcinoma. Most will die of non-intestinal causes such as heart disease and pulmonary disease.[2]

Treatment of Barrett's Esophagus

All patients with Barrett's esophagus should be on once daily proton pump inhibitor therapy as this may reduce the risk of progression to dysplasia and esophageal adenocarcinoma. The use of H2 blockers has not shown to reduce this risk. Twice daily dosing is not routinely recommended and should only be used for poorly controlled gastroesophageal reflux disease or evidence of persistent inflammation. Currently there is not enough evidence to advocate the use of medications such as statins, aspirin or non-steroidal anti-inflammatory drugs as a chemoprevention strategy. Antireflux surgery should not be recommended for treatment of Barrett's alone but may be considered for GERD management.

Surveillance endoscopy intervals are currently determined by the presence and grade of dysplasia. As the risk is low for esophageal adenocarcinoma in patients with non-dysplastic Barrett's esophagus, surveillance upper endoscopy with biopsies should occur every three to five years in these patients. Patients with low or high-grade dysplasia or stage T1a esophageal adenocarcinoma (defined as being limited to the mucosa with no extension to the submucosa) should be managed with endoscopic therapy. Endoscopic management has been shown in multiple randomized controlled trials to effectively eliminate dysplastic and metaplastic epithelium, as well as greatly reduce cancer incidence.[4] Currently the preferred endoscopic therapy for low grade dysplasia is radiofrequency ablation (Figure 1, Panel C). Radiofrequency ablation has largely replaced most other forms of ablation such as argon plasma coagulation and photodynamic therapy because of its high efficacy rate and low complication rate.

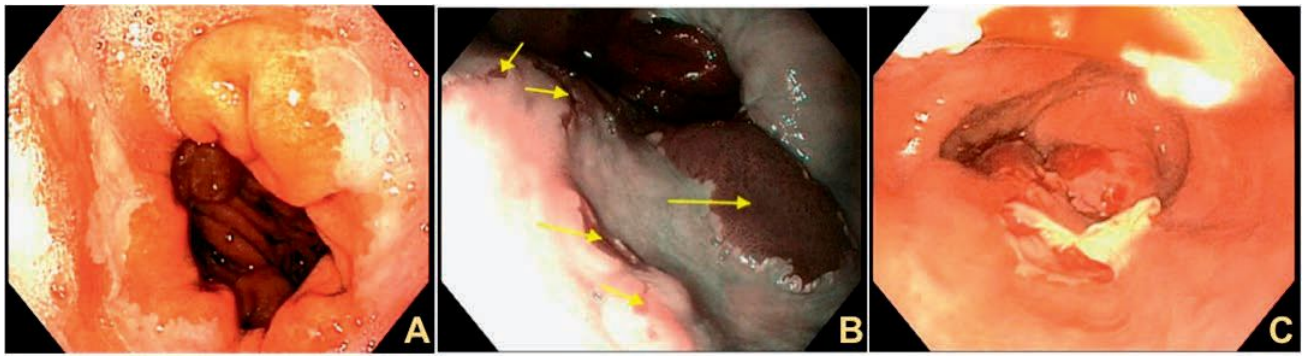


Figure 1. A, Endoscopic view of salmon-colored mucosa typical of Barrett's esophagus in white light; B, Narrow band imaging highlighting the squamous cell epithelium (white mucosa) and tongues and islands of Barrett's mucosa (arrows); C, Burned patch of esophageal mucosa after one session of radiofrequency ablation (white colored mucosa).

For patients with high-grade dysplasia or stage T1a esophageal adenocarcinoma, endoscopic mucosal resection followed by radiofrequency ablation is the preferred treatment. Endoscopic mucosal resection is a procedure designed to remove mucosa and superficial submucosal tissue and serves as both a diagnostic and a therapeutic procedure.

If there are advanced features such as nodularity, ulcers, or strictures seen in the segment of Barrett's esophagus, endoscopic mucosal resection of these lesions should be performed first and treatment based upon histological assessment. These more advanced endoscopic features have been shown to be associated with an increased risk of esophageal adenocarcinoma.[4] Patients with stage T1b (tumor with extension to submucosa) or more advanced esophageal adenocarcinoma should be managed by a multidisciplinary team consisting of oncology, surgical oncology, and advanced endoscopy. These patients likely need adjuvant chemoradiation and consideration of esophagectomy.

In patients who are treated endoscopically and have complete elimination of intestinal metaplasia, subsequent surveillance is based on the severity of the initial disease. In patients with low-grade dysplasia, surveillance endoscopy is performed every six months in the first year and then annually thereafter. In patients with high grade dysplasia or stage T1a esophageal adenocarcinoma surveillance endoscopy is done every three months for the first year, every 6 months in the second year, and then yearly thereafter. For recurrent disease, treatment follows the same histological algorithm that was used before treatment.

Future Technologies

Conventional endoscopy is still considered the gold standard for diagnosing BE. However, current surveillance programs are expensive and time-consuming, creating the need for less invasive and more cost effective screening methods.[6]

Newer technologies such as unsedated transnasal endoscopy,[8] capsule endoscopy, chromoendoscopy, biomarkers, and Cytosponge (esophageal samples are obtained using a sponge at the end of a wire), and risk prediction models will likely become more prevalent and useful as diagnostic and risk stratification tools in the future.

Summary

Barrett's esophagus is a risk factor for EAC. Unfortunately, EAC has a poor prognosis if diagnosed late. Understanding the screening and surveillance practices will help identify patients at increased risk for EAC. Best practices will likely continue to evolve as increased emphasis on risk stratification helps to target those who are most likely to progress to EAC. An ever-expanding armamentarium of therapeutics is now available to help tackle the progression of Barrett's to EAC.

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Disclosure

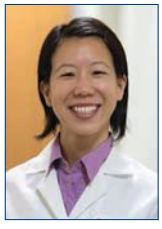
None reported. **MM**

Gastroesophageal Reflux Disease (GERD)

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Gastroesophageal reflux disease affects millions of people worldwide with significant clinical implications.





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Abstract

Gastroesophageal reflux disease (GERD) is a common clinical problem, affecting millions of people worldwide. Patients are recognized by both classic and atypical symptoms. Acid suppressive therapy provides symptomatic relief and prevents complications in many individuals with GERD. Advances in diagnostic and therapeutic modalities have improved our ability to identify and manage disease complications. Here, we discuss the pathophysiology and effects of GERD, and provide information on the clinical approach to this common disorder.

Introduction

Gastroesophageal reflux disease (GERD) is a very common digestive disorder worldwide with an estimated prevalence of 18.1-27.8% in North America.[1] Approximately half of all adults will report reflux symptoms at some time.[2] According to the Montreal definition, GERD is a condition of troublesome symptoms and complications that result from the reflux of stomach contents into the esophagus.[3] Diagnosis of GERD is typically based on classic symptoms and response to acid suppression after an empiric trial. GERD is an important health concern as it is associated with decreased quality of life and significant morbidity.[4] Successful treatment of GERD symptoms has been associated with significant improvement in quality of life, including decreased physical pain, increased vitality, physical and social function, and emotional well-being. While GERD medications are not particularly expensive, the cost of treating GERD patients has been deemed 2-fold more costly than comparable individuals without GERD.[5] This cost difference is likely due to higher morbidity in GERD patients and the higher cost of managing complications of inappropriately treated GERD.

Epidemiology and Pathophysiology

Risk factors for GERD include older age, excessive body mass index (BMI), smoking, anxiety/depression, and less physical activity at work.[6-8] Eating habits may also contribute to GERD, including the acidity of food, as well as size and timing of meals, particularly with respect to sleep. Recreational physical activity appears to be protective, except when performed post-prandially.[6, 9]

Gastroesophageal reflux is primarily a disorder of the lower esophageal sphincter (LES) but there are several factors that may contribute to its development. The factors influencing GERD are both physiologic and pathologic. The most common cause is transient lower esophageal sphincter relaxations (TLESRs). TLESRs are brief moments of lower esophageal sphincter tone inhibition that are independent of a swallow.[10] While these are physiologic in nature, there is an increase in frequency in the postprandial phase and they contribute greatly to acid reflux in patients with GERD. Other factors include reduced lower esophageal sphincter (LES)

pressure, hiatal hernias, impaired esophageal clearance, and delayed gastric emptying.[8, 11]

Symptoms

The classic and most common symptom of GERD is heartburn. Heartburn is a burning sensation in the chest, radiating toward the mouth, as a result of acid reflux into the esophagus. However, only a small percentage of reflux events are symptomatic. Heartburn is also often associated with a sour taste in the back of the mouth with or without regurgitation of the refluxate.

Notably, GERD is a common cause of non-cardiac chest pain.[12, 13] It is important to distinguish between the underlying cause of the chest pain because of the potentially serious implications of cardiac chest pain and varied diagnostic and treatment algorithms based on etiology.[13] A good clinical history may elicit GERD symptoms in patients with non-cardiac chest pain pointing to GERD as a potential etiology.

Although classic symptoms of GERD are easily recognized, extraesophageal manifestations of GERD are also common but not always recognized. Extraesophageal symptoms are more likely due to reflux into the larynx, resulting in throat clearing and hoarseness. It is not uncommon for patients with GERD to complain of a feeling of fullness or a lump in the back of their throat, referred to as globus sensation.[14] The cause of globus is not well understood but it is thought that exposure of the hypopharynx to acid leads to increased tonicity of the upper esophageal sphincter (UES).[14] Furthermore, acid reflux may trigger bronchospasm, which can exacerbate underlying asthma, thereby leading to cough, dyspnea, and wheezing.[15] Some GERD patients may also experience chronic nausea and vomiting.

It is important to screen patients for alarm symptoms associated with GERD as these should prompt endoscopic evaluation. Alarm symptoms may suggest a possible underlying malignancy. Upper endoscopy is not required in the presence of typical GERD symptoms. However, endoscopy is recommended in the presence of alarm symptoms and for screening of patients at high risk for complications (i.e. Barrett's esophagus, including those with chronic and/or frequent symptoms, age > 50 years, Caucasian race, and central obesity). Alarm symptoms include dysphagia (difficulty swallowing) and odynophagia (painful swallowing), which may represent presence of complications such as strictures, ulceration, and/or malignancy. Other alarm signs and symptoms include, but are not limited to, anemia, bleeding, and weight loss.[16]

GERD symptoms should be considered as distinct from dyspepsia. Dyspepsia is defined as epigastric discomfort, without heartburn or acid regurgitation, lasting longer than one month. It can be associated with bloating/epigastric fullness, belching, nausea, and vomiting. Dyspepsia is an entity that may be managed differently from GERD and may prompt endoscopic evaluation, as well as testing for H. pylori.[20]

Complications

Left untreated, GERD can result in several serious complications, including esophagitis and Barrett's esophagus. Esophagitis can vary widely in severity with severe cases resulting in extensive erosions, ulcerations and narrowing of the esophagus.[17] Esophagitis may also lead to gastrointestinal (GI) bleeding. Upper GI bleeding may present as anemia, hematemesis, coffee-ground emesis, melena, and when especially brisk, hematochezia. Chronic esophageal inflammation from ongoing acid exposure may also lead to scarring and the development of peptic strictures, usually presenting with the chief complaint of dysphagia.[11]

Patients with persistent acid reflux may be at risk for Barrett's esophagus, defined as intestinal metaplasia of the esophagus. In Barrett's esophagus, the normal squamous cell epithelium of the esophagus is replaced by columnar epithelium with goblet cells, as a response to acid exposure.[18] Changes of Barrett's esophagus may extend proximally from the gastroesophageal junction (GEJ) and have the potential to progress to esophageal adenocarcinoma, making early detection very important in the prevention and management of malignant transformation.[19]

Diagnosis

GERD is usually diagnosed clinically with classic symptoms and response to acid suppression. Heartburn with or without regurgitation is typically sufficient to suspect GERD, particularly when these symptoms are worse postprandially or when recumbent.[20] The initiation of treatment with histamine type 2 (H2) receptor blockers or proton pump inhibitors (PPIs) with subsequent cessation of symptoms is considered diagnostic. In patients who respond to empiric treatment, in the absence of alarm features or symptoms, no further workup is required.[21]

In some patients, reflux symptoms will persist despite treatment with high-dose PPIs. Additional tests may be warranted to evaluate for other causes of their symptoms and to screen for possible complications of GERD. It is

important to note that the severity of reflux symptoms does not necessarily correlate with the extent of mucosal damage.

The most utilized diagnostic test for the evaluation of GERD and its possible complications is the upper gastrointestinal endoscopy, or esophagogastroduodenoscopy (EGD). The primary benefit of endoscopy is direct visualization of the esophageal mucosa. This assists in diagnosis of complications of GERD such as esophagitis, strictures and Barrett's esophagus. One endoscopic grading system of GERD severity is the Los Angeles classification, graded from A to D, with D being the most severe (Figure 1).[22]

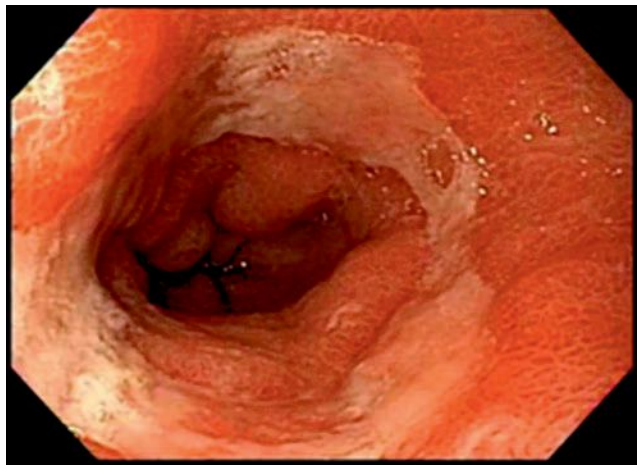


Figure 1. Endoscopic view of Los Angeles grade D esophagitis (circumferential esophageal erosions, ulceration, and inflammation).

Ambulatory pH monitoring is considered the gold standard in the diagnosis of acid reflux. Ambulatory pH monitoring allows for the objective detection of acid reflux events and correlation with symptoms (Figure 2). This is particularly helpful in symptomatic patients with normal endoscopic findings. Ambulatory pH testing can be completed with good reproducibility (84-93%), sensitivity (96%), and specificity (96%).[23] To complete the test, pH probes (catheter or wireless capsule) are placed into the esophagus for 24 to 48 hours. Percent of time with an esophageal pH of less than 4 is the primary parameter used in the diagnosis of GERD. It has the benefit of detecting dynamic changes in pH while upright and recumbent. Furthermore, pH probes record the number of reflux events, the proximal extent of reflux, as well as the duration of reflux events. Symptom correlation is also noted between reflux and symptoms. This test can be performed on or off PPI therapy.

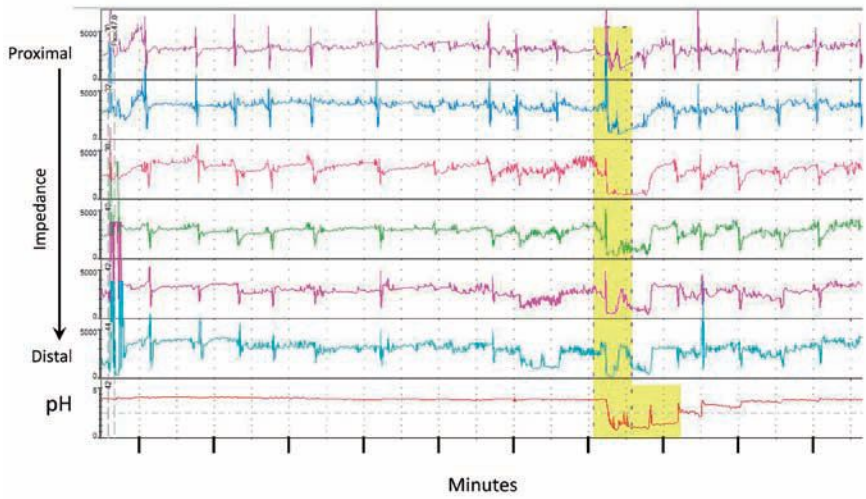


Figure 2. High resolution esophageal impedance and pH tracings. Impedance (measure of electrical conductance) within the lumen of the esophagus is measured simultaneously using multiple probes and the measurements are displayed with the proximal measures at the top progressing distally towards the stomach. The bottom tracing is the pH at the most distal measurement point. Highlighted in yellow are measurements that document liquid reflux from the stomach correlating with a drop in pH indicating reflux of gastric acid. This tracing is a small snapshot of 24 hours of data.

The diagnostic yield of ambulatory esophageal pH testing can be improved with the addition of impedance testing in patients with suspected GERD (Figure 3). This test involves the same procedure of placing probes into the esophagus but measures electrical properties of esophageal contents. For example, liquid reflux has low impedance and high conductance while gaseous reflux, seen in belching, has high impedance with low conductance. Some patients sense reflux symptoms during times of both normal and excessive esophageal acid exposure and combination monitoring allows for detection of nonacid reflux events that would otherwise go unnoticed with pH monitoring alone.[24, 25]

While it has some utility in evaluating patients with dysphagia, the barium esophagram is a poor screening test for GERD. It has a very poor sensitivity (26%) and specificity (50%) for mild esophagitis compared to

endoscopy. Reflux of barium often does not correlate well with reflux of acid in symptomatic patients, and in up to 20% of cases is positive in normal individuals.[16] Sensitivity can be improved by using maneuvers to illicit reflux such as coughing, valsalva, and rolling from supine to the right lateral position.[26] Fluoroscopic barium testing has better yield in the detection of severe esophagitis, peptic strictures, and hiatal hernia. However, even for this indication, it still carries a relatively poor sensitivity and specificity for the detection of acid reflux in comparison to ambulatory pH testing. Therefore, due to its poor utility, it is not recommended for routine diagnosis of GERD.[16]

Treatment

GERD patients should be assessed for alarm features, as these should prompt urgent endoscopic evaluation. If no alarm symptoms are present, initial management of GERD should be geared toward lifestyle modification. However, it is important to note that the majority of studies on lifestyle and dietary changes in GERD have not been well powered. Nevertheless, lifestyle changes remain first-line in management of GERD with a primary goal of symptom reduction and improvement in quality of life.[27, 28]

The only proven lifestyle modification for the management of GERD is head of bed (HOB) elevation.[29] Head of bed elevation has been shown to decrease esophageal acid exposure and esophageal clearance time with subsequent reduction in symptoms in patients with supine GERD. In addition, is it advised that factors contributing to the incidence of TLESRs should also be minimized or avoided. These include smoking, heavy alcohol consumption, large evening meals, nighttime snacks, and high dietary fat intake.[27] Weight loss is strongly encouraged in overweight GERD patients, but there is no documented benefit in those with normal weight.[30] Although obesity is a risk factor for GERD, most bariatric surgeries exacerbate reflux. Additionally, all patients with GERD should avoid non-steroidal anti-inflammatory drugs (NSAIDs) because of their role in disrupting physiologic mucosal protection mechanisms.

Medication therapy for GERD is targeted at symptom reduction and minimizing mucosal damage from acid reflux. While acid suppression is successful in the treatment of GERD, there does not appear to be a clear relationship between GERD severity and high gastric acid levels with the exception being Zollinger-Ellison syndrome.[31]

Many patients with heartburn try over-the-counter antacids prior to seeking medical attention. The primary acid suppressive medications include H2 blockers and proton pump inhibitors. H2 blockers decrease gastric acid secretion by inhibiting histamine stimulation of the parietal cell. Proton pump inhibitors work to decrease the amount of acid secreted from parietal cells into the gastric lumen. H2 blockers have been shown to have some symptomatic benefit above placebo, but in individuals without contraindication, PPIs are the most effective therapy.[32] There is no clear role for prokinetic agents, such as metoclopramide, in the treatment of GERD.[16]

Proton pump inhibitors are the most potent class of antacid medications. They are dosed once or twice daily and are most effective if taken 30 to 60 minutes prior to meals. Many patients will have relapse of symptoms after the cessation of PPI, therefore lifelong therapy is often required.[16] Recently, there has been a rise in concern of PPIs contributing to the development of bone fractures, electrolyte deficiencies, infections (e.g., Clostridium difficile, pneumonia), and renal insufficiency.[33, 34] Given the theoretical risk of side effect from PPI therapy, the lowest dose required for maintenance should be used and periodic trials of weaning should be attempted.[33]

In GERD patients refractory to twice daily PPI dosing, there is some evidence to show that adding a nighttime H2 blocker can be beneficial.[16, 35] In refractory cases, other disorders should be considered, notably: eosinophilic esophagitis, pill esophagitis, delayed gastric emptying, duodenogastric/bile reflux, irritable bowel syndrome, psychological disorders, achalasia, and Zollinger-Ellison syndrome.[36]

The use of anti-reflux surgery (fundoplication) has been controversial. Studies show only minimal long-term symptomatic improvements with surgery over PPI therapy, paired with an increased incidence of dysphagia and dyspepsia. Patients who respond best to surgery are those who also respond well to PPIs and therefore may be managed medically. Conversely, PPI-refractory patients are unlikely to have benefit from surgery.[16] Approximately half of all patients who undergo surgery eventually require surgical revision. Given the near-negligible difference in efficacy between surgery and PPI and the risk for postoperative complications and mortality, surgery should only be reserved for select patients. Choosing the best candidates for anti-reflux surgery remains a clinical challenge.

Summary

GERD is a common clinical problem with significant morbidity and potentially decreased quality of life. Early recognition of symptoms is integral to preventing complications of GERD. Behavioral changes and advances in acid suppression remain integral to its treatment.

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Disclosure

None reported.

MM

Peptic Ulcer Disease and *Helicobacter pylori* infection

by Mechu Narayanan, MD, Kavya M. Reddy, MD & Elizabeth Marsicano, MD

Peptic ulcers are frequently encountered in the primary care setting and understanding associated risk factors is key to disease prevention and management.







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Abstract

Peptic ulcer disease (PUD) is a common condition that both primary care providers and gastroenterologists encounter. Symptoms of peptic ulcer disease are variable and may include abdominal pain, nausea, vomiting, weight loss and bleeding or perforation with complicated disease. Identifying the risk factors and mechanisms that lead to the development of PUD helps to understand the approach behind diagnostic and treatment strategies.

Definition and Epidemiology

Peptic ulcers are acid-induced lesions found in the stomach and duodenum characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria.[1] Lesions that do not reach this depth are called erosions (Figure 1). In the United States, the prevalence of self-reported physician-diagnosed peptic ulcer disease was 10% in 1990, and the approximate incidence is about 500,000 new cases per a year.[2, 3] Overall, however, the risk of mortality and need for hospitalizations due to PUD has been decreasing worldwide. This is most likely secondary to a decline in *Helicobacter pylori (H. pylori)* infections due to treatment and improved hygiene.[4, 5] Increased use of prescription and over-the-counter acid-suppressing medications and greater caution with non-steroidal anti-inflammatory drugs (NSAIDs) may account partially for this trend as well.[5, 6]

Etiology and Pathophysiology

The main risk factors for PUD are *H. pylori* and NSAID use, however not all individuals infected with *H. pylori* or taking NSAIDs develop PUD.[1, 7] Almost half of the world's population is colonized by *H. pylori.*[8] The organism is usually acquired in childhood and persists until treated. Risk factors for acquiring the infection include a lower socioeconomic status and unsanitary conditions or crowding. The prevalence of *H. pylori* is higher in developing countries and more common in certain ethnicities. In the last five years in the United States, there has been a decline in the prevalence of *H.pylori* in all ages. Yet, there are differences based on ethnicity with rates of infection that are over 60% in Mexican Americans versus 30% in the non-Hispanic white population.[9]

H. pylori causes an inflammatory response with neutrophils, lymphocytes, plasma cells, and macrophages within the mucosal layer and causes epithelial cell degeneration and injury. Gastritis is usually more severe in the antrum, with little or no inflammation in the corpus. All patients found to have peptic ulcers should be tested for *H. pylori.* There are both invasive and noninvasive methods for testing that are summarized in Table 1. Of all the noninvasive methods, the urea breath test and stool antigen tests are the

most feasible and are more accurate than serologic testing.[10] Although invasive, endoscopy allows for biopsy and includes a variety of methods for testing such as histology, culture, or rapid urease test. All methods other than serology are affected by use of acid-suppressing medications such as proton pump inhibitors and may produce false negatives.

NSAIDs are widely used for a variety of conditions to help reduce pain and inflammation; however, many users develop gastrointestinal side effects. NSAIDs account for over 90% of all ulcers and approximately 25% of NSAID users will develop peptic ulcer disease.[11] Aspirin users are also twice as likely to develop peptic ulcers as the general population.[12, 13] Others develop a milder degree of topical injury, which is seen as mucosal hemorrhages and erosions and are referred to as NSAID gastropathy. These multiple small erosions are usually located in the antrum but may also be seen in the body.

NSAIDs induce mucosal injury by several mechanisms. The majority of NSAIDs are weak acids and become protonated and cross lipid membranes to enter epithelial cells when exposed to acidic gastric juice (pH 2). In the epithelial cell (pH 7.4), the NSAID ionizes and releases its H+ and cannot cross the lipid membrane and thus becomes trapped. This leads to uncoupling of oxidative phosphorylation, leading to decreased mitochondrial energy production, reduced cellular integrity, and increased cellular permeability. This can result in a topical injury and rapid epithelial cell death, superficial hemorrhage, and erosions.[14]

The other major mechanism by which NSAIDs cause mucosal injury is by inhibition of cyclooxygenase-1 (COX-1), which is responsible for prostaglandin synthesis. Prostaglandins increase secretion of bicarbonate and mucous, increase mucosal blood flow, and inhibit cell proliferation to maintain the mucosal barrier.[5] Aspirin acetylates cyclooxygenase and irreversibly inhibits the

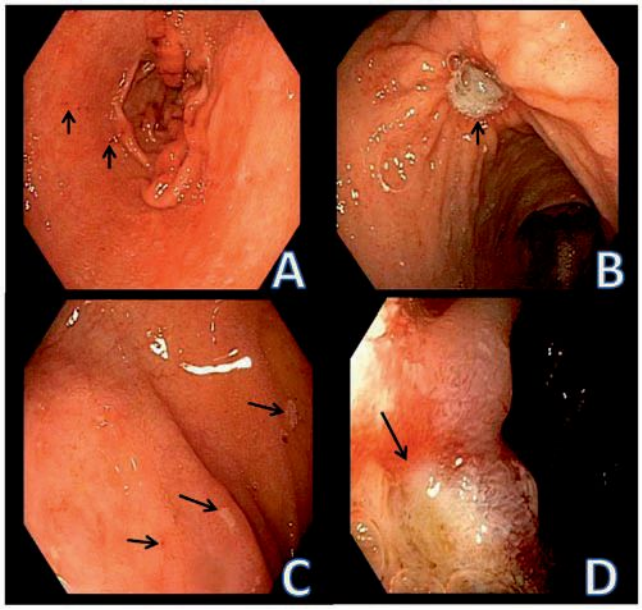


Figure 1. Peptic erosions and ulcers in the stomach and duodenum. A. Small erosions in the gastric antrum. Mucosal breaks with focal hemorrhage are identified by the arrows. B. Benign peptic ulcer in the body of the stomach (arrow). C. Duodenal erosions identified by focal areas of adherent exudate (arrows). D. Duodenal ulcer. The mucosal defect has depth and the margin is identified by the arrow. The surrounding mucosa is edematous.

Table 1. Diagnostic Tests for *H. pylori*

Test	Sensitivity	Specificity	Advantages	Disadvantages
Serology	85-92%	79-83%	Only test not influenced by PPI or antibiotic use	Cannot confirm cure
Urea Breath Test	95%	96%	Confirms cure	Accuracy affected by PPI and antibiotic use
Fecal antigen testing	95%	94%	Confirms cure	Accuracy affected by PPI and antibiotic use
Rapid urease test	98%	99%	Inexpensive, confirms cure	Requires endoscopy, less accurate after treatment or after PPI use
Histology	>95%	>95%	Permits visualization, confirms cure	Requires endoscopy, affected by PPI and antibiotic use
Culture	70-90%	100%	Allows determination of antimicrobial sensitivity, confirms cure	Requires endoscopy, result takes several days, affected by PPI and antibiotic use

PPI, proton pump inhibitor

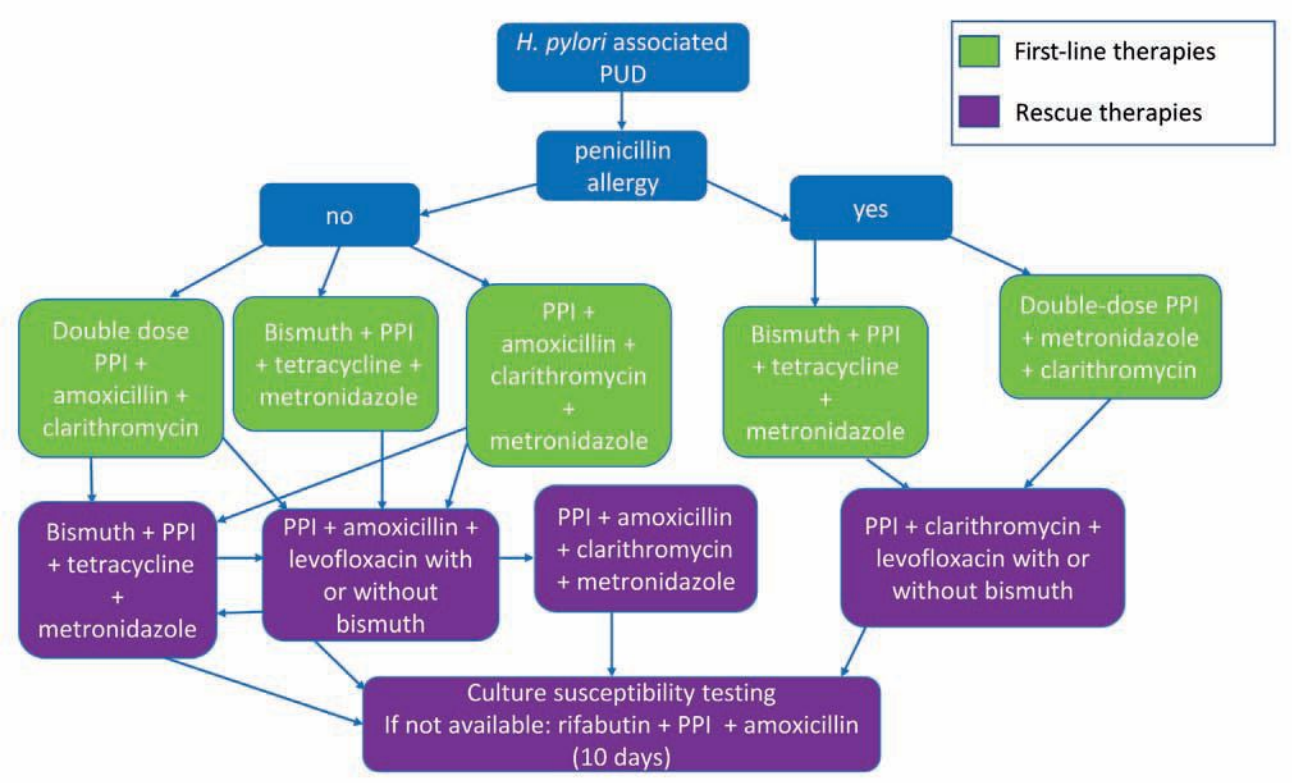


Figure 2. Multiple treatment regimens for H. pylori can be considered and the standard treatment duration is 14 days. The doses of the drugs used are: proton pump inhibitor (PPI, standard or double dose), clarithromycin 500 mg BID, amoxicillin 1 gm BID, bismuth subsalicylate 300 mg QID, metronidazole 500 mg TID, tetracycline 500 mg QID, levofloxacin 500 mg QD, rifabutin 300 mg QD.

enzyme, whereas NSAIDs inhibit the enzyme reversibly in a concentration-dependent manner. Among these pathophysiologic responses, reduction in blood flow is thought to be the primary mechanism responsible for NSAIDs-induced injury.[14]

Two isoforms of COX exist: COX-1 is primarily responsible for prostaglandin synthesis in the GI tract, whereas COX-2 is responsible for prostaglandin synthesis at sites of inflammation. NSAIDs such as ibuprofen, naproxen, aspirin, and indomethacin inhibit both COX-1 and COX-2 and are classified as non-selective. COX-2 specific NSAIDs such as celocoxib or rofecoxib inhibit COX-2 without inhibiting COX-1, making them potentially safer in the GI tract. Endoscopic studies of patients taking COX-2 inhibitors have demonstrated lower incidences of ulceration of approximately 3-5% when compared to traditional NSAIDs which have a 20-40% incidence. However, COX-2 selective NSAIDs have been shown to increase risk of cardiac disease and many have been taken off the market.

Those who are at highest risk for NSAID-induced ulcers are patients with a history of peptic ulcers or hemorrhage, those concomitantly using steroids or anticoagulants, anyone over the age of 65 and those taking high doses or combinations of more than one NSAID (including low dose aspirin). If these patients need multiple agents, they should be started on treatment to prevent ulcers. Furthermore, using medications such as selective serotonin-reuptake inhibitors, corticosteroids, aldosterone antagonists, or anticoagulants increases the risk of bleeding.[15] Older age and a greater number of comorbidities also affect the clinical course of patients with *H. pylori* and NSAIDs.[16, 17] Interaction between *H. pylori* and NSAIDs is controversial but current American College of Gastroenterology guidelines recommend testing and treating for *H. pylori* if an individual is to start long-term NSAIDs and testing could be considered in those taking long term low dose aspirin as well.[5, 18]

About a fifth of PUD cases are not related to *H. pylori*, NSAIDs or aspirin, but the accuracy of this value has been challenged due to false negative *H. pylori* testing or accidental (or underreported) NSAID ingestion.[19,20] This idiopathic PUD may be due to an imbalance between factors that contribute to mucosal integrity and aggressive insults, including a hypersecretory status. Other etiologies for PUD include ischemia causing stress ulcers, medications (steroids, alendronate, potassium chloride, and

chemotherapeutic agents), viral infections (CMV, HSV), gastric bypass surgery, metabolic disturbances, radiotherapy, histamine, eosinophilic infiltration, and basophilia.[5, 21]

Diagnosis

Diagnosis begins with clinical suspicion when patients present with symptoms such as epigastric abdominal pain, burning, post-prandial fullness, or early satiety.[1] Classically, patients with duodenal ulcers complain of worsening abdominal pain on an empty stomach and describe hunger or abdominal pain two to three hours after meals or at night. In contrast, patients with gastric ulcers report nausea, vomiting, weight loss and post-prandial abdominal pain. Elderly patients are often minimally symptomatic and some patients with untreated PUD may have intermittent symptoms due to spontaneous healing and then relapse due to persistence of risk factors, such as continued NSAIDs use or *H. pylori* infection.[5]

If clinical symptoms suggest possible peptic ulcer disease and no alarm symptoms are noted, empiric treatment with anti-secretory therapy can be started. Furthermore, since *H. pylori* is a common cause of PUD, a test and treat strategy with a non-invasive test for *H. pylori* (stool antigen or urea breath test) is recommended in patients less than 55 years of age without alarm features, in geographic regions were gastric cancer is uncommon and the prevalence of *H. pylori* is greater than 20%.[22] In older patients and those with alarm symptoms, endoscopy is recommended to establish a diagnosis. Alarm symptoms include GI bleeding, weight loss, early satiety, dysphagia or odynophagia, family history of upper GI malignancy, iron deficiency anemia or new upper GI symptoms in patients older than 55.[23] Esophagogastroduodenoscopy (EGD) or upper endoscopy is the gold standard for the diagnosis of PUD. It is can be used to detect *H. pylori* with gastric biopsies and can also rule out malignancy.

Treatment

Treatment is usually directed at identifying the factors that lead to PUD. For *H. pylori*-associated PUD, eradication alone will lead to ulcer healing and prevent further mucosal injury. However, due to rising antibiotic resistance in *H. pylori*, treatment has become more difficult (Figure 2). First line therapy for *H. pylori* eradication includes a proton pump inhibitor (PPI), clarithromycin and amoxicillin or metronidazole (for penicillin-allergic patients) for seven to 14 days.[24] PPIs work synergistically with antibiotics to eradicate *H. pylori*.[25] Due to increasing antibiotic resistance, the efficacy of triple therapy has fallen below 70% in many countries. [24] As susceptibility testing is often not available in clinical practice, clarithromycin-based regimens should be avoided when local clarithromycin resistance rates are greater than 15%.[24] Clarithromycin resistance rates are high (>20%) across the United States.[26] When using clarithromycin-based triple therapy, eradication rates can be increased with use of high dose PPI and by extending the duration of treatment from seven to 14 days.[5] For areas with high clarithromycin resistance, bismuth-containing quadruple therapy with a PPI, bismuth, tetracycline and a nitroimidazole (metronidazole or tinidazole) for 14 days or PPI, clarithromycin, amoxicillin, and a nitroimidazole for 14 days is the preferred as first line treatment.[18] There have been issues with the cost and availability of tetracycline and the data have been mixed on whether doxycycline can be substituted. The regimens discussed above yield eradication rates greater than 90%.[5]

All patients treated for *H. pylori,* should be tested to confirm eradication at least four weeks after completing therapy. Second line therapy should be prescribed if a first line regimen fails (Figure 2) and should not include repeating metronidazole or clarithromycin.[18] Furthermore, susceptibility testing should be considered after two treatment failures or after one treatment failure when endoscopy is performed (for other reasons such as follow up of gastric ulcer). If culture for *H. pylori* is not available to evaluate for resistance or after three recommended treatments have failed, rifabutin-based triple therapy (PPI, rifabutin, and amoxicillin) for 10 days can be considered. If symptoms do not improve after *H. pylori* eradication, endoscopy should be pursued if not already performed.

In NSAID- or aspirin-associated PUD, ulcers heal more than 85% of the time with 6-8 weeks of PPI therapy if the offending agent is discontinued. Ulcer healing is still attainable but delayed with continued NSAIDs use. Anti-secretory therapy can be started for prevention of PUD in patients on aspirin. Although PPIs, H2 blockers, sucralfate, and misoprostol can all be considered to treat NSAID-associated PUD, PPIs are far more effective than other agents.[25] Sucralfate is effective for treating NSAID-associated duodenal ulcers but not for the treatment or prevention of NSAID-associated gastric ulcers. In addition to its poor efficacy, misoprostol is often limited by its side effect profile, which includes gastrointestinal upset and abortifacient reactions. In cases of refractory ulcers, both drug compliance with PPI use and inadvertent use of NSAIDs should be explored.[27] All gastric ulcers require repeat endoscopy in six to eight weeks to evaluate for healing. If a gastric ulcer is not healed, biopsies must be taken at time of repeat endoscopy to rule out gastric cancer. For refractory ulcers, doubling the PPI dose can be

recommended for six to eight weeks, although the evidence supporting this is weak. Furthermore, evaluating for false-negative *H. pylori* testing (via serology), malignancies, infections, Crohn's disease, vasculitis, upper abdominal radiotherapy, cocaine use, and Zollinger-Ellison syndrome should be considered for ulcers that have been treated appropriately and have not healed.[5]

Complications

The complications of PUD include unabated symptoms, bleeding, perforation, penetration, gastric outlet obstruction, and gastric malignancy (adenocarcinoma and MALT lymphoma). Bleeding is the most common complication and occurs in about 15-20% of patients. PUD accounts for a large proportion (about 40-60%) of acute upper GI bleeding.[28] Upper GI bleeding is an emergency which requires patients to be evaluated and triaged immediately. Alerting a GI consultant early in the evaluation of a bleeding patient is helpful to coordinate care for critically ill patients. The Glasgow-Blatchford score and Rockall scores have been used for risk stratification.[29] Appropriate resuscitation with IV fluids and blood products to maintain a goal hemoglobin above 7 is vital in management.[30]

Intravenous PPI therapy should be started on all patients considered to have an upper GI bleed immediately on presentation, as IV PPIs reduce the risk of finding high-risk stigmata during endoscopy and in accordance, re-bleeding risk and need for surgery as well.[25] They work by increasing intra-gastric pH, encouraging platelet aggregation and providing clot stability. Prokinetic agents such as erythromycin or metoclopramide can also be considered to improve endoscopic visualization and diagnostic yield.[31] Early endoscopy which is ideally performed within 24 hours provides both prognostic and therapeutic results. After endoscopy, it is recommended to either start or continue PPI (IV if high-risk stigmata of bleeding are found). Studies have shown that IV PPI given twice daily is as efficacious as a continuous PPI drip[32, 33] with significant cost savings. Recurrent bleeding is associated with high mortality and may require repeat endoscopy, angiographic embolization by interventional radiology, or surgery.

If patients have coagulopathy due to warfarin, reversal agents such as vitamin K, fresh frozen plasma (FFP), prothrombin complex concentrates (PCC) or recombinant factor VIIa should be considered as a part of management. These agents need to be used judiciously however, as they can have adverse effects. For instance, high doses of vitamin K can cause prolongation of the time to achieve therapeutic warfarin levels after bleeding stops and therapeutic anticoagulation needs to be restarted (e.g., in the setting of mechanical heart valves). FFP has a risk of causing volume overload and recombinant factor VIIa has an increased risk of thrombosis and is expensive. Novel oral anticoagulants (NOACs) are being used more commonly and these agents cannot be reversed with vitamin K. Compared to warfarin, the NOACs rivaroxaban and dabigatran increase the risk of GI bleeding although apixaban does not seem to have an increased risk of GI bleeding.[34] Activated charcoal can be given within four hours of ingestion to treat a NOAC overdose. Hemodialysis and idarucizumab can be used for life-threatening bleeding associated with dabigatran.[5] Anticoagulant and antiplatelet agents can be restarted once hemostasis has been achieved with the timing dependent on the urgency to restore anticoagulation. Patients on dual antiplatelet therapy after placement of drug-eluting stents should avoid stopping both agents, as they are at high risk for in-stent thrombosis. For patients on aspirin for cardiovascular disease, aspirin should be resumed soon (between one to three days, within seven days) after hemostasis is achieved.[31] For patients with a high risk of thrombosis (such as mechanical mitral valve) bridging with low molecular weight heparin is recommended while warfarin levels are sub-therapeutic.

Perforation is the next most common complication of PUD, occurring in 2-10% of peptic ulcers, and can present as sudden severe abdominal pain with hemodynamic instability or shock.[35] Physical exam findings may include initially hyperactive bowel sounds that can diminish and progress to a rigid abdomen with rebound, suggesting peritonitis. The presence of free air on imaging is supportive of this diagnosis and endoscopy should be avoided in this setting. Surgery is usually the treatment of choice for a perforated peptic ulcer.[3] In patients who are poor surgical candidates and with perforation for more than 24 hours that is contained (based on water soluble contrast studies), medical treatment with nasogastric (NG) suction, IV fluids, antibiotics and acid suppression is an option. Penetrating ulcers can also erode into nearby organs such as pancreas, liver, bile duct, or colon.

Gastric outlet obstruction (GOO) is another complication of PUD and can present with early satiety, bloating, weight loss, indigestion, nausea and vomiting. On physical exam, a succussion splash may be heard due to trapped air and fluid in the stomach. Ulcers that manifest with GOO are often located in the pyloric channel or duodenal bulb. Medical therapy usually involves NG suction and anti-secretory therapy. Endoscopic balloon dilation of pylorus or surgery are options to relieve chronic obstruction.[35]

Conclusion

PUD is a disease with decreasing clinical burden due to the decline in *H. pylori* infections, as well as increased accessibility to anti-secretory therapy and more judicious use of NSAIDs. However, due to its continued high lifetime prevalence and varied clinical presentation, recognition and appropriate management of PUD are key to avoid and minimize significant complications. Testing and treating *H. pylori* as well as limiting mucosal injury caused by NSAIDs (via concurrent PPI prophylaxis or choosing COX-2 selective NSAIDs if available) are the strategies to consider when evaluating PUD. Resuscitation, anti-secretory therapy, endoscopy and management of antithrombotic agents are the key steps in treatment of PUD bleeding, which is the most common complication.

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Disclosure

None reported.

MM

NASH: The Emerging Most Common Form of Chronic Liver Disease

by Meron Tesfay, MD, W. Joseph Goldkamp, MD & Brent A. Neuschwander-Tetri, MD

Nonalcoholic steatohepatitis has emerged as the major form of chronic liver disease of this decade, and NASH cirrhosis is soon to be the leading indication for liver transplantation.







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Abstract

Nonalcoholic steatohepatitis (NASH) is a common cause of chronic liver disease that can progress to cirrhosis and hepatocellular carcinoma. This review provides brief answers to common questions clinicians may have about NASH. The diagnosis of NASH currently requires a liver biopsy, although non-invasive tests are being evaluated and may supplant liver biopsy in the near future. Treatment is focused on lifestyle modifications, with new medications currently in clinical trials.

What differentiates nonalcoholic fatty liver (NAFL) from nonalcoholic steatohepatitis (NASH)?

Nonalcoholic fatty liver disease (NAFLD) is characterized by macrovesicular hepatic fat accumulation in ≥ 5% of hepatocytes in those patients who do not have a secondary cause of steatosis (e.g. alcohol consumption, genotype 3 hepatitis C, medications, protein malnutrition, parenteral nutrition). NAFLD is a spectrum ranging from nonalcoholic fatty liver (NAFL) which includes hepatic steatosis without substantial inflammation or hepatocellular injury, to nonalcoholic steatohepatitis (NASH) which is characterized by steatosis, inflammation and evidence of hepatocellular injury in a characteristic pattern. Both can progress to advanced fibrosis and cirrhosis, but the risk of progression is much greater in patients with NASH compared to NAFL.

Why is it important to distinguish between NAFL and NASH?

NASH, unlike NAFL, has the greatest potential to progress to cirrhosis, liver failure, and liver cancer. A multitude of studies have shown that progression of fibrosis is associated with decreased survival.[1] Differentiating between the two allows for earlier lifestyle changes, medical interventions, cancer screening, and overall improved outcomes.

What factors help identify the patients with NAFLD who are at greatest risk for progression to cirrhosis?

Identifying factors that place patients with NAFLD at risk for progression to cirrhosis is important for determining potential therapeutic interventions.[1] Studies have shown that liver fibrosis, hepatocyte ballooning, and portal inflammation (but surprisingly not the amount of steatosis) correlate with reduced survival.[2] A recent meta-analysis not only identified fibrosis as an independent risk factor for liver-related mortality, but also demonstrated an exponential increase in liver related mortality with worsening fibrosis stage.[3] These data highlights the importance of targeting fibrosis in the treatment of NAFLD, as well as targeting NASH, the driver of that fibrosis.

What is the prevalence of NAFLD and NASH?

Over the past few decades, the rate of NAFLD has been on the rise. This increase parallels the overall trend of increasing obesity and metabolic syndrome, particularly in developed nations. The prevalence of NAFLD is often underestimated, given that patients are typically asymptomatic until they progress to decompensated cirrhosis. Several studies have examined the epidemiology of NAFLD, and often, a wide range of prevalence rates has been found. This variation is partly related to the criteria used to establish a diagnosis (e.g. elevation in liver enzymes, imaging, histology). Younossi et al. studied the global prevalence and incidence of fatty liver disease spanning 26 years, encompassing 22 countries, and including approximately 8.5 million individuals.[4] They estimate that approximately 25% of the adult population worldwide has NAFLD, with the highest prevalence rates in South America (31%) and the Middle East (32%) compared to the lowest rate in Africa (14%).[4] The prevalence of NASH in adults has been approximated to be 1.5% - 6.45%.[4] Furthermore, NASH is a major cause of chronic liver disease in children, even progressing to cirrhosis in teenagers.[5] Comparing years 1999-2002 to 2009-2012, Kabbany et al reported a 2-2.5-fold increase in the prevalence of NASH cirrhosis and NAFLD-associated advanced fibrosis.[6] In light of the rising rate of NAFLD, it is not surprising that the percentage of patients with NASH cirrhosis on the liver transplant list has also increased.[7]

What is the burden of NAFLD on healthcare costs?

Cirrhosis with subsequent decompensation results in frequent hospital admissions and ultimately the need for liver transplantation, although many patients with NASH cirrhosis may not be transplant candidates due to co-existing obesity and cardiovascular complications. The percentage of patients with NASH cirrhosis listed for liver transplantation has been rising and will soon surpass hepatitis C. This reversal is due to a decrease in liver transplants in the latter group which is partly related to new highly efficacious direct acting antiviral therapies for chronic hepatitis C.[7] In the coming decade, NAFLD is projected to be the leading indication for liver transplantation.[8] This change has resulted in NAFLD patients becoming major contributors to increasing healthcare costs. The 64 million people with NAFLD in the United States have been estimated to contribute $103 billion to direct medical costs annually.[9] Similarly, four European nations (Germany, France, Italy, and United Kingdom) are estimated to have 52 million patients with NAFLD with annual combined health care costs of £35 billion.[9]

What conditions have been associated with NAFLD?

Patients with nonalcoholic fatty liver disease are often obese. They typically have some, if not all, of the other components of metabolic syndrome including insulin resistance, type 2 diabetes mellitus, hypertension, and dyslipidemia. This places patients with NAFLD at an increased risk of cardiovascular disease and its associated complications. Even without metabolic syndrome, NAFLD is an independent risk factor for cardiovascular disease.[10] In fact, cardiovascular disease is the leading cause of death in people with NAFLD. Established conditions associated with NAFLD include hepatocellular carcinoma (including in non-cirrhotic patients), extrahepatic tumors (e.g. colorectal cancer) and osteoporosis.[10, 11] There have also been associations between NAFLD and sleep apnea, psoriasis, endocrinopathies, and polycystic ovary syndrome independent of obesity.[5] The importance of recognizing these associations is that it provides clinicians the opportunity to screen patients with NAFLD for these conditions and provide early medical management to reduce morbidity and mortality in this population.

Which patients with NAFLD are at an increased risk for hepatocellular carcinoma?

It has been well established that cirrhosis is a significant risk factor for the development of hepatocellular carcinoma (HCC). A recent study of US veterans has also shown that NAFLD, in the absence of cirrhosis, also confers an increased risk of HCC.[12] Mittal et al concluded that non-cirrhotic NAFLD patients developed HCC more frequently compared to non-cirrhotic patients with other etiologies for their chronic liver disease.[12] Although this data begs the question of whether the criteria for HCC screening should be expanded to include NAFLD patient without cirrhosis, current guidelines recommend screening only those patients with cirrhosis.[5]

How are NAFLD and NASH diagnosed?

Patients with NAFLD are often asymptomatic until they develop signs or symptoms of decompensated cirrhosis. Often it is incidental elevation in serum aminotransferases (ALT and AST) or incidental steatosis on imaging that clue clinicians to the possibility of NAFLD. Persistently elevated aminotransferases can be associated with an increased risk of disease progression. However, even with normal aminotransferases, those patients with metabolic syndrome who are found to have steatosis on imaging are at increased risk for nonalcoholic

steatohepatitis.[5] Up to 30-60% of biopsy-proven NASH patients can have a normal ALT, and it is only through histology that one can distinguish steatohepatitis from steatosis.[13] Although biopsy is the gold standard to delineate among the spectrum of NAFLDs, it is associated with higher costs, increased risk of complications, and sampling error. These hurdles have inspired researchers to seek non-invasive means of assessing hepatic steatosis and hepatic fibrosis.

Ultrasound (US), computerized tomography (CT) and magnetic resonance imaging (MRI) have been used to assess patients for steatosis. US has 93% sensitivity in diagnosing steatosis when hepatic fat accumulation is greater than 33%, but the sensitivity decreases when hepatic fat accumulation is less than 30%.[14, 15] In contrast, MRI is able to detect steatosis greater than 5.56% nearly 100% of the time.[16] CT is also sensitive for detecting liver fat in which the liver appears lower in density than the spleen or paraspinal muscles, but it is not used routinely for this purpose because of the radiation exposure. A significant limitation of imaging studies is their inability to distinguish steatosis from steatohepatitis or detect early stages of liver fibrosis.

Noninvasive assessments of advanced fibrosis currently available include clinical scoring systems (e.g. NAFLD fibrosis score [NFS], Fibrosis-4 index [FIB-4]), imaging techniques (vibration controlled transient elastography [VCTE], MR elastography [MRE]), and biomarkers (e.g. enhanced liver fibrosis [ELF] panel, FibroTest). Of all the risk scoring systems available, NFS (calculated based on age, BMI, hyperglycemia, platelet count, albumin, and AST/ALT ratio) and FIB-4 (an algorithm based on age, platelet count, AST, and ALT) have been shown to be as reasonable at predicting advanced fibrosis as MR is elastography when compared to biopsy-proven NAFLD.[17] VCTE (FibroScan) is a noninvasive measure of liver stiffness used for assessing liver fibrosis. When comparing the two modalities, MRE was better than VCTE at identifying fibrosis stage 2 and above, however, both were equally as effective at detecting fibrosis stage 3 or above.[17] One emerging option is to combine the results of Fibroscan and the FIB-4 index to identify patients needing further evaluation. The ELF panel (comprised of hyaluronic acid, tissue inhibitor of metalloproteinase 1, and N-terminal procollagen III-peptide) has also been shown to have 80% sensitivity and 90% specificity for detecting advanced fibrosis, but it is not available in the United States.[18]

When is a liver biopsy the next step in the evaluation of patients with NAFLD?

Despite the advances in noninvasive methods of assessing steatosis and fibrosis, there are instances when a biopsy is necessary. Liver biopsy is considered in those patients in whom competing etiologies of chronic liver disease (e.g. autoimmune hepatitis, Wilsons, hemochromatosis) cannot be excluded, when noninvasive imaging studies are equivocal, and in those patients who are at increased risk of having steatosis and/or advanced fibrosis (e.g. patients with metabolic syndrome, high NFS or FIB-4 score, or increased liver stiffness measured by MRE or VCTE).[5]

Are there any genetic associations with NAFLD?

There have been genome-wide association studies to identify genetic links found in NAFLD. These studies have elucidated associations between genetic polymorphisms, notably PNPLA-3, and NAFLD.[19] An allele in PNPLA3 has been strongly associated with increased hepatic fat content and inflammation; this allele is most common in Hispanics, the ethnic group with the highest prevalence of NAFLD.[19] However, it will be some time before these genetic associations will be applicable in routine clinical settings. Nonetheless, patients with first degree relatives with advanced NASH should be followed with a higher index of suspicion.

What is the treatment for NAFLD?

The role of treatment approaches currently available and those being studied in clinical trials is shown in Figure 1. The cornerstone of NAFLD management consists of healthy eating habits and regular exercise.[5] Weight loss alone has been shown to decrease histologic features of NASH and induce regression of fibrosis with greatest improvement occurring after 10% weight reduction has been attained.[20] Decreasing daily caloric intake by 500-1000 kcal is an effective method for achieving weight loss, but it is often challenging to maintain this lifestyle modification.[20] Various diets have also been researched, and studies show that the content of the diet may play a role in the treatment of NAFLD independent of weight loss. A recent randomized controlled trial found that a Mediterranean diet aids in the reduction of fat accumulation and liver stiffness in addition to improving insulin sensitivity.[21] Exercise has also been shown to reduce fat accumulation in the liver as well as reduce aminotransferase levels; however, its effect on liver histology remains to be fully established.[22] Nonetheless, exercise provides multiple other benefits including improved cardiovascular health and reduced peripheral, adipose, and hepatic insulin resistance independent of weight loss.[13] Studies suggest that specifically aerobic exercise reduces more intrahepatic fat content compared to resistance exercise, however, further investigation is required to determine the specifics regarding exercise and its impact in the treatment of NAFLD.[22] Although there are no randomized controlled trials evaluating bariatric surgery in patients with NAFLD, cohort studies that have shown

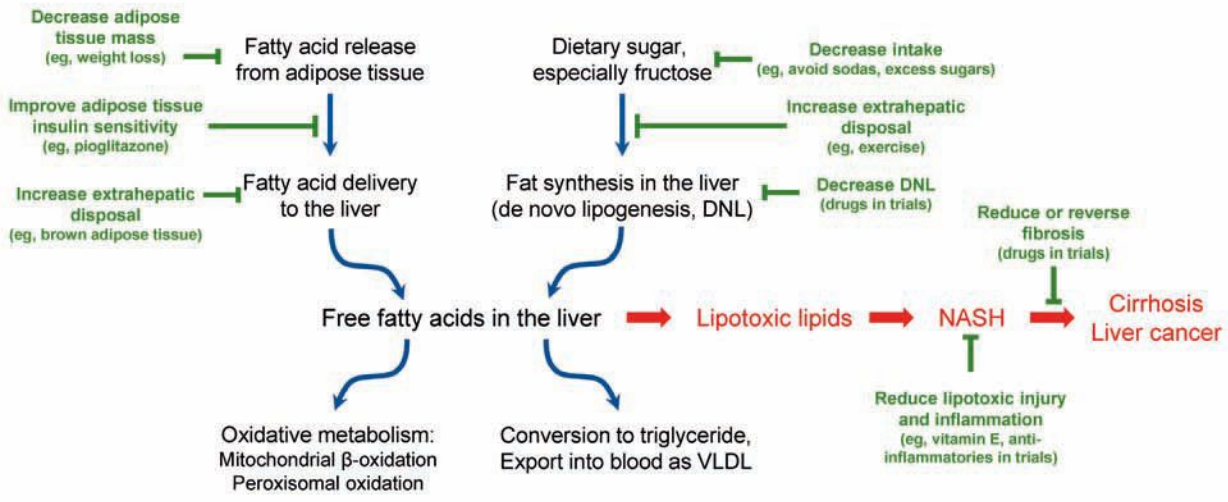


Figure. NASH develops in the setting of excess fat being transported to the liver or being produced in the liver, in conjunction with limitations on the capacity of the liver to oxidize fat or return it to the circulation as very low density lipoprotein (VLDL). Dietary factors such as fructose and glucose consumption contribute to this process. The role of genetics, epigenetic changes, and other modifying factors, such as the gut microbiome, are currently being explored in research studies. Multiple treatment options that target differents steps of these pathways are undergoing evaluation in clinical trials. Reducing caloric intake, especially from carbohydrates, and increasing disposal through regular aerobic exercise remain the primary treatment recommendations.

improvement in steatohepatitis following bariatric surgery, which suggests that surgery may be a reasonable option in a subset of NAFLD patients.[23]

Are there any pharmacologic agents recommended for the treatment of NAFLD?

In addition to lifestyle modification, pharmacologic agents for the management of NAFLD have been explored. Currently, there are no medications approved for the treatment of NAFLD, but studies have identified subgroups of NASH patients who may benefit from vitamin E or pioglitazone. In a randomized controlled trial, both vitamin E and pioglitazone were shown to significantly improve nonalcoholic steatohepatitis in non-diabetic patients.[24] A recent trial also demonstrated improvement in steatohepatitis and fibrosis in diabetic patients who took pioglitazone.[25] These findings have influenced current AASLD guidelines, which recommend considering treatment with vitamin E in non-diabetics and pioglitazone in patients with biopsy confirmed NASH.[5] Additionally, obeticholic acid (an FXR ligand), elafibranor (a PPARγ/PPARδ ligand), selonsertib (an ASK-1 inhibitor) and cenicriviroc (a chemokine receptor 2 and 5 inhibitor) are currently in phase 3 trials as potential therapies for NASH.

Are statins safe for the treatment of dyslipidemia in patients with NAFLD?

Cardiovascular disease is common in patients with NAFLD, and it accounts for twice as many deaths as those that occur by liver-related causes.[13] It is vital for health care providers to remain vigilant regarding the recognition and early management of cardiovascular risk factors that place NAFLD patients at highest risk of morbidity and mortality. Despite the overwhelming benefit of statins in cardiovascular disease, physicians have been hesitant to utilize these medications in their NAFLD patients given concerns for potential hepatotoxicity. Studies have confirmed the safety of statin use in NAFLD patients; furthermore, there is no proof that pre-existing liver disease is a reason to avoid statins to reduce cardiovascular disease risks.[26] There is no clear evidence that statins result in improvement in the underlying liver disease itself but statins should certainly be considered for cardiovascular risk reduction.

What are the concerns regarding tamoxifen use in the development and progression of NAFLD?

Multiple medications have been identified as steatogenic with the potential to cause or worsen nonalcoholic fatty liver disease. Tamoxifen is an anti-estrogen medication frequently used as adjuvant therapy in patients with estrogen receptor positive breast cancer. Studies have demonstrated that NAFLD develops in 30-50% of patients treated with tamoxifen.[27] A small proportion of these patients, especially those with metabolic syndrome, have the potential to progress to NASH.[28] Tamoxifen is thought to cause NAFLD by inhibiting mitochondrial beta-oxidation of fatty acids and

suppressing estrogen synthesis.[27] It is important for health care providers to understand the association between tamoxifen and NAFLD when considering treatment options for estrogen receptor positive breast cancer, especially in patients who also have some or all of the components of metabolic syndrome.

Summary

NASH has emerged as a common cause of chronic liver disease, cirrhosis and hepatocellular carcinoma. Identifying patients with NASH has historically required a liver biopsy, although non-invasive markers may soon be validated as diagnostic tools which may be used in the management of these patients. Current treatment is focused on healthy eating habits, exercise, and weight loss. Vitamin E and pioglitazone may play a role in the treatment of selected patients. Multiple new drugs being evaluated in ongoing clinical trials may be available in the next 2-5 years. NASH is a complex disease that likely results from a combination of environmental and genetic factors that may vary among different patients. Thus, treatment in the future will likely be personalized to each patient based on their risk factors.

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Disclosure

None reported.

MM

Pancreatic Adenocarcinoma

by Ashley A. Vareedayah, MD, Samer Alkaade, MD & Jason R. Taylor, MD

Pancreatic cancer remains a devastating diagnosis and the management of patients is facilitated by the coordinated efforts of specialists in gastroenterology, radiology, oncology, and oncologic surgery.







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Abstract

Pancreatic cancer is a common gastrointestinal malignancy, and is often associated with a poor prognosis. Challenges to effective screening for pancreatic cancer include low disease prevalence and high cost of screening modalities such as endoscopic ultrasound and cross-sectional imaging. Further, most patients are asymptomatic during the early course of disease, which often leads to delay in diagnosis. Treatment options include surgery, chemotherapy, and palliative care.

Introduction

Pancreatic cancer is the second most common gastrointestinal malignancy in the United States. Approximately 53,000 people will be diagnosed with pancreatic cancer this year.[1]

Interestingly, it is more common in African-Americans, slightly more common in men, and is usually a disease of older adults.[1] Despite its relative low incidence compared to other more common malignancies (prostate, lung, colorectal, etc), pancreatic cancer represents the fourth leading cause of death in men and women. Cigarette smoking appears to be one of the strongest risk factors, and is likely associated with as many as one quarter of all pancreatic tumors.[2] Diabetes mellitus is also suspected to play a role in the development of pancreatic cancer, though the precise mechanism by which this occurs is not clearly established.[3] Patients with type 2 diabetes often have years or decades of insulin resistance with compensatory hyperinsulinemia. The mitogenic properties of insulin may explain the association between type 2 diabetes and many types of malignancy. Other known risk factors for pancreatic cancer include alcohol use, obesity, and various genetic syndromes, although these account for less than 10% of all pancreatic cancer. Concomitant risk factors are felt to be synergistic.[2]

In general, the prognosis for pancreatic cancer is poor. The overall one- and five-year mortality rates are 24% and 6%, respectively.[1] Approximately 80% of patients have regional spread or metastatic disease at the time of diagnosis. This highlights the need for improved screening modalities, early detection, accurate pre-operative staging, and improved treatment options.

Pancreatic Adenocarcinoma

The term "pancreatic cancer" is typically used to refer to pancreatic adenocarcinoma. There are other types of pancreatic cancer, but this review will focus on discussion of pancreatic adenocarcinoma. More than 95% of malignant neoplasms of the pancreas arise from the exocrine portions of the gland (ductal and acinar cells), and demonstrate features consistent with adenocarcinoma.[4]

Patients with pancreatic cancer who have two first-degree relatives

with a history of pancreatic cancer meet criteria for familial pancreatic cancer.[5] Though hereditary causes account for only approximately one tenth of pancreatic cancers, it is important to identify those patients with higher risk due to genetic mutations early in order to determine appropriate screening and surveillance strategies. Patients with BRCA2 gene mutations account for the highest proportion of known causes of inherited pancreatic cancer.[6] Another common etiology of hereditary pancreatitis is an autosomal dominant mutation of the *PRSS1* gene on chromosome 7.[7] The cumulative risk for development of pancreatic cancer in these patients by age 75 is greater than 50%.[7] Other genetic syndromes associated with elevated risk of pancreatic cancer include Peutz-Jeghers syndrome (*STK11* gene mutation), familial atypical mole-malignant melanoma (FAMMM) syndrome (germline mutation in the *P16* gene), hereditary nonpolyposis colorectal cancer (mutations in *MLH1, MSH2*, *MSH6*, *PMS2*, or the *EPCAM* gene), and mutations in *PALB2*.[8]

Challenges to effective screening for pancreatic cancer include low disease prevalence and cost of screening modalities such as endoscopic ultrasound and cross-sectional imaging. Current medical practice relies on family history as the primary assessment of risk for pancreatic cancer.

Patients who carry a known genetic mutation that increases risk for pancreatic cancer and have a family history (as above) that meets criteria for pancreatic cancer screening should be enrolled in a screening program. This includes endoscopic ultrasound and/or magnetic resonance cholangiopancreatography (MRCP), though there is no consensus regarding initiation of screening. Those who meet criteria should be screened every 6 months with MRI or EUS on an alternating schedule. Many practitioners start screening at age 40-50 in accordance with recommendations by the CAPS consortium.[5] However, the American Gastroenterological Association (AGA) recommends screening patients with hereditary pancreatitis at age 35, and in other familial pancreatic cancer syndromes, 10 years prior to the age of the index case.[9]

Autopsy data show that approximately 60-70% of tumors are located in the head of the pancreas, 5-10% in the body, and 10-15% in the tail.[10] At diagnosis, the average size of pancreatic cancers located in the head of the pancreas is approximately 3 cm, while those in the body or tail are approximately 6 cm. This is explained by the earlier development of signs and symptoms in proximal tumors related to obstruction of the common bile duct and pancreatic duct. Distal cancers in the body and tail of the pancreas have a higher propensity for extra-pancreatic extension into retroperitoneal tissues, and vasculature such as the portal vein and superior mesenteric artery and vein. Other sites of invasion with extra-pancreatic extension include the spleen, stomach, colon (transverse colon or splenic flexure), and the left adrenal gland. In more advanced disease, common sites of distant metastases include lymph nodes, liver, and peritoneum. Less common sites of metastases are lung and bone.[2]

Common Presentation

Unfortunately, most patients do not note symptoms during the early course of their disease, which often delays diagnosis. Jaundice is one of the main presenting symptoms, especially with pancreatic head tumors. Some patients present with pancreatic exocrine insufficiency, which can manifest as a wide spectrum of symptoms, including steatorrhea (fatty, frothy, loose, greasy, foul-smelling stools), malabsorption, weight loss, abdominal discomfort, and abdominal bloating. Yet others can present with dull, nonspecific pain, which usually occurs as a result of tumor invasion of celiac or superior mesenteric arterial plexus. Other common clinical manifestations of pancreatic cancer include nausea, anorexia, weight loss, and new-onset diabetes mellitus.

Diagnosis

Routine lab tests are usually non-specific, though elevated liver tests may suggest biliary obstruction. Serum amylase and lipase levels are occasionally elevated.

Serum markers have some utility in the evaluation of pancreatic cancer, though they are not routinely used for screening purposes. Cancer-associated antigen 19-9 (CA 19) is the most well-known and likely the most useful. It serves as an adjunct in diagnosis, and in monitoring response to treatment.[11, 12] However, it should be noted that false-positive results (high values of CA 19-9 in the absence of malignancy) can be seen with cholestasis related to non-malignant obstruction (ie choledocholithiasis, cholangitis, and chronic pancreatitis.[13]

Radiologic Imaging

Though many patients presenting with jaundice often undergo trans-abdominal ultrasound as part of the initial evaluation for jaundice, MRI of the pancreas (with

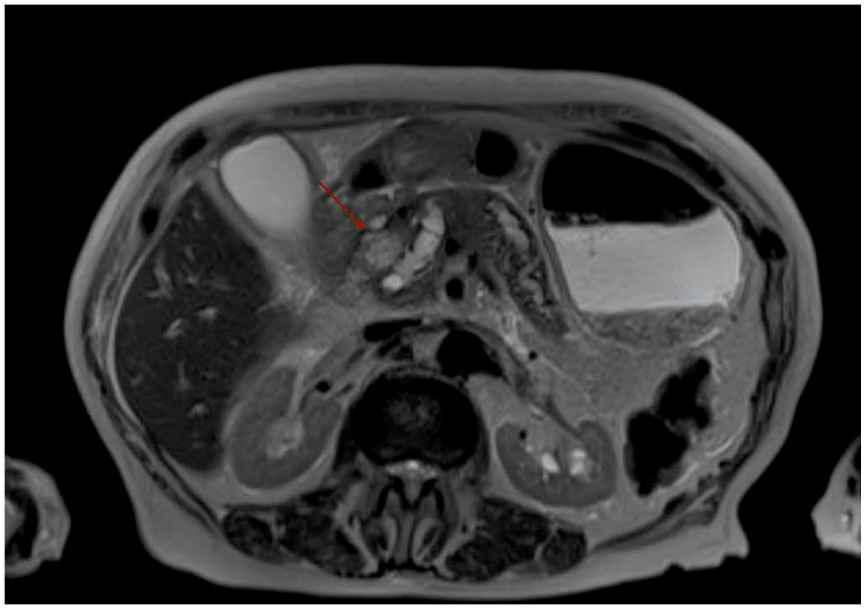


Figure 1. MRI abdomen showing pancreatic head mass (red arrow). Adjacent to the mass is a dilated pancreatic duct.

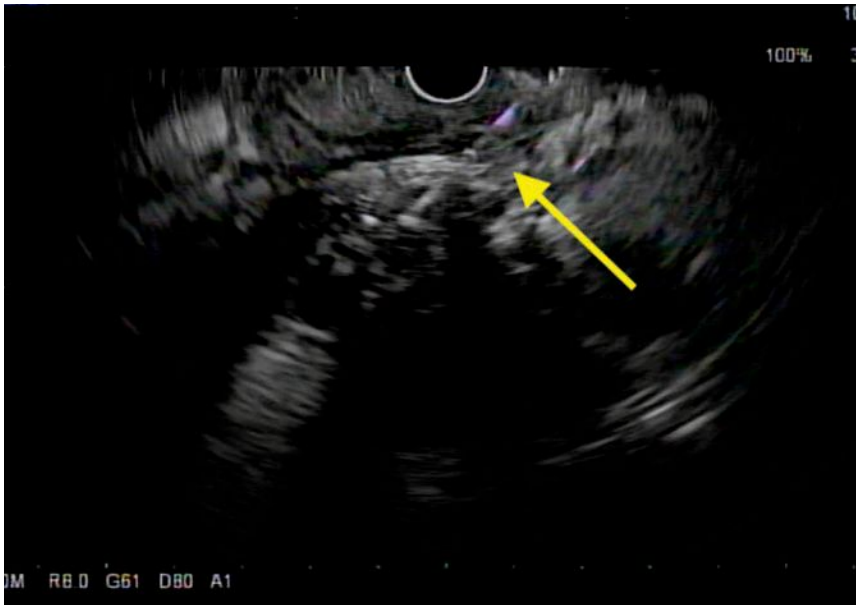


Figure 2. EUS-guided fine-needle aspiration with a 22-gauge needle (yellow arrow points to the needle) of the same pancreatic head tumor via transduodenal approach. The tip of the needle is seen inside the mass.

MRCP) or CT of the pancreas (pancreatic protocol CT) are the preferred radiologic modalities to identify and help stage pancreatic cancer, with MRI being preferred to CT (Figure 1).

CT is associated with a high degree of accuracy in defining unresectable pancreatic cancer, for which the criteria is met with any one of the following: distant metastases (liver, peritoneum, etc), and certain arterial/vascular involvement (celiac axis or superior mesenteric artery, or occlusion of the portal vein or superior mesenteric vein) which may be institution-specific.[14] Advantages of magnetic resonance imaging (with MRCP) include lack of radiation and iodine-free contrast. Cost and limited availability are the main limitations to MRI/MRCP.[15]

Positron emission tomography (PET) combined with CT is not useful as a primary diagnostic imaging study for pancreatic cancer due to lack of anatomic detail. However, PET/CT may be useful in assessing tumor recurrence after resection, or after neoadjuvant chemotherapy, and can be helpful in identifying sites of distant metastases.

Endoscopic Imaging

Endoscopic ultrasound (EUS) is felt to be the most accurate test for the diagnosis of pancreatic cancer.[16] It has been shown to have a higher sensitivity and specificity

Table 1. TNM Pancreatic Cancer Staging (American Joint Committee on Cancer.)

Stage	Definition
Primary Tumor (T)	
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*
T1	Tumor limited to pancreas, ≤ 2cm
T2	Tumor limited to pancreas, ≥ 2cm
T3	Extension into peri-pancreatic tissues (excluding arteries)
T4	Tumor involves celiac axis or superior mesenteric artery
Regional lymph nodes (N)	
Nx	Regional lymph nodes not assessed
N0	No metastatic regional lymph nodes
N1	Metastatic regional lymph nodes
Distant metastases (M)	
M0	No distant metastatic disease
M1	Distant metastatic disease

American Joint Committee on Cancer (AJCC) TNM staging system, September 6, 2013. American Cancer Society. Available at http://www.cancer.org/cancer/pancreaticcancer/detailedguide/pancreatic-cancer-staging. April 5, 2016; Accessed November 28, 2017.

for detecting pancreatic masses than CT, although there have been no prospective head-to-head studies comparing the two modalities.[16] The ability to add fine needle aspiration (FNA) cytology to EUS increases the specificity of detecting pancreatic cancer, compared to imaging studies (Figure 2).

The caveat, however, is that EUS has a high level of operator dependence, and requires significant experience. Therefore, this study is best when performed at a high volume center.[17]

Endoscopic retrograde cholangiopancreatography (ERCP) allows for radiographic visualization of the biliary and pancreatic ducts via X-ray. However, ERCP should be reserved for therapeutic treatment of ductal obstruction and not used as the sole tool to evaluate for pancreatic cancer. ERCP does allow for tissue sampling as well as interventions such as biliary or pancreatic stenting, if necessary.[15, 18] A "double duct" sign, which represents simultaneous dilatation of the common bile duct and pancreatic duct due to obstruction, is a worrisome finding seen on ERCP (and on imaging studies such as CT or MRI) as it can represent obstruction due to pancreatic cancer. When this "double duct" sign is seen, it is of paramount importance to evaluate for pancreatic cancer before being complacent with other diagnostic possibilities.

Staging of Pancreatic Cancer

The American Joint Committee on Cancer (AJCC) staging system was recently revised in July 2017, and is shown in Table 1.[19]

Once the diagnosis of pancreatic cancer has been made, staging can include CT or MRI of the chest, abdomen, and pelvis with IV contrast. EUS is also very important not only for tissue acquisition for diagnosis, but for staging as well.

With staging, patients are often placed into one of four distinct groups, which determines treatment plan. Patients in the first group are those with stage 1 (clearly resectable) disease, and should be referred as soon as possible to a surgeon, to determine if they are candidates for resection based on other medical comorbidities. The second group includes those with "borderline resectable" disease; these patients are more likely to derive benefit from neoadjuvant chemoradiation. Third, we include those with locally advanced disease, without metastases, but are still unresectable. These patients may be candidates for neoadjuvant chemoradiation, and potentially surgery after successful downstaging. The fourth and final group is comprised of patients with metastatic disease, who do not benefit from surgical resection. Treatment for this group of patients includes chemotherapy and palliative care.

Approximately 1 in 4 patients with CT-demonstrated localized pancreatic cancer are found to have metastatic disease at laparoscopy.[20, 21] As a result, staging diagnostic laparoscopy is recommended (to identify small lesions with visual inspection that may be missed on imaging studies) in most patients prior to surgical exploration.[6, 22]

Treatment Options

Surgery

Surgery is the only treatment modality for pancreatic cancer that is potentially curative.[23] Unfortunately, as mentioned above, only 15-20% of patients are candidates for pancreatectomy, due to the high proportion of advanced disease at presentation. An absolute contraindication to surgery is extra-pancreatic disease. Vascular involvement is a relative contraindication – in some cases, vascular resection and reconstruction are performed with good success.

Routine pre-operative ERCP and biliary duct stenting to relieve jaundice has not been shown to improve outcomes, and is not currently recommended in patients with resectable tumors.[24] Patients for whom pre-operative ERCP may be appropriate include those with an expected delay in surgery, and those receiving neoadjuvant therapy. In patients with comorbidities that preclude surgery, ERCP with biliary stenting (with expandable metal stents) is an excellent palliative option.

The most common surgical procedure for pancreatic cancer localized to the head or uncinate region or both is pancreaticoduodenectomy, commonly referred to as the Whipple procedure. This involves en bloc removal of the head of the pancreas and duodenum, distal common bile duct, and proximal jejunum. A pancreaticojejunal anastomosis is also established. The mortality rate with the Whipple procedure has improved significantly and is now less than 3% when performed at a center of excellence for pancreatic surgery.[25] Patients with tumors localized to the body and or tail who are surgical candidates typically undergo distal pancreatectomy and splenectomy.

Predictors of better outcomes after surgery include tumor size < 3 cm, lack of lymph node metastases, negative resection margins, well-differentiated tumors, and intra-operative blood loss of < 750 mL.[26]

Still, prognosis for pancreatic cancer remains poor, even after potentially curative surgery. The five-year survival rate after resection remains approximately 25%, similar to that of 30 years ago.[1]

Adjuvant and Neoadjuvant Therapy

Neoadjuvant therapy is defined as treatment (chemotherapy and/or radiation) administered prior to surgery. Potential benefits include early therapy to decrease the likelihood of distant disease and tumor downstaging to optimize surgical resection. One concern with neoadjuvant therapy is the possibility that during therapy, the cancer may progress from potentially resectable to unresectable terminal cancer. It should also be noted that neoadjuvant therapy protocols tend to be institution-specific.

Adjuvant therapy is defined as treatment administered after surgery, with the goal of preventing recurrence. Recurrence of pancreatic cancer typically manifests as distant metastatic disease, and isolated local tumor bed recurrence only occurs 10-15% of the time. Though current guidelines from the National Cancer Center Network recommend adjuvant therapy, its value has been questioned.[12]

Chemotherapy for metastatic disease is not curative. Further, the potential for toxic side effects is significant. Current recommendations for treatment of patients with metastatic disease include combination therapy with FOLFIRINOX (folinic acid, fluorouracil, irinotecan, oxaliplatin) or gemcitabine plus nab-paclitaxel or gemcitabine alone (based on the patient's performance status).[12] Response to treatment is assessed with serial imaging studies, serum markers (such as CA19-9), and changes in tumor-related symptoms.

Locally advanced pancreatic cancer may be treated with stereotactic body radiation therapy (SBRT), a form of radiation therapy that involves high-dose targeted radiation over a short time course – usually three to five days.[12] This usually requires EUS-guided placement of fiducial markers at the site of the tumor. Common treatment-related toxicities include fatigue, nausea, and less common risks are gastrointestinal bleeding and perforation.

A new ablation therapy for locally advanced pancreatic cancer is irreversible electroporation (IRE). It achieves soft tissue ablation with short (70 to 90 microseconds), high voltage (3,000 volts) pulses causing cell membrane perforation, electrolyte instability with disruption of cellular homeostasis, and apoptosis.[27] It is unique in that it does not cause coagulative necrosis, such as in radiation therapy, but immune-mediated cell death. A major advantage is that surrounding structures and vasculature are not injured.[27] Though not a standard-of-care practice at this time, with further research, IRE may serve as a useful adjunct in the optimal treatment of pancreatic cancer.

Palliative Care

Patients with unresectable disease often have significant jaundice and duodenal obstruction. These patients benefit greatly from either endoscopic biliary or duodenal stenting. Endoscopy is associated with a high success rate of palliation, as well as low procedure-related morbidity and mortality.

Pain in patients with unresectable pancreatic cancer can be difficult to manage. These patients should be referred for EUS-guided celiac plexus neurolysis given the high-success rate of 70-80% reduction in pain post-procedure.[28] Patients who are deemed non-treatment candidates or who do not wish to pursue treatment should be referred to hospice. Finally, several nonprofit organizations are useful resources for patients

with pancreatic cancer as well as for their families. One such organization is PANCAN, the Pancreatic Cancer Action Network.

Summary

- Pancreatic cancer is the second most common gastrointestinal malignancy in the United States, and carries a poor prognosis, with overall one- and five-year mortality rates of 24% and 6%, respectively.
- Risk factors include older age, cigarette smoking, type 2 diabetes mellitus, and various genetic syndromes.
- Endoscopic ultrasound (EUS) is felt to be the most accurate test for the diagnosis of pancreatic cancer. It has been shown to have a higher sensitivity and specificity for detecting pancreatic masses than CT.
- Patients with stage 1 disease should be referred promptly for evaluation for surgical resection, as surgery is the only treatment modality for pancreatic cancer that is potentially curative
- Surgery, chemotherapy, radiation therapy, and other modalities of treatment are best decided after discussions with the patient, at a high volume referral center with a multi-disciplinary approach.
- Patients with advanced disease should be referred for palliative chemotherapy and/or hospice.

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Disclosure

None reported. **MM**

Constipation: Evaluation and Management

by Bhairvi Jani, MD & Elizabeth Marsicano, MD

Constipation is a common and challenging complaint, but a systematic approach to evaluating patients with constipation can lead to effective treatments.





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Abstract

Constipation is defined as the infrequent passage of stools or difficulty with evacuation of stools. Constipation can be classified as primary or secondary, and primary constipation can be further divided into slow transit constipation or outlet obstruction. The diagnostic workup involves focused lab tests and structural evaluation, followed by a therapeutic trial of fiber and laxatives, and finally, specialized tests. Treatment can consist of dietary changes, medications, physical therapy, and possibly surgery in refractory cases.

Background

Constipation is defined as infrequent passage of stools or difficulty with evacuation of stools. It is associated with various symptoms including hard stools, straining, sensation of anorectal blockage, incomplete evacuation, abdominal discomfort and bloating.[1] The prevalence of constipation is 15% in the general population with a higher female to male ratio and a higher prevalence in the elderly especially over 65 years.[2, 3] This disease poses a great economic burden related to direct health care costs and indirect costs.[4]

Etiology

Causes of constipation can be divided into primary (slow transit or outlet obstruction) or secondary causes. Secondary causes can include simple dehydration or inadequate fluid intake, metabolic disturbances, medications, neurological disorders, myopathic disorders and structural abnormalities (Table 1).

When evaluating patients with constipation, secondary causes should be considered first and after secondary causes of constipation have been ruled out, the patient should be evaluated for primary or functional constipation. Risk factors for functional constipation include advanced age, low fiber diet, low socioeconomic status, immobility, abdominal or pelvic surgery and polypharmacy.[5-7]

Diagnosis of Functional Constipation

Since there are no specific tests to identify functional constipation, this diagnosis is based on criteria established by expert consensus called the Rome criteria.[8] These have been sequentially refined over time and the Rome IV criteria define functional constipation as fulfilling at least 2 of the 6 criteria listed in Table 2.

Functional constipation can be divided into 2 groups, slow transit constipation and outlet dysfunction.[8] Slow transit constipation refers to delayed passage of fecal contents through the colon and is more common in women. The exact pathophysiology of slow transit constipation is unknown, however, it appears to involve a number of underlying causes including

Table 1. Secondary Causes of Constipation

Secondary causes of constipation	
Metabolic disturbances	Diabetes, hypothyroidism, hypercalcemia, panhypopituitarism and pheochromocytoma.[30-32]
Medications	Analgesics like opioids and nonsteroidal anti-inflammatory agents, anticholinergics including antidepressants and antipsychotics, anti-hypertensives like calcium channel blockers, diuretics and iron supplementation.[32, 33]
Neurological disorders	Parkinson's disease, multiple sclerosis, dementia, Hirschprung's disease and spinal cord lesions.[32, 34]
Myopathic diseases	Scleroderma, myotonic dystrophy and amyloidosis.[32, 35]
Structural disorders	Colon cancer, strictures and a large rectocele.[36]

Table 2. ROME IV Criteria

ROME IV criteria for functional constipation (must have at least 2 of 6):
• Fewer than 3 bowel movements per week
• Straining during >25% of the time
• Lumpy or hard stools > 25% of the time
• Sensation of anorectal obstruction > 25% of the time
• Sensation of incomplete evacuation > 25% of the time
• Manual maneuvers required to aid defecation > 25% of the time
In addition to the above, the following three criteria should also be met to diagnose functional constipation: (1) Loose stools should rarely be present without the use of laxatives (2) Insufficient criteria for IBS (3) Present for at least 3 months during a period of 6 months.

alterations in colonic muscle or nerve activity, enteric neurotransmitters and loss of interstitial cells of Cajal. The interstitial cells of Cajal are electrically active cells believed to act as the pacemakers for the intestines.[7, 9]. Studies have also found that excess methane production by colonic bacteria may be responsible for slow transit in some patients.[10]

Opioid-induced constipation is one of the most common side effects of opioid analgesic use in patients with cancer and non-cancer pain or chronic opiate use for other reasons. It is a common cause of slow transit constipations, and is thought to arise from increased non-propulsive segmental motility and decreased propulsive peristalsis due to μ-opioid receptor activation. The μ-opioid receptors are expressed in the myenteric and submucosal plexuses of the enteric nervous system in the gastrointestinal tract.

Outlet dysfunction is characterized by impaired rectal evacuation from inadequate rectal propulsive forces or increased resistance to evacuation or both.[1, 8] Dyssynergic defecation is a form of outlet dysfunction and is defined by the inadequate relaxation or paradoxical contraction of the anorectal muscles while attempting to pass a bowel movement. Its pathophysiology is incompletely understood, however anxiety, psychological stress, and chronicity of constipation can contribute to the development of dyssynergic defecation.[8, 11]

Diagnosis

During evaluation of constipation, a careful history and physical examination should be conducted. Performing a complete digital rectal exam (DRE) is an important part of the clinical evaluation that includes squeeze and push maneuvers.[12] An overview of the diagnostic algorithm is shown in Figure 1.

After the initial history and physical examination, a set of focused tests should be obtained to assess disorders that are either treatable (like hypothyroidism) or important to diagnose early (like colon cancer). Guidelines agree that a complete blood cell count should be performed, however, further testing should be chosen based on history and physical.[13] Although metabolic tests (thyroid-stimulating hormone, serum glucose, creatinine, and calcium) are often performed when evaluating patients with constipation, their diagnostic utility and cost-effectiveness have not been demonstrated. A structural evaluation of the colon may be beneficial, especially if the patient has alarm symptoms (weight loss, abdominal pain and hematochezia), has abrupt onset of constipation or is older than the recommended screening age for colonoscopy and has not undergone previous screening for colorectal cancer.[1]

If this evaluation reveals a secondary cause for constipation, the appropriate treatment can be offered. The patient's medications should be adjusted when possible to limit those with constipating effects.

Those patients who do not respond to initial treatment with laxatives should undergo anorectal testing for evaluation of possible outlet dysfunction.[1] Anorectal manometry measures the rectal and anal pressure at rest and during attempted defecation (Figure 2). It is also able to assess rectal sensation, recto-anal reflexes and rectal compliance. During the maneuver, when a patient mimics defecation, or tries to bear down, there should be a rise in the rectal pressure along with relaxation of the internal

and external anal sphincters. The inability to relax the external anal sphincter and/or the puborectalis (Figure 2 is an example), along with inability to expel a 50cc water-filled balloon within one minute, is diagnostic of dyssynergic defecation.[14]

A balloon expulsion test can be done during anorectal manometry or as an independent test. It involves filling a balloon with 50cc of saline and asking the patient to expel it. Patients with normal defecation are able to expel the balloon within 1 minute. If the patient has difficulty expelling the balloon in this time frame, dyssynergic defecation should be suspected.[15]

After excluding outlet dysfunction with anorectal manometry and balloon expulsion, colonic transit should be evaluated using radiopaque markers (sitzmark study) or a wireless motility capsule.[16, 17] A sitzmark study can measure colonic transit time by administering 24 radiopaque markers and obtaining a plain abdominal x-ray on day 5. A prolonged colonic transit time is identified when there are more than 20% of the markers or more than 5 markers remaining in the colon on day 5.[16] The wireless motility capsule is a wireless capsule which measures pH, temperature and pressure throughout the entirety of the gastrointestinal tract, therefore providing gastric, small bowel and colonic transit time without radiation exposure. [17]Defecography and Magnetic Resonance Defecography are additional tests that can be obtained. These record the pelvic anatomy of the patient during attempted defecation and are useful for evaluating conditions like rectocele or sigmoidocele, intussusception, rectal prolapse, and megarectum.[8]

Treatment

Once secondary causes of constipation are excluded, patients should be advised to increase their fiber and fluid intake, engage in regular physical activity and conduct timed toilet training.[18]

Most patients with constipation require the use of laxatives at some point in their course. For chronic use, bulk laxatives (fiber) and polyethylene glycol 3350 ("PEG," e.g., Miralax) are tolerated best. Bulk laxatives include psyllium (Metamucil) and methylcellulose (Citrucel). Stimulant laxatives like senna and bisacodyl (Dulcolax) can produce excessive cramping and should therefore be used sparingly. Emollient stool softeners such as docusate (e.g., Colace) are best used for short-term prophylaxis, for example, in the post-operative setting.[19]

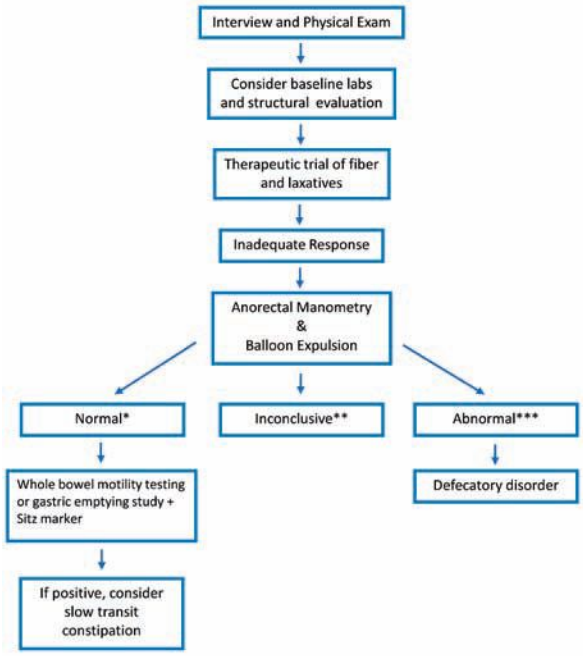


Figure 1. Diagnostic algorithm for constipation
*Normal or negative manometry study is normal balloon expulsion with no paradoxical contraction
**Inconclusive manometry is normal balloon expulsion and paradoxical contraction OR abnormal balloon expulsion and no paradoxical contraction
***Abnormal or positive manometry is abnormal balloon expulsion and paradoxical contraction

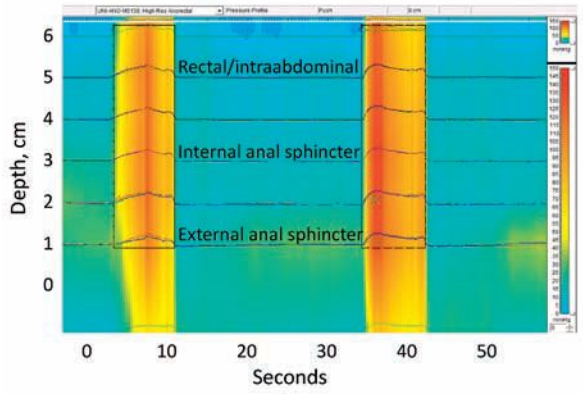


Figure 2. High resolution anorectal manometry. A catheter with multiple pressure transducers is introduced through the anal canal and into the rectum and provides real-time pressure measurements at the external anal sphincter, internal anal sphincter and within the rectum. The patient is asked to try to expel the catheter by increasing intraabdominal pressure and relaxing the external sphincter. As shown in this example, two attempts to expel the catheter (from 3 to 11 seconds and 34 to 42 seconds) resulted in appropriately increased intraabdominal pressure but dyssynergic contraction of the external sphincter and no relaxation of the internal sphincter. The color pressure scale is shown on the right from low pressure (blue) to high pressure (red).

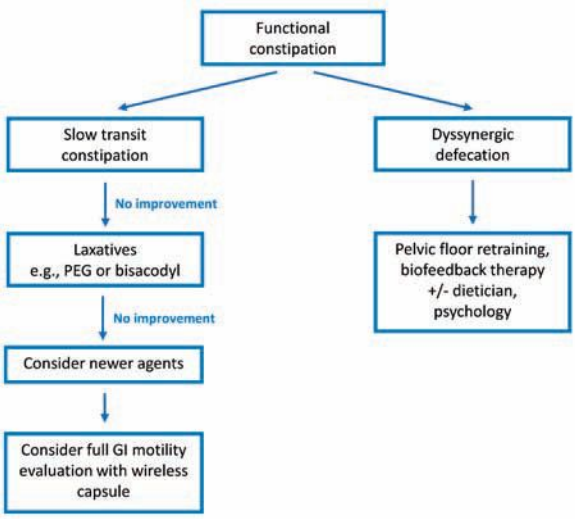


Figure 3. Treatment algorithm for functional constipation. Once secondary constipation has been excluded and functional constipation has been characterized, treatment can be focused on the underlying disorders.

Osmotic agents include polyethylene glycol (PEG)-based solutions, magnesium citrate–based products, sodium phosphate–based products (e.g., Fleets), and non-absorbable carbohydrates (e.g., sorbitol). These hypertonic products work by the osmotic effect, retaining water in the colon.

The PEG and electrolyte lavage solutions used for colonic cleansing before procedures are typically not used for chronic constipation and are iso-osmotic with plasma; bowel evacuation is achieved with these by high-volume lavage rather than an osmotic effect.[20]

Newer medications include lubiprostone, an agent that activates chloride channels much like the cholera toxin and increases luminal fluid secretion. It has been shown to decrease stool transit time and improve symptoms of chronic idiopathic constipation.[21] Linaclotide, a guanylin analog, works by stimulating the guanylyl cyclase-C receptor to increase chloride secretion like the enterotoxin from E. coli, and has been shown in studies to have neuromodulatory benefits in patients with IBS-C as well as decrease stool transit time.[22] Plecanatide is another agent that also stimulates the guanylyl cyclase inhibitor and causes increased chloride and bicarbonate entry into the lumen via the activation of the cystic fibrosis transmembrane conductance regulator (CFTR) ion channel. Tegaserod is a serotonin type 4 (5-HT4) receptor partial agonist that is thought to trigger a peristaltic reflex via 5-HT4 activation, which enhances motor activity and normalizes impaired GI motility.[23]

Colchicine, which is a cytotoxin used to treat gout, is not usually recommended for regular clinical use for constipation because of its side effect profile, particularly when renal function is impaired. However small studies have shown that it may be useful in a subset of patients with chronic constipation who are refractory to medical management.[24] Misoprostol is a prostaglandin E_1 analogue that increases intraluminal fluid and bicarbonate secretion, effects that have been exploited to reduce the severity of refractory chronic constipation in small studies.[25, 26]

For patients with functional outlet obstruction, biofeedback has been shown to be very helpful. Trials have demonstrated that biofeedback is extremely useful in patients with dyssynergia, and is superior to standard therapy alone.[27]

First-line treatment for opioid-induced constipation typically involves a combination of pharmacological and non-pharmacological interventions such as laxatives and increased dietary fiber. A more targeted pharmacological approach to the treatment of refractory opioid-induced constipation is the development of peripherally acting μ-opioid receptor antagonists (PAMORAs), which aim to reverse opioid-induced constipation by selectively blocking opioid actions at peripheral μ-opioid receptors, including those in the enteric nervous system, without affecting analgesia in the CNS.[28, 29] Drugs in this class currently approved for the treatment of opioid-induced constipation include naloxegol, methylnaltrexone, alvimopan and naldemidine. These agents should be avoided if bowel obstruction is suspected.

Surgical options, such as colectomy, should be a last resort for those patients who have failed medical management.

An algorithm for treatment decisions in functional constipation is shown in Figure 3.

Conclusion

Constipation is a very common complaint, especially in older adults, with a significant impact on healthcare costs. A careful history, physical examination and blood tests can help exclude secondary causes of constipation. Management of chronic constipation includes patient education, behavior modification, dietary changes, and laxative therapy.

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Disclosures

None reported. **MM**

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A Bridge to Nowhere? Challenging Outpatient Transitions of Care for Acute Pain Patients in the Opioid Epidemic Era

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Valiant efforts to promote responsible opioid prescribing are necessary to reverse the ill effects of the current epidemic.



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Abstract

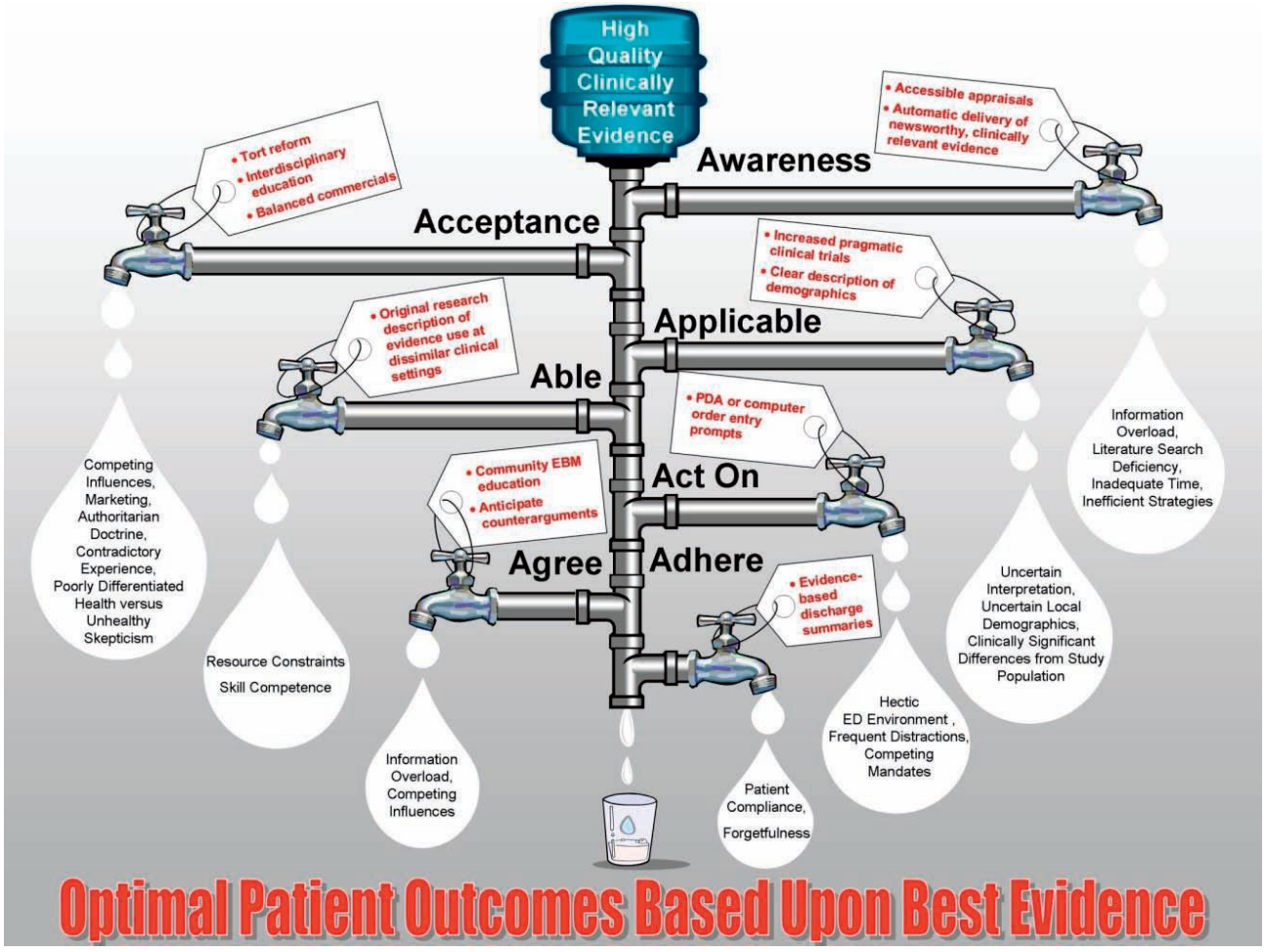
Opioid misuse is reducing Americans' life expectancy, thereby catalyzing professional societies and legislators to action. Efforts to combat the opioid epidemic must work hand-in-hand with appropriate efforts to reduce the severity and duration of suffering. Pharmacologic analgesia is temporizing. Current opioid prescribing guidelines focus on reducing the frequency and quantity of narcotics prescribed, but lack attention to alleviation of the source of pain. Conditions eliciting acute pain sometimes require additional specialist management following discharge from the emergency department. Patients frequently lack timely access to these specialists, particularly if underinsured. This essay explores acute dental pain, extremity fractures, and back pain as three common examples whereby complex healthcare systems must efficiently adapt in order to serve the dual objectives of reducing the risk of opioid-related adverse consequences and minimizing the duration of patient suffering.

Background

The United States (US) is in the midst of an epidemic confronting a 400% increase in opioid overdose deaths between 1999 and 2010.[1] For the first time since the 1960s, life expectancy in the US has decreased for two consecutive years, partially as a consequence of increasing opioid misuse.[2] The scope of this public health crisis motivated the Division of Emergency Medicine at Washington University in St. Louis to host an interdisciplinary health policy symposium in August 2017 in order to engage frontline healthcare providers, hospital administrators, addiction specialists, legislators, and afflicted families in proactive problem solving.[3] *Missouri Medicine* is supporting a series of essays stemming from that symposium. This inaugural essay explores the challenges of and opportunities for interdisciplinary improvement of patient-centric outpatient transitions of care for common subsets of acute pain patients from the emergency department (ED).

On average, the ED accounts for 47% of hospital-associated medical care delivered in the US with acute and acute-on-chronic pain as common precipitants for an ED encounter.[4] Pain is a subjective ailment and

Figure 1. The Knowledge Translation Pipeline (from Reference 3)



physical exam measures like vital signs do not correlate well with reported pain.[5] Two decades ago a constellation of events laid the foundation for the current opioid epidemic, including pain society lobbyists' support of Patient's Bill of Rights, poor quality data implying acceptably low risk of addiction,[6,7] aggressive and misleading pharmaceutical industry marketing,[8,9] and Centers for Medicare and Medicaid Services financial incentives based upon patient satisfaction with pain control.[10] A predictable consequence of this perfect storm was increased opioid prescribing in office-based and ED practices (277% and 275%, respectively) between 1996 and 2012.[11] Observational research suggests that 17% of discharged ED patients are prescribed opioids, most commonly for extremity fractures, back and abdominal pain, and dental issues.[12] Notably, significant variability exists between providers regarding opioid prescribing criteria. The risk for any patient to develop opioid use disorder is associated with the type and dose, frequency, and duration of the opioids prescribed.[13] ED providers generally prescribe only immediate-release formulations in small pill counts.[12]

An early response by specialty organizations, hospitals, and governments has been promotion of guidelines to encourage or legally restrict the quantity of opioid analgesics that providers prescribe. Two Philadelphia hospitals established ED guidelines dissuading discharge opioid prescriptions exceeding a seven-day supply and completely avoiding long acting narcotics, and a policy against refilling of opioid prescriptions. Their rate of opioid prescribing declined 23% between 2012 and 2014.[14] The Ohio Governor's Cabinet Opiate Action Team released prescribing guidelines in 2012 encouraging ED physicians to check the state's prescription drug monitoring program, prescribe less than four days' supply, and provide referral to primary care or pain specialists. While opioid prescribing diminished prior to introduction of the governor's report,

this trend accelerated to a 12% statewide reduction after the guideline's release.[15] Three Rhode Island hospitals of varying size implemented prescribing guidelines in 2013, noting a reduction in all three sites most pronounced among the higher baseline prescribers.[16] Nationally, the American College of Emergency Physicians provides analgesia prescribing clinical policy recommendations,[17] while federal legislation in the Comprehensive Addiction and Recovery Act proposes limiting opioid prescriptions to three days for acute pain without exception.[18] Some emergency providers view prescribing guidelines as a shield to justify limiting prescriptions at discharge with the added benefit of diverting problematic drug-seekers away from their ED.[19] On the other hand, patients report that ED providers rarely discuss opioid alternatives or the anticipated duration of pain.[20]

Astonishingly, the recommendations and effectiveness of these guidelines focus exclusively on prescribing. This disease-centric perspective neglects and fails to contemplate the patient viewpoint or priorities, including establishing a timely plan for definitive management of the underlying cause of pain in a fragmented healthcare system.[20] The public realizes that the ED is the only reliable 24/7/365 resource available to address immediate needs like pain. The vast majority of ED patients with acute pain desire definitive, permanent alleviation from suffering – the ED provides only temporary management. Many patients understand that analgesics provide temporizing, variable relief of pain and that opioids carry the risk of addiction.

Efforts to reduce opioid prescribing in acute pain scenarios will largely succeed or fail depending upon how well they incorporate implementation science principles, including alignment with patient priorities. The Knowledge Translation Pipeline (Figure 1) illustrates the "leaks" occurring at the physician-patient level before research evidence (prescribing guidelines) becomes routine practice. The first five leaks occur at the physician provider level including awareness of the new practice approach, acceptance of the superiority or non-inferiority of the recommended change, applicability to their setting and patients, and ability to do so with available resources. The last two leaks constitute patients and their families agreeing with the diagnosis and management plan and then adhering to the elements of that plan. If patients perceive an inadequate or unreliable pain management plan at the time of ED discharge, other pain remedies will be sought. For example, some patients will opt for supra-therapeutic dosing of over-the-counter medications like acetaminophen. Acetaminophen is already the leading cause of acute liver failure in the US with almost half of these overdoses unintentional.[21,22] Additionally, patients may purchase prescription narcotics illicitly with street drugs often adulterated with potent synthetic opioids increasing the risk of unintentional overdose.[23] Some frustrated and uncomfortable patients will predictably return to the same or another ED with persistent undertreated pain and no alternatives available in the days to weeks ahead. Ensuring timely post-ED access to care to the appropriate specialists for pain management must be included in prescribing guidelines to serve the dual aim of reducing opioid-prescribing related addiction risk and ensuring patient-centric alleviation of suffering. In the disjointed US healthcare system with priorities and motivating influences between hospital administrators, physicians, payers, and patients often misaligned, complex system thinking is paramount.[24] Definitive care for dental pain, extremity fractures, and acute-on-chronic back pain may require subspecialty management not only unavailable in the ED, but also unavailable to vulnerable patients for months after discharge from the ED, which is a significant and underreported obstacle to combating the opioid epidemic.

Toothache and Acute Dental Issues

Toothache is the fifth most common reason for an ED visit.[25] Many Americans lack dental insurance and do not receive adequate preventative dental care. This results in dental emergencies comprising 1% to 4.3% of all ED visits each year at an estimated cost of about $1 billion per year.[26,27] In choosing their initial site of care (dental clinic versus ED), patients may mistakenly assume that ED staffing includes a dentist. Providing toothache management recommendations with a list of nearby dental clinics reduces both ED return visits and opioid prescriptions.[28] Most dental care-related ED encounters (92%) do not include any other acute health issues, 94% are discharged from the ED, and 40% involve patients with no Medicare, Medicaid, or dental insurance.[27] ED visits for dental issues also likely reflects a degree of patient convenience as indicated by the finding that greater travel distances to the ED are associated with lower rates of ED use for dental care.[29] Ironically, an ED visit for a dental complaint is inversely associated with dental follow-up within six months, offering an opportunity for low-risk ED diversion programs for Medicaid patients if reasonably

rapid follow-up can be collaboratively developed with dentists in the community.[30]

Lacking dental training beyond the basics of acute tooth trauma or recognition of infectious maxillofacial conditions like Ludwig's angina[31] – yet compelled to display more empathy than "sorry, I can offer ibuprofen, acetaminophen, or nothing"[32] – ED providers sometimes prescribe antibiotics despite evidence of ineffectiveness as a substitute for opioid analgesics.[33] Alternatively, ED providers sometimes advocate for nerve blocks as a substitute for opioids. Unfortunately, nerve blocks only provide analgesia for a few hours, which may be inadequate if follow-up is delayed. Although emergency physicians may prescribe opioid analgesics for dental pain, non-opioid alternative are often effective. Extrapolating surgical extraction data to non-traumatic toothache patients, non-steroidal anti-inflammatory drugs (NSAIDs) achieve similar analgesia at a median of 30 minutes compared with acetaminophen/codeine and sustain relief for 17 hours longer than the opioid agent.[34] The effectiveness of codeine as an analgesic depends upon an individual's metabolism of codeine into the active molecule, so alternative opioids are considered more predictably effective. The combination of oxycodone and ibuprofen (5 mg and 400 mg, respectively) more effectively relieves dental pain at six hours than hydrocodone 7.5/acetaminophen 500 mg combinations.[35] However, dentists are also increasingly encouraged to select non-opioid management of acute odontalgia,[36] which may encourage some patients to seek opioid prescriptions from the ED despite access to a dentist. Mutual understanding between EDs and dental clinics regarding non-opioid analgesia recommendations and reasonable follow-up intervals will be required to prevent asynchronous messages to patients or further ED crowding by those seeking a second prescriber.

Dental insurance has historically been separate from medical insurance, despite the reality that oral health is associated with pain, social status, and overall well-being.[37] Opportunities to improve transitions of care between EDs and primary care clinics with definitive dental care confront daunting logistical and financial challenges. Community emergency dental clinics that rely on philanthropy and foundation support struggle to sustain care for indigent populations.[38] As primary care is redesigned for more conscientious opioid prescribing,[39] dental analgesia protocols need to adapt, including provision of timely access to dental care. Adaptive transition of care responses to simultaneously reduce opioid prescribing and alleviate the duration of patient suffering might include EDs or hospitals contracting with a dental clinic via mobile applications,[40] linking dentists' electronic medical records with EDs for free exchange of appointment availability and patient care plans, or substantial financial incentives for dentists providing timely access and definitive management for acute dental pain crises in economically vulnerable populations.[37]

Extremity Fractures

Alleviating acute fracture pain often requires appropriately compassionate opioid prescribing.[39] Post-ED fracture management usually involves orthopedic referrals, which are often challenging to obtain within weeks or even months of an ED encounter for underinsured patients. In addition, underinsured patients are sometimes referred from one hospital's ED to another neighboring ED despite the availability of orthopedic services at the initial ED. These "insurance transfers" increase the financial challenges to the receiving, often non-profit, hospitals. In addition, receiving hospitals also tend to be further away from the patient's home, which renders follow-up more challenging. In one Texas hospital estimated six month uncompensated orthopedic care for the receiving hospital was $1.7 million.[41] While the link between underinsured orthopedic transfers and opioid prescribing remains undefined, these transfers are likely associated with delays to timely analgesia in the ED, prolonged waiting times for all patients in the receiving ED, and delays to timely outpatient follow-up as the receiving hospital's orthopedic clinics seek to preferentially schedule insured patients and/or await Medicaid registration for referrals.[42,43] Transferring fracture patients from one orthopedic-capable hospital to another safety net hospital could be dissuaded by modifying the Disproportionate Share Hospital non-profit rule to disallow hospitals from including costs of transferred patients from public reimbursement claims or non-profit status.[41] While the Emergency Medical Treatment and Labor Act (EMTALA) was intended to reduce preventable transfers related to ability to pay, some modifications to EMTALA could improve this objective, including alignment of Medicaid reimbursements with Medicare and random audits for appropriateness of Medicaid transfers for uncomplicated fractures linked to penalties if acceptable thresholds are consistently breached.[44] Additional ED transition of care adaptations targeting the dual objective of reduced opioid prescribing

with timely outpatient orthopedic evaluation could include empowering ED case managers to schedule appropriate next day follow-up appointments in conjunction with shared decision making to align risks/benefits of different analgesic options with patient priorities while differentiating subjective pain from the philosophy of suffering.[45] Telecare also provides an opportunity for more timely orthopedic evaluation, though technology and payer barriers await resolution.[46]

Acute-on-Chronic Back Pain

Acute low back pain accounts for 3% of ED visits and represents the leading cause of disability under age 45 years.[47] Clinicians traditionally learned that low back pain is a self-limited problem with resolution within six weeks in 90% of patients regardless of analgesic prescribed or referral to physiotherapy, imaging, or specialist. Back pain as a generally self-limited problem now appears to be an oversimplification that may misinform patients and fuel disparities in timely analgesia.[48] Multiple recent systematic reviews highlight that two-thirds of acute non-specific low back pain patients report persistent and often disabling pain at one-year.[49,50]

Therefore, to affect and sustain reductions in opioid prescribing, both ED providers and primary care providers must learn to manage expectations rather than meet them. A tiered analgesic approach is worthwhile since both acetaminophen and NSAIDs compare favorably to morphine.[17,51] ED back pain patients should certainly be referred back to their primary care providers for re-evaluation to guide additional medical or sub-specialty referrals. However, many acute back pain patients have no identifiable primary care provider. Others present to the ED frustrated with their primary care provider, expressing misalignment between their understanding of back pain and the degree of relief obtained with their current opioid or non-opioid analgesic. Referrals to physiotherapy or Pain Medicine services from the ED might alleviate patient angst and accelerate recovery,[52] but insurers often refuse reimbursement for direct ED referrals whereas insurers pay for opioids which are easily obtained at the pharmacy. In addition, when back pain patients are already under the care of a pain medicine physician, ED providers frequently lack access for referral or discussion with that physician to help provide timely follow-up or non-opioid management recommendations. Telemedicine between the ED and Pain Medicine may provide one viable alternative to these barriers,[53] although simple accessibility by telephone might be equally effective. Another concept worthy of exploration is the "ambulatory pain physician" using anesthesiology as an in-person ED consultant to provide short- or long-term opioid and non-opioid options for back pain patients.[54]

Conclusion

Valiant efforts to promote responsible opioid prescribing are necessary to reverse the ill effects of the current epidemic. Decreased subscribing alone is inhumane and unethical with an imminent threat of swinging the pendulum from an emphasis on pain as a fifth vital sign with little concern for adverse effects of opioid analgesia to an illogical one-size fits all legislated rationing of effective analgesia without connecting patients to providers in a reasonably timely fashion. Successful patient-centric ED transitions of care for acutely painful conditions require a paradigm shift that engages emergency medicine, follow-up specialists and primary care providers, insurers, and patients.

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Disclosure

None reported.

MM

Not Salt But Sugar As Aetiological In Osteoporosis: A Review

by James J. DiNicolantonio, PharmD, Varshil Mehta, MBBS, Sojib Bin Zaman, MBBS & James H. O'Keefe, MD

The other ubiquitous white crystal, sugar, may lead to osteoporosis by increasing inflammation, hyperinsulinemia, increased renal acid load, reduced calcium intake, and increased urinary calcium excretion.





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Abstract

Salt has notoriously been blamed for causing an increase in the urinary excretion of calcium, and thus is a considered a risk factor for osteoporosis. However, the increase in the urinary excretion of calcium with higher sodium intakes can be offset by the increased intestinal absorption of dietary calcium. Thus, the overall calcium balance does not appear to be reduced with a higher sodium intake. However, the other ubiquitous white crystal, sugar, may lead to osteoporosis by increasing inflammation, hyperinsulinemia, increased renal acid load, reduced calcium intake, and increased urinary calcium excretion. Sugar, not salt, is the more likely white crystal to be a risk factor for osteoporosis when overconsumed.

Epidemiology of Osteoporosis

Osteoporosis is considered to be a major concern for the elderly population which is characterized by decreased bone mineral density or mineral content affecting both the measures of bone quantity and quality.[1] Reduction in the bone mass or its architectural disruption often results in an enhanced risk of fragility and fractures.[2]

Osteoporosis-related fractures are known to cause significant morbidity leading to a permanent disability in the elderly population which increases the economic burden on the health care system.[3] Moreover, osteoporosis is not only under-diagnosed but also, under-treated even among those who are at high-risk or who have had previous fractures. Osteoporosis not only leads to a decline in quality of life (QOL) but also the quality-adjusted-life-year (QALY).[4] Therefore, osteoporosis is regarded as an important worldwide public health concern and its prevalence is continuing to escalate, especially in women and the elderly. It is estimated that 200 million people are suffering from the negative consequences of osteoporosis globally.[5]

Approximately one quarter of men and half of women over 50 years of age will have an osteoporosis-related fracture in their lifetime. Indeed, 1.5 million fractures are reported annually due to osteoporosis related causes which includes 0.25 million wrist fractures, 0.3 million hip fractures, more than 0.3 million fractures at other body sites, and 0.7 million vertebral fractures.[6] These fractures are associated with substantial pain, morbidity, and even mortality. Furthermore, a global increase in longevity has lead to a significant rise in the proportion of the population who are at risk for osteoporisis.[7]

While, it is obvious that the burden of hip fractures is increasing globally, the greatest impact is observed in Asia. It is hypothesized that due to the increased number of senior citizens

in Asia, the prevalence of hip fractures will rise to 37% in 2025 which was 26% in 1990.[8] Moreover, almost half of all hip fractures are projected to occur in Asia, particularly in China by the end of 2055.[9] Currently, 10 million Americans have either experienced or have osteoporosis.[10]

Various factors play a vital role in the pathogenesis of osteoporosis. However, the impact of salt or sugar on bone health is not well known. The aim of this review paper was to determine the impact of a diet high in salt and/or sugar on bone health and osteoporosis risk.

Risk factors for Osteoporosis

Among the non-modifiable risk factors, older age, gender, genetics, and ethnicity are associated with osteoporosis. Reduced sunlight exposure, lower intake of calcium-rich foods, as well as hypovitaminosis D are modifiable risk factors for osteoporosis.[7, 1] Lower amounts of estrogen can further decrease bone formation and growth of new bone leading to osteoporosis. Hence, post-menopausal women or women with low estrogen levels during the reproductive years may be at a higher risk of osteoporosis.[12]

Dietary consumptions of sodium chloride (salt) and excess protein are known to increase urinary calcium excretion.[13] Therefore, a high salt intake is considered one of the major risk factor for osteoporosis due to increased calciuria.[14-16] The calciuria can be hypothesized to be partly due to salt-induced volume expansion which might lead to an increase in glomerular filtration rate (GFR), and partly due to competition between sodium and calcium ions for reabsorption in the renal tubule.[17] Therefore, low calcium intakes may contribute to a compensatory response leading to increased bone remodeling and bone loss, which might be perpetuated by an increase in dietary salt consumption.

Association of salt with osteoporosis

There is a large fraction of body sodium deposited in the bone,[18] suggesting that bone might serve as a sodium reservoir which is mobilized during homeostatic stress. Salt also has a crucial role in maintaining positive magnesium and calcium balance. If a reduction in serum sodium occurs, the bone may be stripped of sodium (as well as magnesium and calcium) to maintain normal serum sodium levels. Indeed, a low-salt diet has been shown to lead to negative calcium and magnesium balance which could result in osteoporosis.[19] Thus, a low-salt diet may cause osteoporosis by stripping the bones of sodium, calcium, and magnesium.

Theoretically, a high-salt diet may lead to hypercalciuria. However, its effect on bone health is unclear. Recent research indicates that a high-salt diet may increase bone resorption among postmenopausal women,[14] however other studies have not found this to be the case.[20] Animal studies also suggest that elevated levels of aldosterone may lead to magnesium and calcium loss in the urine potentially leading to a loss of bone minerals and bone strength.[21] Thus, a low salt diet, which increases aldosterone levels, may harm rather than improve bone health.

A previous study conducted on over 4,000 postmenopausal women from the Women's Health Initiative (WHI) concluded that, "Higher levels of sodium intake and intakes above the WHI population median were associated with significantly fewer hip fractures."[2] There are other studies which have not found any significant association between sodium intake and bone mineral density (BMD).[22,23] Another previous study also concluded that a high sodium intake may not be detrimental to bone health in elderly patients whose dietary calcium intake is adequate.[24]

A high sodium is consistently cited as a risk factor for osteoporotic fractures, especially if the calcium intake or calcium absorption is also low.[15,25-27] However, the regulation of sodium balance within the human body is quite complex. Normal sodium levels are of utmost importance and normal sodium intakes help to maintain central blood volume and renal perfusion. Thus, sodium levels in the body are tightly regulated by homeostatic defense mechanisms primarily mediated by the renin-angiotensin-aldosterone system (RAAS).

A lower sodium intake (< 3,000 mg per day) in an average-weight adult can lead to low sodium levels in the blood and activation of the RAAS both of which may induce osteoclastic activity.[28-30] Osteoclasts resorb bone, and if bone breakdown exceeds bone building this can lead to osteoporosis. In experimental studies, it was shown that activation of RAAS or an infusion of angiotensin II lead to an increase in bone resorption with the absence of angiotensin receptor type 1 being associated with greater bone strength. It is interesting to note that greater salt intake was found to be associated with a high bone mineral densit .[31,32]

Sustaining low sodium levels in blood are not only potentially harmful for bone health but also seems to increase the risk of cardiovascular morbidity and mortality. In fact, even normal sodium levels at the lower-normal range (136-138 mEq/L) significantly increases the risk

of major morbidity (cardiovascular complications) when compared with the upper normal range of sodium (139-143 mEq/L).[33]

Hyponatremia or low sodium levels in the blood is most common electrolyte abnormality, and this condition occurs frequently in the elderly population both in and out of the hospital setting. Hyponatremia may lead to unsteadiness, which predisposes to falls and injuries particularly in older individuals.[33,34] For the elderly, falls can be hazardous, as they can lead to fractures and even death. A recent review paper noted that, "The increased bone fragility together with gait instability makes chronic hyponatremia a new risk factor for fractures, especially in the elderly."[35] The study even suggested that correcting even minor hyponatremia may help to lower the risk of fracture related events.[35] In fact, hyponatremia can potentiate the increased risk of fractures after a fall by around four-fold.[36]

Studies conducted on animals indicate that chronic hyponatremia can cause or accelerate the condition of osteoporosis, organ dysfunction, and senescence.[37,38] Moreover, two cohort and case-control studies suggest a significant association between osteoporosis or fracture and hyponatremia,[36,39-41] and a recent case report described a patient who had reversal of severe osteoporosis after correction of chronic hyponatremia.[42]

Another way that hyponatremia may lead to weak bones is by causing a deficiency of vitamin C. It is well documented that vitamin C absorption in the intestine depends on sodiu,.[43,44] Thus, hyponatremia may directly or indirectly worsen the bone health by causing vitamin C deficiency.[45] Interestingly, animal studies report that hyponatremia is responsible for decreased activity of the sodium-dependent vitamin C transporter, which not only reduces the uptake of ascorbic acid into the bone but also increases oxidative stress, which may also apply to humans.[46]

Sugar and Osteoporosis

The present literature suggests that nutritional deficiency (both the undernutrition and over-nutrition) may be a substantial risk factor for osteoporosis. The groups that appears to be most affected by both overnutrition with concomitant undernutrition are children and teenagers who consume excess refined carbohydrates and added sugars.[47] Adolescents who consume the greatest amounts of added sugar may be particularly vulnerable to the detrimental effects of dietary sugar on peak bone mass.

The regular consumption of soft drinks is a notoriously high source of added sugar, and is associated with an increased in the risk of developing fractures which may be in part due to the replacement of calcium-rich beverages.[48-51] Studies have found that soft drinks lack important nutrients.[48-51] Furthermore, the intake of sweet beverages, including non-carbonated fruit juices and carbonated cola beverages, are significantly associated with a higher risk of fractures. An increase of one-half of a can per day of fruit juice and cola beverages, increased the likelihood of developing bone fractures by 1.6-fold and 1.7-fold, respectively[5.

One study reported that the ingestion of 100 grams of galactose and glucose in healthy subjects significantly increased the urinary excretion of calcium, magnesium, and potassium (suggesting an increased need for these minerals after ingestion of sugar). The authors noted no effect of sugar consumption on sodium excretion.[52]

In another such study, by Lemann et al. it was observed that despite inducing a reduction in glomerular filtration rate leading to reductions in the rates of filtration of calcium and magnesium, glucose ingestion augmented urinary calcium and magnesium excretion. They further hypothesized that the reason behind this augmentation could be the inhibition of re-absorption of calcium and magnesium within the tubules.[53]

In a study conducted by Holl and Allen, there was a significant increase in both urinary calcium excretion (peak at 1.5 hrs) and serum insulin levels after ingestion of 2 gram/kg of sucrose. The reabsorption of calcium from the renal tubules first decreased from 99.1% at 0 min. to 97.3% at 90 mins. The investigators noted that sucrose consumption was responsible for an increase in the urinary excretion of zinc and sodium, however the renal re-absorption of zinc and sodium was not found to be impaired. The possible reason was due to increase in serum insulin levels, which might be responsible for inhibiting calcium reabsorption in the tubules.[54]

Experiments in animals have observed urinary mineral loss after the ingestion of dietary sugar.[55-57] Borle et al.[58] in their experiments on mouse metaphysis concluded that addition of glucose to the medium lead to a dramatic increment of bone lactate production. Lactic acid formed from osteoclast metabolism of glucose may dissolve the mineral salts from the bone and high glucose levels may reduce osteoblast proliferation.[5] Also, osteoclasts trigger the production of hydrolases which can dissolve the organic bone structures.[60,61]

In a study conducted by Ericson in subjects after consuming either 100gm of sucrose or glucose, a strong positive association between calcium and magnesium

excretion rates was observed ($P < 0.01$ to < 0.001).[62] This study showed that the consumption of dietary sugar leads to an increase in the urinary excretion of of both calcium and magnesium. The authors wrote, "[…] the calcium loss is not compensated for during the hours following the calcium hyperexcretion shown by the results of Thom et al. […] which reported an average net loss of 40 mg Ca/day during a week with doubled intake of sucrose and total carbohydrate, and 100 mg Ca/day during a week with three-fold intake."[62]

Furthermore, sugar consumption is also associated with a decrease in the active form of vitamin D, leading to a reduction in the intestinal absorption of calcius.[63] Thus, a diet high in sugar may drive both calcium and vitamin D deficiency. The overconsumption of sugar may also impair bone formation by causing high glucose levels in blood.[64] Moreover, hyperglycaemia (which is commonly driven by a diet high in sugar[65]) is associated with lower bone quality and density.[66]

Another recent study concluded that dietary fructose can be responsible for a reduction in calcium transport in both the intestine and the kidneys due to reduced levels of 1, 25 dihydroxy vitamin D3 (1, 25(OH) 2D3). The hypothesis involved an increased expression of 24-hydroxylase (CYP24A1) and decreased expression of 1α -hydroxylase (CYP27B1), suggesting that fructose might enhance the renal catabolism and impairs the synthesis, respectively, of 1,25-(OH)2D3.[10]

Moreover, it is observed that a diet high in sucrose decreases the formation of dentin[67] and reduces the mineralization[68] during the primary dentinogenesis in rats. As the dentin and bone formations share a common matrix of calcium hydroxyapatite[69] it might be logical to infer that their osteoblastic activities may be similarly impacted by the influences of a high sucrose diet.

Saffar et al. observed adverse sucrose-induced changes that took place in the femurs of the young golden hamsters.[70] The researchers conducted another study where they found that the effect of diet-induced osteoporosis might involve not only the endosteal structure of bones but also the bone remodelling process.[71] According to the findings derived from the experiments on rats, glucose seemed to cause serious harm to the bones as compared to dietary sucrose.[72]

Lorincz et al.[73] presented a study on 9-week-old female C57BL/6 mice where they were given a high fat sucrose (HFS) diet for 10 weeks, and observed a detrimental impact on bone structure with negative morphological properties in cortical bone. Most of these effects were due to the increased osteoclastic activity, which was associated with an inflammatory environment. Moreover, long-term ingestion of an HFS diet for 24 months in female rats, also showed an adverse effect on the cortical bone, histology of the vertebrae and femoral neck, along with changes in mechanical properties.[73]

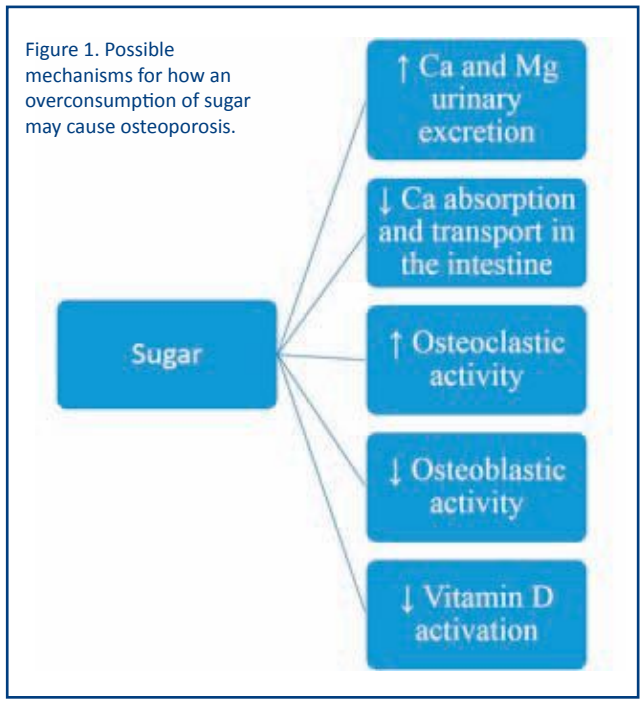


Figure 1. Possible mechanisms for how an overconsumption of sugar may cause osteoporosis.

In contrast to HFS studies, there are some experiments which used a fructose-rich diet (FRD) to forecast the metabolic syndrome (MS) animal model, where they assessed the consequences of FRD-induced MS on mice particularly focusing the growth in area of long bone histomorphometry and bone tissue regeneration.[74] Based on these FRD experiments, the researchers concluded that there was a 20% and 30% decrease in the osteocytic density of femoral trabecular bone and in osteoclast-covered (TRAP-positive) bone surface in the primary spongiosa, respectively.

Another study conducted by Felice et al. also evaluated the impact of FRD-induced MS on bone tissue regeneration, and concluded that fructose ingestion not only decreases the re-ossification, but also significantly reduces the osteocytic density. The study also suggested that further reduction of the osteoclastic activity particularly in the lesion site, might lead to a decrement in bone formation and remodelling. Moreover, it was also noted that the FRD-induced MS might diminish the ex-vivo osteogenic potential of marrow stromal cells (MSC) components and could lead to an increase in the ex vivo adipogenic potential of MSC,

which may lead to a reduction in Runt-related transcription factor (Runx2) and an increase in Peroxisome Proliferator Activator Receptorr γ (PPAR γ) expression under basal (undifferentiated) conditions. All the above mentioned data suggest that fructose can lead to a deleterious effect on overall bone health.[75] The final mechanism that by which fructose can lead to an overall negative impact on bone health is due to insulin resistance and hyperglycemia.[65,76,77] Indeed, diabetes and hyperglycemia are associated with higher risks for osteoporosis, bone fractures, impaired bone strength and bone remodelling. Figure 1 summarizes the possible mechanisms whereby an overconsumption of dietary sugar may lead to osteoporosis.

Conclusion

In summary it appears we have blamed the wrong crystal: it's not salt, but sugar that presents a greater risk factor for osteoporosis. The overconsumption of dietary sugar has the potential to increase the risk of osteoporosis by: a) increasing the urinary excretion of both calcium and magnesium, b) reducing the intestinal absorption of calcium by lowering the levels of active vitamin D, and c) impairing bone formation by reducing osteoblast proliferation and increasing osteoclast activation as well as lactic acid production.

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Disclosure

None reported.

MM

IgG-4 Related Disease: An Introduction

by Orwah M. Al-Khalili, MD & Alan R. Erickson, MD

Glucocorticoids remain the main initial therapy agents with expected good and quick response.



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Abstract

IgG4-related disease (IgG-RD) describes a group of fibroinflammatory diseases that affect a variety of tissues resulting in tumor-like effect and/or organ dysfunction. Clinical presentation varies according to the tissue(s) involved, and diagnosis relies on tissue findings of dense infiltration of IgG4-positive plasma cells and a characteristic storiform fibrosis. Treatment is mainly with glucocorticoids, while multiple immunosuppressive medications can be used as adjuvant agents. Rituximab has showed promising results, but further studies are needed.

Introduction

IgG 4 related disease (IgG4-RD) is a systemic fibroinflammatory disease characterized by dense infiltration of IgG4-positive plasma cells in the affected tissue(s) with or without elevated plasma levels of IgG4.[1] The inflammatory infiltration along with a characteristic storiform fibrosis can lead to the development of chronic damage and/or tumefactive lesions[1] that may affect any organ. In 2001, Hamano and colleagues published a study that showed the association between elevated plasma IgG4 levels and sclerosing pancreatitis [2], which is now called type 1 autoimmune pancreatitis (AIP). Immunohistochemical examinations of AIP tissues revealed severe infiltration with IgG4-positive plasma cells that further enlightened the existence of an IgG4-RD with a possible systemic process.[3] In the years to follow, several previously described syndromes were linked to IgG4 infiltration and now they are labeled as IgG4-RD affecting different tissues or organs. These syndromes include Mikulicz disease[4], chronic sclerosing sialadenitis (Kuttner's tumor)[5], Riedels' thyroiditis[6], mediastinal fibrosis, retroperitoneal fibrosis (Ormond's disease), periaortitis, idiopathic hypocomplementic tubulointerstitial nephritis, multifocal fibrosclerosis, and inflammatory pseudotumor.[1]

Epidemiology

The incidence of IGG4-RD remains unknown. This is due to challenges in making the diagnosis as the disease is often unrecognized or misdiagnosed. A cohort of 125 biopsy proven IgG4-RD showed a mean age of 55 years old at diagnosis (50 years old at onset of symptoms); 78% were white and 61% were males. Head and neck tissues were the most affected sites.[7] Mayo Clinic reported 166 patients with IgG-RD; the median age of onset was 61 years old and the male to female ratio was 3:1; 80 % of patients were white. In the Mayo Clinic report; hepatobiliary IgG4-RD was the most common entity.[8] One study from Japan reported 114 of

cases with a similar male to female ratio of 3:1. The higher incidence of the disease in males persisted regardless of the tissue affected with the only exception of IgG4-RD in the head and neck (sialadenitis or dacryoadenitis) where the male to female distribution was equal. In this cohort the average age at diagnosis was 64 years old.[9] The disease seems to be less common in the pediatrics population. A systematic review found 22 cases of IgG4-RD in children with a median age of 13 years old (age range was 22 months to 17 years); 64% were females in contrast to the male predominance in the adult disease. In the pediatric population ophthalmic IgG4-RD was the most common entity and it was seen in 44% of the cases.[10]

Pathogenesis

Most studies on the pathogenesis and the genetic associations of IgG4-RD were conducted in Asian populations with AIP. Both human leukocyte antigen (HLA), and non-HLA genes were associated with IgG4-RD. A study from Japan reported that the frequencies of HLA serotypes DRB1_0405 and DQB1_0401 were significantly higher in patients with AIP than in healthy individuals and in patients with chronic calcifying pancreatitis not related to AIP. In addition, single nucleotide polymorphisms (SNPs) in non-HLA genes were linked to AIP. Those genes include Cytotoxic T-Lymphocyte Antigen-4 (CTLA-4) and Tumor necrosis factor (TNF)- alpha promoter genes. The frequency of CTLA-4_ 49A and TNF- alpha promoter _863 haplotypes were higher in Chinese AIP patients than in healthy individuals. A Japanese study found that the CTLA-4_49A haplotype is associated with a higher risk of disease relapse. Another study reported an association between AIP and Fc receptor-like 3 (FCRL3) _110A/A genotype.[11]

While impaired function or a decreased number of regulatory T cells (Treg cells) is believed to be an important step in the development of autoimmune disorders[11], Treg cells seem to play an important role in the pathogenesis of IgG4-RD. The expression of Th2 cytokines (IL-4, IL-5, and IL-13) and regulatory cytokines (IL-10 and TGF-β) was up-regulated in the affected tissues of type 1 AIP[12], and in IgG4-related tubulointerstitial nephritis.[11] Similar findings were reported in Mickulicz disease.[13] The overproduction of IL-4, IL-5, and IL-13 can explain the higher frequency of peripheral eosinophilia and IgE levels in patients with IgG4-RD. IL-10 causes increased production of IgG4 and can lead to fibrosis by increasing the expression of Transforming Growth Factor- beta (TGF-β), which is a fibrogenic cytokine.[12] A recent study showed that CD4+ effector/memory T cells with a cytolytic phenotype were expanded in IgG4-RD patients. These CD4+ cytotoxic lymphocytes (CD4+ CTLs) might play a major role in the pathogenesis of the disease. Plasmablasts, which are increased in IGG4-RD, are thought to be responsible for the reactivation of the CD4+CTLs and induce them to make fibrosing-inducing cytokines including IL-1β and TGF-β1.[14]

Clinical Presentation

The symptoms of IgG4-RD vary considerably depending on the organ(s) or tissues involved. The most common presentation is a mass lesion or organ enlargement. The most commonly affected organs are salivary and lacrimal glands, pancreas and biliary tract, and the kidneys; but any organ could be involved and multiorgan disease can be also seen.[15] The inflammatory infiltration and fibrosis can result in tissue or organ dysfunction in addition to tumor-like effects that can cause obstruction or compression complications.[16] Among the clinical features observed are exophthalmos including orbital pseudotumor, salivary gland enlargement, pancreatic failure, lymph node enlargement, retroperitoneal fibrosis, kidney disease with proteinuria and subsequent renal failure, and aortitis-related aortic aneurysm.[17] A number of cases will present as an incidental finding on imaging. Presentation is usually subacute, and some patients might have more than one organ affected at the same time or years after the initial diagnosis. Many patients have an existing allergic condition. Peripheral eosinophilia is not uncommon while fever is rare.[1]

Diagnosis

The diagnosis of IgG4-RD can be challenging and the approach to diagnosis will depend on the site affected. A thorough process should always be followed to rule out the different diseases that can mimic IgG4-RD. These diseases include a broad spectrum of conditions including malignancy, lymphoproliferative disorders, Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis, sarcoidosis, Sjogren's syndrome, Castleman's disease and others.[16, 17]

It is important to remember that elevated plasma IgG4 levels are neither specific nor sensitive for IgG4-

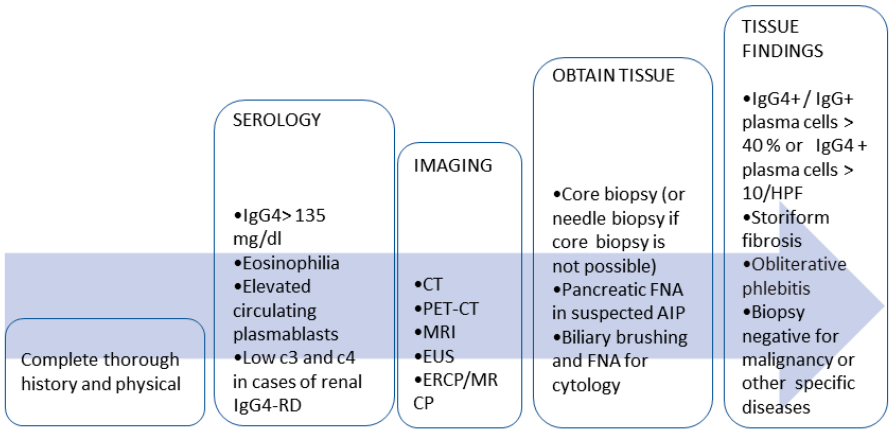


Figure (1). Suggested flow chart for IgG4-RD diagnostic work up. HPF: high-power field. FNA: Fine needle aspiration.

RD. Normal IgG4 can be seen in nearly one-fourth of the cases[9], and using a cutoff level for IgG4 of 135 mg/dl has a positive predictive value for IGG4-RD of only 34%.[18] While tissue biopsy is very helpful in ruling out cancer and other possible disease processes, IgG4+ cellular staining on biopsy alone is not sufficient to make a definite diagnosis of IgG4-RD as the presence of IGG4+ plasma cells in the tissue can be seen in other diseases including malignancy. In addition, certain sites affected by IgG4-RD, like the retroperitoneum, orbital cavity and pancreas, are very difficult to biopsy.[1,16,17] Elevated numbers of circulating plasmablasts can be seen in a variety of inflammatory conditions but a significant elevation (>2,000 cells/ml) was observed in IgG4-RD and may serve as a marker for both diagnosis and measurement of disease activity. Plasmablasts elevation in IgG4-RD was seen even in patients who had normal IgG4 levels.[19] However, the testing of plasmablasts might not be readily available in all clinical settings and more studies are needed to advise a universal use of this test.[17] Comprehensive diagnostic criteria for IgG4-RD and organ-specific IgG4-RD (like AIP and IgG4-related kidney disease) exist and they take in consideration the clinical, serological, radiographic and histopathologic al manifestations.[16] However, some of the proposed criteria had low sensitivity (as low as 70%).[16] Also, a major caveat was the ability to make IgG4-RD diagnosis without obtaining a biopsy, which can be problematic.[17] The use of these criteria should not replace the need for obtaining a biopsy from the suspected lesion.

The assessment should start with complete history and physical examination. Then when the disease is suspected lab testing and appropriate radiology evaluation will depend on the site involved. Plasma IgG4 levels should be obtained in all patients. Most cases of renal IgG4-RD will have low complements[17], which often correlates with disease activity[17], thus complement levels should be obtained when renal IgG4-RD is suspected. Circulating plasmablasts measurement, if available, can be helpful especially if the serum IgG4 level is normal. Selection of the imaging modality in the assessment of IgG4-RD will depend on the organ under evaluation, local radiology expertise, and availability. Computed tomography (CT), CT with positron emission tomography (CT-PET), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), Endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS) are modalities that are commonly used to evaluate IgG4-RD.[17] Biopsy remains the cornerstone step in evaluation. As noted, the presence of high level of IgG4+ plasma cells (> 10/HPF or IgG4+/IgG4>40%) is typical but not diagnostic.[9] Findings of storiform fibrosis and obliterative phlebitis increase the specificity of the diagnosis.[16.17] Diagnosing biliary or pancreatic IgG4-RD is even more challenging due to difficulties in obtaining adequate tissue samples. The characteristic imaging findings and serologic testing become the main diagnostic criteria. Fine needle aspiration of the pancreas and brush cytology of the biliary system, however, remain important to rule out malignancy.[16, 17]

The diagnosis is made by clinical correlation of the laboratory, imaging and histopathologic findings in absence of malignancy or other disease processes that could explain the presentation (Figure 1).

Treatment

Some patients with asymptomatic IgG4-RD can be watched without treatment, e.g. asymptomatic lymphadenopathy or mild submandibular gland enlargement.[17] However, most patients will require initiation of therapy. Special attention should be made to active IgG4-RD in the pancreas, biliary tree, aorta, mediastinum, kidneys, retroperitoneum and mesentery as in those cases starting therapy in an urgent fashion must be considered.[17] Pachymeningitis is one of the manifestations of IgG4-RD that also requires urgent treatment. [17]

Glucocorticoids remain the main initial therapy agents with expected good and quick response. A meta-analysis that included 62 different studies with total number of 3034 patients showed that glucocorticoids are the most commonly used medication to initiate therapy (74% of reported cases) with a mean starting dose of 0.6 mg/kg. The reported response rate for glucocorticoids monotherapy was 97% but a complete response rate was 65 %.[15] Also, relapse can occur after stopping glucocorticoids. The actual rate for relapse is unknown but one study reported a relapse rate of 54 % after cessation of steroids therapy in AIP.[20] The efficacy of corticosteroids was less in American studies compared to studies from Asia.[15]

Initial glucocorticoids dose should be maintained for 2-4 weeks then tapered slowly over 3-6 months depending on response.[17] Adding a steroid-sparing agent is reasonable especially if prednisone can't be tapered because of persistently active disease. Options include Methotrexate, Azathioprine, Mycophenolate, 6-Mercaptopurine and cyclophosphamide.[17] To date there is no randomized controlled studies that compared prednisone monotherapy to combination of steroids with any immunosuppressive agent in IgG4-RD. The use of Rituximab (RTX) monotherapy to induce remission has demonstrated promising results. Rituximab was associated with significant reductions in both IgG4 levels[21, 22], and circulating plasmablasts.[22] A prospective study of Rituximab showed that 77% patients met the primary outcome of response with no relapses for six months.[21]

Maintenance therapy for IgG4-RD after remission induction is recommended for patients with higher risk of organ dysfunction or high risk of relapse. There is no consensus on the optimal regimen or duration for maintenance therapy, however. Maintenance with small dose of glucocorticoids is the most practiced approach in Japan for AIP.[17] A steroid sparing agent and Rituximab for maintenance can also be used. Disease relapse or flares should be managed with glucocorticoids and if the patient is not already on another immunosuppressive then starting an agent should be strongly considered.[17]

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Disclosure

None reported. **MM**

Missouri State Medical Association
160th ANNUAL CONVENTION



OFFICIAL MINUTES & REPORTS

March 23-25, 2018
Renaissance St. Louis Airport Hotel
St. Louis, Missouri



Meet MSMA's 2018-2019 President

Joseph A. Corrado, MD, FACS
Mexico, Missouri

Contact: bigdocjoe@sbcglobal.net

Joseph A. Corrado, MD, FACS, a Diplomate of the American Board of Surgery, from Mexico, Missouri, will serve as President of the Missouri State Medical Association in 2018-2019. He will be formally installed in St. Louis tonight, March 24, 2018, during MSMA's 160th Annual Convention.

Dr. Corrado was born in Everett, Massachusetts, grew up in Revere, Massachusetts, and earned his BS in Biology from Boston College. He received his MD from the Saint Louis University School of Medicine in 1976. His residency, including Chief Resident in Surgery, was at the Albany Medical Center and affiliate hospitals in Albany, New York. In 1981, he trained as Chief Fellow and the American Cancer Society fellow at Lahey Clinic Medical Center in Burlington, Massachusetts.

Dr. Corrado is currently the Chief of Surgery at SSM-St. Mary's Audrain Hospital in Mexico, Missouri. He has served as Chief of Staff, Cancer Liaison and Chairman, and has been on each committee of the Audrain Medical Center in the last 36 years.

A long-time supporter of organized medicine, Dr. Corrado is a Fellow of the American College of Surgeons, and a member of the Missouri Chapter of the American College of Surgeons (Past President and Governor) Missouri State Medical Association, American Medical Association, and an Audrain County Medical Society Past President. Additionally, he is a member of numerous medical and specialty organizations, including the Society of Surgical Oncology, Society of Breast Surgeons, Southwest Surgical Society, Society of Gastrointestinal Endoscopic Surgeons, American Trauma Society, and a Charter Member of the American Society of General Surgeons.

He has been appointed and is currently serving as Instructor/Preceptor in Surgery, A.T. Still Kirksville School of Osteopathic Medicine; Instructor/Preceptor in Surgery, Saint Louis University School of Medicine; and Instructor/Preceptor in Surgery, Washington University School of Medicine, St. Louis. Presently, he is on the American College of Surgeons Committee on Coaching the Next Generation.

Dr. Corrado has been recognized with several awards, including the American College of Surgeons 30 Year Cancer Liaison Physicians Award; the Commission on Cancer, American College of Surgeons Outstanding Performance Award; and National Cancer Institute Certificate of Appreciation. He also served on the Board of Governors as a Governor at Large for the American College of Surgeons.

He and his spouse, Donna Glasford Corrado, have five children and eleven grandchildren. Dr. Corrado has remained active in the town of Mexico, Missouri, and surrounding communities since his arrival in 1982, including the Chamber of Commerce, Knights of Columbus, Elks, and Lions clubs. He has been a musician in the church choir at St. Brendan's Catholic Church, and is a guitarist, playing bass, for "Blues Highway."

Under his tenure as MSMA President, Dr. Corrado will be promoting:

- The Patient First Concept;
- Rural Medicine;
- The benefits of organized medicine.

MM

Alliance Installs 2018-2019 President

Gill Waltman

St. Louis, Missouri

Contact: gillian.waltman@gmail.com



Gillian Waltman, 2018-2019 Alliance President, was born and raised in England, the oldest child of Michael and Sheila Roper-Hall, both still living independently at home at almost 95. Gill has one sister and two brothers, all still in England. Her father is a retired ophthalmic surgeon and the family has a strong tradition in the medical field with several generations of physicians.

Gill, still known as 'Roper-Hall' in her professional world, was educated in England and did her specialty training in binocular vision and eye movements at Moorfield's Eye Hospital in London.

She came to the United States in the 1970s to pursue a fellowship in neuro-ophthalmology at Washington University – where she heard a lot about a very shy, very bright young cornea surgeon and former resident and was away at the time serving as a major in the U.S. Army at Walter Reed Hospital. She and Steve Waltman met at an ophthalmology conference in Las Vegas.

After a short transatlantic romance, Gill returned to Washington University to accept a position in the Department of Ophthalmology where Steve was already back on the faculty, and they were married soon after. The Waltmans have lived in St. Louis since then. Steve rose quickly through the academic ranks at Washington University establishing the cornea transplant service and Eye Bank for the bi-state area and becoming a full professor at a young age.

Gill and Steve have two children; Belinda and Michael now in their mid-30s. Belinda is a physician, currently Medical Director of a Los Angeles County Health initiative for the underserved. She is married to Matt, a biophysicist doing stem cell research at Caltech in Pasadena, and have two children. Mike is a business strategist for a series of startup companies in the Bay Area. He and his wife Michelle (an entrepreneurial culinary expert) have one child.

Gill is currently a full Professor of Ophthalmology at Saint Louis University. She is a prolific author, and an experienced reviewer and board examiner who is internationally recognized for her clinical expertise and research experience in the field of adult strabismus and neuro-ophthalmology. She considers herself an "ambassador" for the university and the profession as she travels around the U.S. and abroad.

Gill is also involved in other activities. She plays a lot of tennis, loves to hike with her women's hiking group, and is on the board of the Saint Louis Chamber Chorus serving as vice president for the past four years.

Between her busy schedule at the hospital, with lots of work travel to present papers at various conferences, regular family visits to California, England and Long Island, and heading off on exotic trips with Steve (now all seven continents), Gill has always found time for the Alliance. She became a member back in 1986 when Chris Bohigian was president, being elected to the board a year later when she was elected as the SLMMS Alliance Vice President for Health. Since then she has held numerous positions as an officer at the local and state level.

She has been on the SLMMS Alliance board in various positions and held three consecutive terms as its president from 2003-2006 and was co-president more recently from 2015-2017.

Gill has held leadership positions as MSMA Alliance Vice President for Health, Legislation, and many years as Recording Secretary before being elected as the president-elect. **MM**

State of the Association: Presidential Address

by Warren C. Lovinger, Jr., MD, MSMA President

It has been my great honor to serve the Missouri State Medical Association during this past year as your President. I have loved every minute of this personal adventure, having traveled over 16,000 miles to visit every county in this state, as well as the city of St. Louis. I have usually been accompanied by my wonderful wife, Marilyn. You have seen some of the pictures we have taken—including county courthouses, individual doctors, and medical groups. We have had the pleasure of meeting many impressive physicians and physicians in training across the state—from Marysville to Caruthersville and from Pineville to Cahoka. In each case, we were struck by the optimism and sense of community service our Missouri physicians embrace. Though we have many challenges, I can confidently say that we are blessed to be in a great profession, serving a great state, and supported by an effective and respected organization—the Missouri State Medical Association.

Let me enumerate some of the good things that have happened during the past year within our profession and organization.

1. The sale of Primaris to a private group was completed, with the $3.5M income added to our Health Education Foundation to help support this meeting and other CME activities for years to come.

2. The SHINE program has been successfully launched as a statewide Health Information Exchange that will connect patient information to our many different EHRs. It is patterned on the successful Kansas system, and will offer a great benefit to MSMA membership.

3. Our MSMA staff in Jefferson City has undergone successful transitions, as Patrick Mills accepted the Executive Vice President reins from Tom Holloway while Heidi Geisbuhler joined our lobbyist team, and Stephan Foutes joined our membership team.

4. David Barbe, MD, of Mountain Grove, has brought great honor to our state and organization as the first Missouri President of the American Medical Association in 90 years! Dave embodies everything good about our profession as he represents us with great eloquence.

5. With the advocacy of the AMA and sub-specialty groups, the 2018 Federal budget bill was passed and signed in Washington DC in February. It achieved several of our goals, including elimination of the Independent Practice Advisory Board (IPAB) and funding of the critical CHIPS program for the next six years.

6. In Missouri, efforts have been successful in getting Anthem BC/BS to review or rescind its controversial Emergency Room retrospective approval program and modifier 25 cuts.

7. The Assistant Physician program, which MSMA helped establish with ground breaking legislation in 2014, has now "taken off." Approximately 35 APs are employed in Missouri, as they await their match into a residency program. Missouri's program has become the model across the U.S.

8. In membership matters, great strides have been made. The Mentor Program, initiated this year as a pilot at MU Columbia medical school has had good participation by both medical students and their physician mentors from across the state. Through the work of the MSMA Alliance and the Missouri State Medical Foundation, an increasing number of scholarships are given annually to students at each of our six medical and osteopathic schools. MSMA's Resident and Fellow Section has been reinvigorated by enthusiastic leadership, with growing numbers and participation. Among practicing physicians—both independent and employed—strides have been made to increase the many benefits of MSMA membership. Our award winning publications promote connectedness.

In addition to these positives, we also have many ongoing challenges to our profession and the provision of healthcare to Missouri's citizens. You can be confident that the MSMA and its leadership will be working hard to optimize these issues—some of which include:

1. Developments that threaten the funding of health care and physician services:

The MIPS and ACO concepts that CMS is using to transition physician payment from volume to quality measures will prove a rocky road for many of us. The mega mergers between insurance companies and pharmacy benefit managers—such as Aetna with CVS, and Cigna with Express Scripts—threaten to form monopolistic giants. Prior authorization requirements have become a nightmare of time consuming, unfunded responsibilities for physicians, pharmacies, and hospitals.

2. Developments that threaten our patients' well being. The opioid crisis is real and pervasive. Considerable education has been provided so far, with our MSMA Alliance being particularly effective. However, much

Top, from left: MSMA President Elect Joe Corrado, MD, MSMA President Warren Lovinger, MD, AMA President David Barbe, MD, MSMA Speaker Lancer Gates, DO, and MSMA Vice Speaker Sam Page, MD.

Below, left: David Chalk,MD, lauds the Missouri State Medical Foundation and its scholarship programs.

Below, right: Dr. Lovinger visits with daughter and physician Sarah Florio, MD, and Betty Drees, MD.







remains to be done, including expansion to a statewide PDMP. The uncontrolled acceleration of prices for generic medications makes it impossible for many of our patients to afford insulin, inhalers, and other essential medications. Healthcare access is becoming especially difficult in rural areas, where the epicenter of health care—our community hospitals—are in desperate financial condition. This threatens the patients, the economy, and the future of these towns—where medical facilities are often the largest employer.

3. Scope of practice battles. There is encroachment on the traditional medical model, which should be physician guided, from almost every other type of healthcare provider. These issues arise daily in the Missouri legislature, and require the constant vigilance of our lobbyists, visiting physicians, and all of you who regularly contact your legislators.

Despite the challenges that exist, we should always 'Dwell on the Positive.' Let's emphasize the many good things about our profession, our organization, and our role in society. We must advance the issues and actions that are critical to good healthcare, our fellow citizens, and our communities.

In closing, I want to again thank all of you for giving me the honor to serve as your Missouri State Medical Association President during this past year. I hope that you will agree with me that we have had a great year together. It has certainly been a life adventure that I will always treasure! **MM**

Physicians Are More Than Just Providers

by Joseph Corrado, MD, FACS
2018-2019 MSMA President



Dr. Corrado, (right) with the official MSMA "Bones" gavel, takes the reins from Dr. Lovinger.

Let me begin in personally thanking all of you for being here this evening. I come here with great anticipation as others have before me.

I would especially like to thank the Missouri Military Academy choir, under the direction of Mr. Freddie Lomas and MMA's president Mr. Charles McGeorge. The very Reverend Father Mark Porterfield my friend and pastor of Saint Brendan Catholic Church in Mexico for his gracious invocation and Dr. Thomas Welsh from Meridian, Mississippi, a colleague and friend for reading the Hippocratic Oath. All of the great talented MSMA staff, for without them we could not do what we do and be successful. To the Alliance, I would like to congratulate Gill Waltman on her new role as president.

Thank you, Dr. Ray Wilbers for taking me into your practice, and all of my loyal colleagues and friends from Audrain County who could join me this evening. I really appreciate you guys and am honored you could make it.

Let's also please take a moment to acknowledge those physicians who could not be here. Those that are home working and taking care of thousands of patients throughout the state.

I especially want to thank all the patients we serve daily who entrust in us their care, for without them there would be no need for us.

To Dr. Warren Lovinger who has done a superb job as president this past year. I doubt I will be able to fill his shoes visiting all 114 counties that's incredible no small feat. Again, thank you Warren for your leadership.

I would like to acknowledge Mr. Philip Gustafson, CEO and president of SSM Health mid-Missouri, and Mrs. Donna Jacobs, president SSM Health St. Mary's Audrain for being here tonight, along with the many hospital staff members, with whom I work with daily.

Also I'd like to acknowledge some truly special guests here tonight. All of our past presidents, my exceptional staff Mrs. Joy Dodge and her husband Brad, my nurse Missy Hoer and husband Matt, who's combined service spans more than a half a century, they are truly dedicated and I am grateful.

And finally first and foremost my lovely wife Donna of 42 years whom I love and cherish, for without her as my life partner, office nurse, and the Alliance's past president, I would not be as good as, or be doing this tonight.

Also it's of course all about family, if they would please stand as I call their names. I have my five extraordinary children and their spouses who I am so proud of and love. First, my son Jason and wife Charlotte Corrado, Jamie and Matt Jackson, Meredith Hume and twin sister Melissa Corrado, all the way from Bangkok,Thailand, Matthew and Danielle Corrado, and all of my 11 fantastic grandchildren: Isabella, Sophia, Eva, August, Josephine, Homer, Clementine Juniper, Georgianna, Nicola and baby Marius. They all think it's great to be here at grandpa's party, you can just imagine what Italian holidays are like at my house.

I also want to thank my brother Paul from Maine, my brother Peter and sister Linda and husband Gunter-Rosenthal from Montreal, Canada, and mother-in-law Faye Varney. And of course last but not least, I am so blessed and proud to have my parents Joe and Anna Corrado from Boston, to be able to share this occasion with me.

My mom tells everyone I practice in St. Louis and wants to know if I am a specialist or just a general surgeon. So mom now you know. Thank you and I love you.

If I could also specially acknowledge my dad, who left the twelfth grade to serve in the South Pacific during World War II, just two years ago was honored and given his original high school diploma, which they still had by the way, at age 90. Dad, thank you for your service, inspiration and support. We are truly proud.

It seems very fitting that it was here, in St Louis four decades ago, that I was bestowed the degree of doctor of medicine.



The family of Joe Corrado, MD, at the MSMA Presidential Inauguration.

As I stand here before you, I am filled with pride and honor that you have given me the opportunity to be your 160th president, representing all the physicians of this great state of Missouri. I promise to do the very best I can and ask your indulgence in doing so, hopefully I'll make you proud.

In my research I've found that I would be the third president of MSMA from Mexico, Missouri, a town of 12,000. The first was Dr. J. Frank Harrison in 1932, but I am so grateful to the second and last president from my hometown in 1986. You all may remember the late Dr. Pete Ekern and, thank you Nancy, for being here this evening, It's because my mentor Pete three and half decades ago, who brought me as a young surgeon to my first MSMA meeting and introduced me to organized medicine. I have been here ever since.

One good thing about being "out state" is that you're here on the council forever. I believe this will be my fourth executive VP. So Mr. Mills, I expect you to be here a long time!

In preparing this evening I thought that maybe a little past history may be helpful. Where have we come from and how can a rural community like Mexico make a difference?

It was 168 years ago on May 18, 1850, that the Missouri State Medical Society was formed, meeting in St. Louis. Your annual membership was only two dollars. At that first meeting they talked about recording and standardizing proper registration of births, deaths, and marriages for the state. I thought just how long ago that was and what it must have been like at that time?

Well, Washington DC was a town in pasture, with grazing cows and sheep and bare dirt paths; a great war hero General Zachary Taylor was only the twelfth president of the United States after his most famous victories in the Mexican War, old "rough and ready" became president at age 64. An interesting aside is, that's how Mexico, Missouri, got its name because of the recent battle "remember the Alamo."

The most feared disease at this time was cholera, the president had to hide his slaves from the public view, and Congress was agitated on whether the federal government had the power to prohibit slavery in the new territories acquired as a result of the recent Mexican war. California was admitted as only the thirty-first state of the union, and the compromise of 1850 was being debated in Congress.

Shortly thereafter president Taylor would be only the second president to die in office. The first being William Harrison, remembering at that time his medical treatment was bleeding; cupping with hot metal cups to create acute blisters; he was given calomel, laudanum, castor oil and powders with increasing doses of opium, along with whiskey and roots.

As for Taylor, the story goes that on that hot fourth of July after being at the Washington monument for an event, he gorged on ripe cherries, cream and sugar. The president got stomach cramps, and doctors came from Baltimore. He was given herbs and laxatives, and later that day the president died, he was embalmed and lay in state at the White House as the Vice President Millard Fillmore became the thirteenth president, all in one day.

I also learned that the MSMA actually has met on two occasions in Mexico for the Annual Meeting, first in May 1881, converging at 4:15 pm in the Audrain County Opera House they were welcomed by the president of the city council, the newly formed Audrain Medical Society organized in 1872, which was then a branch of the Union District Medical Society which at that time included most of northeast Missouri.

By 1892 there were eight counties including Audrain, Montgomery, Warren, Boone, Pike, Callaway, Lincoln, and St. Charles, then called the Lenten District Medical Society boasting about 100 physicians. Audrain met every fourth Friday at the Ringo Hotel.

Again in May 1900, the Medical Association of the State of Missouri was entertained in my fair city Mexico. An event of great importance to the county physicians, as the forty-third Annual Meeting was called to order in the opera house at 9:30 am. The topics discussed were ophthalmology, cancer, syphilis, smallpox, hysteria, coxa vera, gallstones, the progress of gynecology, the cure of old sinuses, and the modern treatment of appendicitis presented by Mexico's own Dr Pinckney French.

The city made a formidable impression upon the state wide assembly. For three days they met at the Ringo, Planters, and Windsor hotels, which are all long gone. The closing banquet, however, was a fitting finale for the doctors, meeting at the elegant Windsor hotel dining room they were served green turtle soup, Saratoga chips, caviar on toast, lobster salad and lambs tongue, topped off with ice cream, sherry and cigars, just like tonight.

But what were the medical conditions like around 1900 in Audrain County. At that time if one was sick in the community they were placed on the front page of the newspaper on the sick list. Cholera was lessening, malaria was diminishing, but the cause was still not clarified, smallpox had not been eliminated, diphtheria was woefully present as was typhoid, scarlet fever, whooping cough, and measles.

The lives of all children were precarious. There was a very high mortality rate in anyone under five years gold. Countless babies never made it past their second summer. Frequently families would suffer the death of several offspring with faded notations in their family bible dwindling from a dozen to only two or three children who would reach adulthood.

In those times, living conditions contributed to enormous health problems; there were no indoor plumbing or bathrooms. With unpaved streets, garbage, and animals were running wild and polluting common drinking wells; flies and mosquitoes swarming everywhere.

Surgery was very limited and attacks of appendicitis were referred as "knotted bowels" and left for nature to take its course. However after 1890 more often were subject to a surgeon's knife, most likely on the kitchen table.

The family stood by at that time making sure that the doctor took out something so that they could get their monies worth; remarkably many were successful.

One case in 1890, a Dr Carson was called to Mexico from St Louis. After performing an appendectomy at the patient's home and leaving him in the care of the local doctor, the surgeon went back to St. Louis, sending a bill for his services of $1,200. The patient survived but had to sell his business to pay the bill. It was called the largest doctor's bill ever known in Mexico at that time. Later they found a similar operation only a few months earlier by a local doctor who had only charged $38. See, there is a good reason for getting your care locally. By the way, the average lifespan in the United States then was only 47. So that's a glimpse at what medicine was like and how Mexico has been an integral part of Missouri medicine's history.

In all seriousness I would like to make a few comments and say to you that we are not merely just providers. That term bothers me. I would like to discuss with you the importance of the role of being a physician, and what that means. What a privilege, a calling, unlike any other. With extraordinary demands and personal sacrifice to you and family. The importance you have to your community and patients.

Just think how much time and effort you have spent getting where you are. When kids ask me, "how long does it take to become a doctor?" I tell them for me after graduating high school it was like starting all over again from kindergarten and going to the twelfth grade again. I don't always remember the long road it took in becoming a physician. Those sleepless nights-in-training, the never-ending call, the years of sacrifice in your personal lives, and years of missed time with your family and friends. However, you should never lose sight of all the lives you've touched during those "lost times."

Just think of the injured you have cared for, the deadly diseases you've encountered, or even the simple "repairs" in people's lives as a rare event like an operation which you may have performed.

Because of this gift and your talent. Whether, in the lab doing research, or in a community health clinic, it truly is a calling in service to patients and the public, we're doing more than just providing. Imagine the surgeon who can repair a congenital malformation in utero. This is more than just providing! Or the neonatologist agonizing over saving a premie - more than just providing!

Remember that the greatest reward we get in our profession is the trust we receive from our patients. As others before me have said, for us it may be just another day at the office, or that patient in room 2049, but to the patient before you it may be one of the most important times in their lives.

A week doesn't go by, that I sit across from a patient and family and have to give them a new diagnosis that their biopsy was positive for cancer. Just as you once they hear those words, they become numb, and their personal lives and those of their families are thus changed forever.

They may never remember anything else you said to them that day, but then I tell them the good news that we can usually do something about this. In fact, I tell them that as they leave the room, if they look on the wall there are photographs of women who were diagnosed with breast cancer some 25, 30, and 35 years ago who are still doing quite well, and that I still have the privilege of caring for them…just as they were sitting in front of me at that time, getting the same shattering news, now they are quite well and thriving. In fact, when my staff reminds me I try to bring them a bottle of sparkling grape juice on their twenty-fifth anniversary year of survival, it gives them great hope that they can be there for their own families a quarter of a century from now.

Oh, the joys of being in a small town. Again, I would say that is more than being a provider.

I would never have imagined myself a rural surgeon, a dinosaur, solo practitioner in the middle of the country. Coming from Boston, a proud product of immigrant grandparents living an impoverished existence in their native Italy, coming here, as so many do, for a better life in America. Like many of you, I ask how and why are you here? I don't have the answer, could it be fate?

Medicine has changed, as I have described, over the past 168 years, but what do you think it will be like in the year 2186? None of us will be here; can you just imagine? When I started there were no ER doctors, nor even that specialty, I remember physically having to come in and see every patient who came through the ER as the "nubie." Oh, the good old days. Not really.

I'll never forget one of the first cases I saw was a woman who had put her hand in a corn auger. Looking at her mangled hand I said "what the he… is a corn auger?" I'm from Boston. So I told the nurse "call plastics or ortho," and I'll never forget, Sue stood there and said … "Doctor, you are plastics and ortho," At that moment I realized what I had got myself into.

Looking back, I wouldn't have changed a thing. Being in a small community, as Warren knows, is different. When I was at the great tertiary care centers in Boston, I would see the patients maybe once or twice, but never outside the hospital.

Now a day doesn't go by that I don't see my patients at the grocery store, in the bank, or on the square, or even showing me their incisions on aisle 3 in Walmart. When the banker's wife perforates her colon, before I get home my family knows about the patient and how they did. So much for HIPPA! And they better have done well, know what I mean?

In short, doing what every one of you do on a daily basis is extra ordinary. You are more than providers! You make a difference every day in your lives and careers as physicians. Patients depend on and trust you for their personal care and you help them through the most monumental decisions of their lives. And for that I applaud each of you. Please continue the great work you do with passion.

I recently saw a commercial on television that said, "If it was easy, everybody would become a doctor because it's the best job in the world." I still think it's the best job in the world.

Another point I would like to share with you is "get involved" and "make a difference." I know I am preaching to the choir, because those of you who are here ARE already involved.

When I say get involved, I know every one of you, on a daily basis is involved with face to face patient contact, involved with nursing service, medical records departments, and insurance companies. Yes, it's true that a lot of things we do, take us away from patient care. For that's what we do best.

It's important that you get involved in your hospital, in their bylaws and on the medical staff, and the various and sundry committees that you may be asked to serve on. It's most important that WE as physicians continue to represent ourselves. That we make a difference here. Make

a difference in your community, it is very important that you be a physician leader, whether on your local school board, or just going to a PTA meeting. It's important that they see you as a community leader. As I told you before, living in a small town is like living in a fishbowl. It can be both a blessing and a curse.

We all understand the problems of burnout in our profession. Don't hang around the doctor's lounge too long. You surely will be discouraged. But I truly believe that if you get involved in both your personal and professional life you will be a better person and a better physician. It's most important that you get involved with your friends and family, with your church, your spouse, and your children. That's what's most important, so that at the end of the day, at the end of this great professional career you can say YOU made a difference.

There may be a few blips along the way, remember as Warren said last year, dwell on the positive!

The mayo clinic proceedings recently showed that those physicians who are uncomfortable with EHRs are more likely to reduce hours and leave practice. Some of the unintended consequences have been decreased efficiency and increased clerical burdens which also increases burnout.

It is said that four minutes of keyboard time for every one minute of true face to face time with the patient, not only increases fragmented care during the patient visit, while doctors often choose navigating their records over communicating with them, causing frustration and shortchanging both parties.

I know most of you sitting here ARE already involved in organized medicine. If not, please get involved. Be active in your county and state societies. You may ask "what does organized medicine do for me?" They see and follow hundreds of bills a year at the state house, many in some way impacting medicine.

We represent each and every specialty every day. Remember not long ago we were fighting for tort reform and caps on malpractice premiums and what insurance companies can and will do with premiums and payment.

It is very important that we stay involved as individuals and also collectively as a state medical society. Every year we are fighting scope of practice issues. We are on the front lines in confronting the opioid epidemic in America.

We have issues with telehealth, we are partnering with Kansas to create a health information exchange so that we can share clinical data. We are trying to get a PDMP passed in this state, and fighting insurance companies such as Aetna from retroactively denying Emergency Room visit payments, this is all in a day's work.

Remember we have exceptional lobbyists battling with us at MSMA fighting for us every day. I have firsthand experience, and just had the pleasure of returning from Washington DC with Warren and visiting with all of our Missouri congressmen and senators.

We were also very proud and honored to have with us, our own Dr. David Barbe, president of the AMA, fighting there beside us. Thank you Dave, we are ALL proud of you and your accomplishments!

We will continue to be there for you, but we, of course, need your backing. We are very much committed in Graduate Medical Education, and making sure the future physicians have the same opportunities as we in their practices.

Medicine is changing, the majority of physicians now are, or will be employed. I understand that now women make up the majority of medical students and that my perspective as a private practitioner may be obsolete.

Lastly, I feel it important that we must always put the patient first. If we do, we will never go wrong. If WE take the attitude of "what would I do if this were my mother, wife or daughter?" If you always do what is right for the patient, you will never regret it, and neither will the patient.

Wise mentors before me have said, "to be successful remember the three A's: Be Available, Affable and Able," in that order. And that has worked well, I can tell you.

There is a saying on the wall of my private office that I got in Italy when I visited with my Grandfather Pasquale in 1973. Boy, would he be proud today. It says: "Il denaro fa l'uomo ricco, ma educazione lo fa signore" which basically means money makes men rich, but education makes them gentlemen.

We as educated physicians make a difference every day in our patient's lives and don't you ever forget it. Continue to do what YOU DO with a passion and make a difference. You are more than providers, you are physicians with more than 16,000 hours of training on average. Be proud of your professional degrees.

I want to again thank all of you for being here. My friends, family, and fellow members of the Missouri State Medical Association. Again, I am truly honored for the opportunity to represent you and work with the great MSMA staff.

Thanks again to all of you, God bless you and God bless America. **MM**

Recipients of the 50-Year Physician Pin

Twenty-two career physicians earned their 50-Year Physician Pin during the MSMA Presidential Inauguration from MSMA President Ravi Johar, MD. After the Installation, many celebrated at the reception. Below is the listing of all pin recipients.

- Richard Baldwin, Jr., MD, St. Louis
- Frederick Bauschard, MD, St. Louis
- Lynn Carlton, MD, Springfield
- Salvador Chavez, MD, St. Louis
- Jonathan Dehner, MD, St. Louis
- Royal Garner, MD, St. Pete Beach, Florida
- Robert Gibbons, Jr., MD, Prairie Village, Kansas
- John Hoehn, III, MD, St. Louis
- John McGarry, MD, Crystal City
- Jay Peterson, MD, Shawnee Mission, KS
- Wilma Rajcher, MD, Columbia
- Philip Robbins, MD, St. Louis
- Perry Schoenecker, MD, St. Louis
- Stanley Sides, MD, Cape Girardeau
- Emily Smith, MD, St. Louis
- John Weed, Jr., MD, Kansas City
- Robert Westerman, MD, St. Louis



Fifty-Year Physician Pin Recipients, from left: Jay Peterson, MD, Shawnee Mission, KS; President Lovinger, presenting; Jonathan Dehner, MD, St. Louis; Wilma Rajcher, MD, Columbia; and Robert Gibbons, MD, Prairie Village, KS.



Middle and bottom: Physicians enjoy meeting with vendors during the Convention Tradeshow.



160th House of Delegates Resolution Actions & Decisions

Resolution #1 – Sale of Tobacco Products in Pharmacies

Action: Amended Resolution #1 Adopted

Resolved, that the Missouri State Medical Association declare the practice of selling tobacco and vapor products in pharmacies as imprudent from a public health perspective; and be it further

Resolved, that the Missouri State Medical Association encourages its members and all physicians to encourage their patients, when possible, to support pharmacies that do not sell tobacco and vapor products.

Resolution #2 – Creating Sustainable Strategies to Enhance Primary Care in Missouri

Action: Substitute Resolution #2 Adopted

Resolved, that the Missouri State Medical Association develop a working group to study and address long-term sustainable strategies that enhance the number of practicing primary care physicians in underserved areas of Missouri.

Resolution #3 – Support for Legislation Creating Needle Exchange Programs in Missouri

Action: Substitute Resolution #3 Adopted

Resolved, that the Missouri State Medical Association support legislation authorizing needle exchange programs in the state of Missouri.

Resolution #4 – Statewide Adoption of the St. Louis County Prescription Drug Monitoring Program

Action: Resolution #4 Adopted

Resolved, that the Missouri State Medical Association support legislation to adopt the St. Louis County Prescription Drug Monitoring Program (PDMP) as the State of Missouri's PDMP.

Resolution #5 – Create Standardized Priority Menu for Physicians Calling in Prescriptions

Action: Resolution #5 Referred to MSMA Council

Resolved, that the Missouri State Medical Association, in partnership with the Missouri Pharmacy Association, work to create a standardized priority menu option for physicians when calling in a prescription to a pharmacy; and be it further

Resolved, that this standardized priority menu concept be taken to the American Medical Association for implementation at a national level.

Resolution #6 – Medical Records Custodial Storage

Action: Resolution #6 Referred to MSMA Council

Resolved, that the Missouri State Medical Association work with the Missouri Board of Registration for the Healing Arts to address the issues of custodial records storage upon retirement or relocation.



Reference Committee A: from left, Lauren Umstattd, MD, Columbia; Ted Groshong, MD, Columbia; Michael O'Dell, MD, Kansas City, Chair; Jeff Copeland, MD, St. Charles; and Kirsten Dunn, MD, St. Louis.



Reference Committee B: from left, Brian Biggers, MD, Springfield; Jon Dehner, MD, St. Louis; I.J. Singh, MD, St. Louis, Chair; Charles Van Way, III, MD, Kansas City; and Ms. Lauren Drake, Kirksville.

Resolution #7 – Maternal Mortality Review Board

Action: Substitute Resolution #7 Adopted

Resolved, that the Missouri State Medical Association support the creation and funding of a Missouri Maternal Mortality Review Board; and be it further

Resolved, that the Missouri State Medical Association encourage the State of Missouri to use the CDC WISDOM Database Program for analysis and storage of data.

Resolution #8 – Opioid Continuing Medical Education Programming

Action: Amended Resolution #8 Adopted

Resolved, that the Missouri State Medical Association promote or develop a voluntary web-based opioid education program and make it available at no cost to MSMA members with continuing medical education credit.



MSMA's Legislative Award is presented to Representative Holly Rehder, (left), by President Lovinger, (right).



Charles H. Sincox, MD, (right), receives the MSMA Distinguished Service Award for his leadership and dedication to the Missouri Physicians Health Program from President Lovinger (left).

Resolution #9 – Membership Applications Included with Licensing Information Packets

Action: Resolution #9 Adopted

Resolved, that the Missouri State Medical Association approach the Missouri Board of Registration for the Healing Arts and request that MSMA and local component society member applications be included in the initial mailing to new physicians licensed to practice in the State of Missouri.

Resolution #10 – Collection of Breastfeeding Data at Well-Baby Visits in First Year of Life

Action: Substitute Resolution #10 Adopted

Resolved, that our MSMA explore the feasibility of a study on the collection of breastfeeding data with state Practice Based Research Networks and relevant specialty medical associations.

Resolution #11 – Allow the Missouri DEA Professional Staff Curriculum Time at Missouri Medical Schools to Present Information on Scheduled Drug Prescribing Practices in Missouri

Action: Resolution #11 Not Adopted

Resolved, that the Missouri State Medical Association encourage the Medical Schools to negotiate with the DEA on a suitable number of hours devoted within the curriculum for Missouri DEA Professional Staff to educate the students on scheduled drug prescribing practices within Missouri.

Resolution #12 – Ensuring Safe and Collaborative APN Scope of Practice

Action: Resolution #12 Not Adopted

Resolved, that our MSMA study methods for advancing the scope of advanced practice nurses which include specific safety mechanisms for practice within the state of Missouri; and be it further

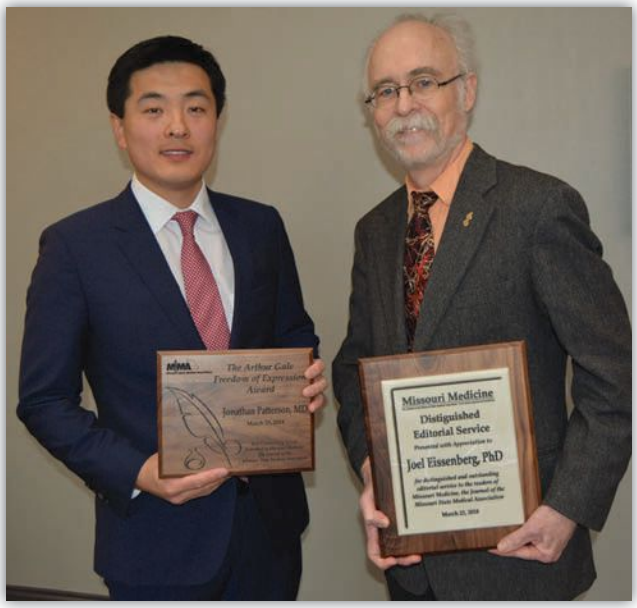
Resolved, that our MSMA work with relevant stakeholders to set parameters for expanding scope of practice, such as establishing a governing organization (such as/or similar to the Missouri Board of Healing Arts) whereby complaints or concerns about an advanced practice nurse operating with expanded scope of practice can be investigated by those with appropriate qualifications to judge inadequate practice; and be it further

Resolved, that if advance practice nurses within Missouri be offered the opportunity for practice without collaboration, that our MSMA work to make this program optional (i.e. that advanced practice nurses wishing to have physician oversight can remain in a collaborative agreement) and that those wishing not to have a collaborative agreement are mandated to meet requirements for independent practice that are comparable to and as rigorous as those faced by practicing medical physicians.

Resolution #13 – Improved Nomination Process

Action: Resolution #13 Referred to MSMA Council

Resolved, that the Missouri State Medical Association appoint an Ad Hoc Committee or Task Force to bring the Council a recommendation for a Nominations process that includes the following: 1) announcement of the candidates to the membership at least 90 days prior to the House of Delegates meetings, 2) open call or self-nominations from the membership, and 3) a reasonable vetting process for all candidates by the Nominations Committee; and be it further



Awardees, from left: Jonathan Patterson, MD, receives the annual "Arthur Gale, MD, Freedom of Expression Award," for Best Perspective in *Missouri Medicine*. Right, Joel Eissenberg, PhD, receives the award for "*Missouri Medicine* Distinguished Editorial Service."



From left, Marc Taomina, MD, Jim DiRenna, DO, and Thomas Allen, MD.

Resolved, that the MSMA Council receive this recommendation by their July meeting, so that a more improved process can be voted on at the 2019 House of Delegates meeting.

Resolution #14 – Return to Prudent Layperson Standard for Emergency Services

Action: Substitute Resolution #14 Adopted

Resolved, that the Missouri State Medical Association oppose the arbitrary denial of payment for emergency services based on diagnostic coding alone, and support the use of the prudent layperson standard; and be it further

Resolved, that this resolution be forwarded to the AMA.

Resolution #15 – Healthcare Finance in the Medical School Curriculum

Action: Substitute Resolution #15 Adopted

Resolved, that our AMA study the extent to which medical schools and residency programs are teaching topics of healthcare finance and medical economics; and be it further

Resolved, that our AMA make a formal suggestion to the LCME encouraging the addition of a new Element, 7.10, under Standard 7, "Curricular Content," that would specifically address the role of healthcare finance and medical economics in undergraduate medical education; and be it further

Resolved, that our MSMA will create a list of resources available on healthcare finance topics and make the list available to undergraduate and graduate medical programs in Missouri. This list will include AMA resources.

Resolution #16 – Content of Advertisement for Pharmaceuticals, which Appear in Medical Journals

Action: Resolution #16 Not Adopted

Resolved, that representatives of your Missouri State Medical Association shall propose Federal regulatory change, to be implemented by the FDA, to enact new regulatory language which mandates that all advertisements for medications must describe that medication's pharmacologic mechanism of action; and be it further

Resolved, that representatives of your Missouri State Medical Association (MSMA) shall carry forward a resolution designed to advocate for this regulatory change, to be considered by the American Medical Association (AMA) at the next meeting of its House of Delegates, in Chicago, in June of 2018; and be it further

Resolved, that the explicit purpose of such a resolution will be to promote regulatory change within the FDA, via governmental outreach by agents such as lobbyists employed by your AMA, to cause there to be a new regulation that requires that a medication's pharmacologic mechanism of action be stated clearly within the product advertising; and be it further

Resolved, that delegates from your MSMA to the next meeting of the House of Delegates of your AMA shall make a reporting of the action, or lack thereof, taken by the AMA House of Delegates, toward this resolution, in a timely fashion.



MSMA members of the Resident and Fellow Section and Medical Student Section. Thank you for participating!

Resolution #17 – Cerebral Palsy

Action: Resolution #17 Not Adopted

Resolved, that your Missouri State Medical Association (MSMA) will collect scientific documentation of the lack of any relationship between events recorded during perinatal monitoring and the outcome of Cerebral Palsy; and be it further

Resolved, that the purpose of this documentation shall be to support the development and passage of a new law, which would bar any alleged tort that purports any alleged relationship between events recorded on a fetal monitoring record and the presence of Cerebral Palsy in a child born in Missouri; and be it further

Resolved, that your MSMA will reach out to the Missouri Hospital Association (MHA), to coordinate a campaign of public information, designed to educate the public and elected officials that perinatal monitoring, although able to provide real-time data about fetal heart rates, lacks any documented efficacy to impact the incidence of Cerebral Palsy; and be it further

Resolved, that your MSMA will initiate a lobbying campaign, alone or with the MHA, to publicize these facts to the elected state legislators within the State of Missouri regarding the lack of efficacy of perinatal monitoring to impact the incidence of Cerebral Palsy; and be it further

Resolved, that your MSMA will lead a scientifically-based initiative, designed to enable outreach to Missouri legislators, to result in the passage of legislation which will eliminate "birth injury" as a possible alleged tort, because perinatal monitoring has no efficacy toward reducing the incidence of Cerebral Palsy; and be it further

Resolved, that representatives of your MSMA shall carry forward a resolution designed for the same purpose, to be considered by the American Medical Association (AMA) at the next meeting of its House of Delegates in Chicago, in June of 2018; and be it further

Resolved, that the explicit purpose of such a resolution will be to promote legislative change by the Congress of the United States, via outreach by agents such as lobbyists employed by your AMA, to procure legislation to outlaw alleged torts purporting a causal relationship between data from perinatal monitoring and the diagnosis of Cerebral Palsy; and be it further

Resolved, that delegates from your MSMA to the next meeting of the House of Delegates of your AMA shall make a reporting of the action, or lack thereof, taken by the AMA House of Delegates, toward this resolution, in a timely fashion.

Resolution #18 – Medicaid

Action: Resolution #18 Not Adopted

Resolved, that in the public discourse regarding the payment for health care goods and services, your Missouri State Medical Association (MSMA) shall forever refrain from making reference to Medicaid coverage as "Health Insurance," because the Medicaid program fails the test of being a type of insurance; and be it further

Resolved, that during the public discourse regarding the payment for health care goods and services, when representatives of the print or electronic media make reference to Medicaid coverage as a form of Health Insurance, representatives of your MSMA shall attempt to contact the reporter who makes such a report, in order to educate them, with this education conveying to the reporter



MSMA Alliance awardees, from left: Jana Wolfe, receives the "Sandra Mitchell Member of the Year" Award; Jennifer Gast receives the "Jean Wankum Spirit of the Alliance Award;" and Sue Ann Greco receives the "Jean Duensing Literary Award."

the fundamental differences between the Medicaid program and Health Insurance; and be it further

Resolved, that your MSMA shall provide data to educate the public that the purchase of health care goods and services by the Medicaid-covered patients occurs at a sizably discounted sum, compared to the sums that would accrue if units of government paid for these goods and service at "market rates"; and be it further

Resolved, that your MSMA shall advocate to its membership, and to members of the print and electronic media, that the Medicaid program should be viewed by leaders of the various units of state or Federal governments as a tremendous benefit provided at a large discount, and not as a tremendous financial burden; and be it further

Resolved, that representatives of your MSMA shall carry forward a resolution designed for the same purpose, to be considered by the American Medical Association (AMA) at the next meeting of its House of Delegates in Chicago, in June of 2018; and be it further

Resolved, that delegates from your MSMA to the next meeting of the House of Delegates of your AMA shall make a reporting of the action, or lack thereof, taken by the AMA House of Delegates, toward this resolution, in a timely fashion.

Resolution #19 – Continuing Medical Education

Action: Resolution #19 Not Adopted

Resolved, that your Missouri State Medical Association will advocate within the state that representatives of one medical specialty shall not mandate any specific number of hours of CME/CPD credits to be completed in any time period, directly, or indirectly, by organizations representing a specialty different from the individual physician's board certification specialty; and be it further

Resolved, that your Missouri State Medical Association shall advocate for a parallel policy at the national level, by introducing an appropriately-worded Resolution at the next meeting of the House of Delegates of the American Medical Association, advocating that no specialty shall directly or indirectly prescribe a minimum number of specialty-targeted CME/CPD requirements for members of another medical specialty that has its own certifying board; and be it further

Resolved, that your Missouri State Medical Association shall specifically acknowledge that it is currently advocating for such limitations, at the state and national level, upon certifying bodies for "Trauma Centers," "Stroke Centers," and "CP Centers."

Resolution #20 – The Opioid Death Epidemic

Action: Resolution #20 Not Adopted

Resolved, that your Missouri State Medical Association (MSMA) shall attempt to persuade Missouri Attorney General Josh Hawley (or his successor) to pursue a civil tort against corporations such as Purdue Pharma, seeking a damage award that would be crippling to the function of companies such as Purdue Pharma, due to their culpability in the current opiate use and death epidemic, for the good of the citizens of Missouri; and be it further

Resolved, that your MSMA shall attempt to persuade Attorney General Hawley to join the four cities in West Virginia, and also pursue an alleged tort against JCAHO, due to their demonstrable negligence in contributing greatly to the current opiate crisis; and be it further

Resolved, that your MSMA shall attempt to obtain a damage award from the JCHAO that will represent a meaningful portion of their assets, such that they will become more motivated to heed rather than to ignore the voices of caution from physicians, which were expressed but ignored by JCHAO leadership frequently after 2001, regarding their misguided policies; and be it further

Resolved, that your MSMA shall carry forward a resolution advocating for pursuit of a civil tort against Purdue Pharma and the JCHAO by the Attorney General of every other state, for consideration at the Annual Meeting of the American Medical Association in Chicago, in June of 2018; and be it further

Resolved, that your MSMA shall develop a press release, suitable to be released to representatives of the print and electronic media, outlining this planned course of action and the rationale by which we shall justify it.

Left, MSMA Alliance President Gill Waltman and spouse Stephen Waltman, MD.

Right, from left: Edmond Cabbabe, MD, Jeff Thomasson, MD, Brian Curtis, MD, and Jo-Ellyn Ryall, MD.











Above, MSMA Past President Jim Wolfe, MD, and spouse, Jana.
Middle, from left: Alliance members Carol Jean DeFeo, Allene Wright, Diana Corzine, Anne Turnbaugh, Mary Catherine Heimburger, and Sandra Murdock.
Lower right: MSMA Past President Fred Hahn, MD, and spouse, Marge.

Winners of MSMA Exhibit Hall Drawings

Congratulations to Bill Turner, MD, Nevada; Tom Greco, MD, St. Louis; Myrna Gover-Havener, MD, Union; and Christopher Swingle, DO, Glendale. They each won $200 for visiting vendors in the Exhibit Hall.

Winners of Convention Evaluation Drawings

Congratulations to Keith Ratcliff, MD, Washington and Karen Goodhope, MD, St. Louis.
They each won $100 for answering MSMA's Convention Evaluation Survey.

Winners of Post-Convention Survey Drawings

Congratulations to Timothy Swearengin, MD, Springfield and David Hardy, MD, Richmond Heights.
They each won $100 each for answering MSMA's Post-Convention Survey.

Sponsors & Exhibit Partners

MSMA thanks the following Sponsors and Exhibit Partners who supported the Annual Convention through educational grants.

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- Medical Group Mgmt Assoc of MO
- Medical Waste Services
- MedPro Group
- Missouri Million Hearts
- Missouri Physicians Health Program
- MO DHSS – Bureau of Vital Records
- MO Drug Card
- MO Registration for the Healing Arts
- MoDocs
- Moneta Group Investment Advisors
- MPM-PPIA
- MSMA Insurance Agency
- MSMA Health Education Foundation
- National Diabetes Prevention Program
- Premier Specialty Network
- Saint Louis University School of Medicine

Credentials & Appointments

The 160th Annual Convention of the Missouri State Medical Association was held at the Renaissance St. Louis Airport Hotel, March 23-25, 2018. Lancer Gates, DO, Kansas City, Missouri, presided as Speaker of the House of Delegates. Parliamentarian was Jo-Ellyn Ryall, MD, St. Louis.

The Committee on Credentials announced that there were 8 Officers, 18 Councilors, and 52 Delegates in attendance for the Opening Session of the House of Delegates.

This report and the minutes of the 159th Annual Convention as published in the May/June 2017 issue of Missouri Medicine were approved.

At the Second Session of the MSMA House of Delegates, the Committee on Credentials reported that there were 9 Officers, 19 Councilors, and 102 Delegates in attendance.

Reference Committee A members were Michael O'Dell, MD, Kansas City, Chair; Lauren Umstattd, MD, Columbia; Ted Groshong, MD, Columbia; Kirsten Dunn, MD, St. Louis; and Jeffrey Copeland, MD, St. Charles. Reference Committee B members were I.J. Singh, MD, St. Louis, Chair; Jonathan Dehner, MD, St. Louis; Brian Biggers, MD, Springfield; Charles Van Way, III, MD, Kansas City; and Ms. Lauren Drake, Kirksville.



The MSMA Nominating Committee members were: Organized Medical Staff Section – James Conant, MD, St. Joseph, Chair; 1st District – Tom Weigand, MD, St. Joseph; 2nd District – Sandra Ahlum, MD, Hannibal; 3rd District – Edmond Cabbabe, MD, St. Louis; 4th District – Martin Willman, MD, St. Louis; 5th District – Mohammad Agha, MD, Columbia; 6th District – William Haynie, MD, Butler; 7th District – Michael O'Dell, MD, Kansas City; 8th District – Brian Curtis, MD, Joplin; 9th District – Omofolarin Fasuyi, MD, Rolla; 10th District – Douglas Wallace, MD, Cape Girardeau; International Medical Graduate Section – Louis DelCampo, MD, Springfield; Young Physician Section – Sarah Florio, MD, Lee's Summit; Resident and Fellow Section – Daniel Young, MD, St. Louis; Medical Student Section – Calli Morris, Columbia.

MSMA Elects Leadership

MSMA Officers

President
Joseph Corrado, MD, Mexico
President Elect
James DiRenna, Jr., DO, Gladstone
Secretary
Brian Biggers, MD, Springfield
Treasurer
David Pohl, MD, St. Louis
1st Vice President
Michael Bukstein, MD, Hannibal
Honorary Vice President
William Huffaker, MD, St. Louis
Honorary Vice President
Robert Gibbons, Jr., MD, Prairie Village, KS
Immediate Past President
Warren Lovinger, MD, Nevada
Speaker
Lancer Gates, DO, Kansas City
Vice Speaker
Sam Page, MD, St. Louis

Councilors

Chair, MSMA Council
George Hruza, MD, Chesterfield (3rd District)
Vice Chair, MSMA Council
Alexander Hover, MD, Springfield (8th District)
1st District
Robert Corder, MD, St. Joseph
2nd District
John Memken, MD, Hannibal
3rd District
Elie Azrak MD, Chesterfield
Robert Brennan, MD, St. Louis
Inderjit Singh, MD, St. Louis
4th District
Kevin Weikart, MD, Lake Saint Louis
5th District
George Hubbell, MD, Osage Beach
Lisa Thomas, MD, Columbia
6th District
David Kuhlmann, MD, Sedalia
7th District
Betty Drees, MD, Kansas City
Lancer Gates, DO, Kansas City
8th District
Mathew Stinson, MD, Springfield
9th District
Lirong Zhu, MD, Rolla
10th District
Sharon Wallace, MD, Cape Girardeau
Organized Medical Staff Section
Peggy Barjenbruch, MD, Mexico
International Medical Graduate
Sri Devi Kolli, MD, St. Louis
Young Physician Section
Ramona Behshad, MD, Chesterfield
Resident & Fellow Section
Nathanial Barbe, MD, Jefferson City
Medical Student Section
Craig Yugawa, St. Louis

Vice Councilors

1st District
Robert Weigand, MD, St. Joseph
2nd District
Sandra Ahlum, MD, Hannibal
3rd District
J. Collins Corder, MD, St. Louis
4th District
Keith Ratcliff, MD, Washington
5th District
Clark Andelin, MD, Mexico
6th District
Benjamin Wilson, MD, Nevada
7th District
Marc Taomina, MD, Lee's Summit
8th District
Brian Curtis, MD, Joplin
9th District
Omofolarin (Fola) Fasuyi, MD, Rolla
10th District
Douglas Wallace, MD, Cape Girardeau
Organized Medical Staff Section
James Conant, MD, St. Joseph
International Medical Graduate
Louis DelCampo, MD, Springfield
Young Physician Section
Sarah Florio, MD, Lee's Summit
Resident & Fellow Section
Daniel Young, MD, St. Louis
Medical Student Section
Scott Berndt, Kansas City



Nathan Nolan, MD, Columbia, provides testimony during the Reference Committees.

AMA Delegates & *Alternate Delgates

Elie Azrak, MD, Chesterfield
Edmond Cabbabe, MD, St. Louis
James Conant, MD, St. Joseph
Rebecca Hierholzer, MD, Leawood, KS
Warren Lovinger, MD, Nevada

*Joseph Corrado, MD, Mexico
*Ravi Johar, MD, Chesterfield
*Michael O'Dell, MD, Kansas City
*Shannon Tai, Lisle, IL, Student
*Charles Van Way, MD, Kansas City

AMA President
David Barbe, MD, Mountain Grove

Alliance

President
Gill Waltman, St. Louis
President Elect
Diana Corzine, St. Joseph

Summary of Council Actions: 2017-2018

Meeting of March 30, 2017 – Kansas City

Warren Lovinger, MD, Nevada, President, presided. Joseph Corrado, MD, Mexico, was elected President Elect. James DiRenna, DO, Gladstone, was elected Chair. George Hruza, MD, St. Louis, was elected Vice Chair. Brian Biggers, MD, Springfield, was elected Secretary. David Pohl, MD, St. Louis, was elected Treasurer.

Meeting of July 16, 2017 – Lake of the Ozarks

The MSMA Council heard at its July 16 meeting at Lake of the Ozarks that the parties involved in the Anthem-Cigna and Aetna-Humana mergers have dropped their pursuit of appeals, so the federal court rulings blocking these mergers stand. MSMA, AMA, and a handful of other states have worked very hard on this issue, and it is a big victory for both organized medicine and patients.

In other advocacy efforts, Anthem has notified its Missouri members that beginning June 1, it will no longer cover emergency department services for conditions deemed not a true emergency. See front page article, above, for more explanation.

The Missouri Department of Health and Senior Services has announced that it will begin rigorously enforcing a law that requires an attending physician to report within 45 days any complications resulting from an abortion procedure. It has issued an official reporting form that includes about a dozen complications. Failure to comply subjects the physician to revocation of license and conviction of a Class A misdemeanor. This applies not only to the physician performing the abortion, but also to any physician treating any complication that arises from an abortion procedure.

MSMA and AMA are working to educate physicians on the federal Quality Payment Program (QPP) which is the current Medicaid physician payment system and what they need to do now in order to avoid payment penalties in 2019. More information, including a helpful instructional video, is on MSMA's website.

MSMA staff reviewed the 2017 legislative session and gave an update on summer advocacy objectives. The Council also heard a review of the rules and regulations promulgated by the Department of Insurance, and are developing legislation for the 2018 legislative session. David Barbe, MD, AMA President, gave a national perspective on some federal issues.

MSMA President, Warren Lovinger, MD, reported on his travels to visit members throughout the state. He has visited 67 of the 114 counties in Missouri. He also represented MSMA at meetings of the Mid-Missouri Medical Society in Rolla and the Tri-County Medical Society in Washington. He attended the annual meetings of Arkansas, Oklahoma, and Iowa, and plans to attend annual meetings in Nebraska and Kansas.

Resolution #11 was referred to MSMA Council by the House of Delegates. The Council adopted the following substitute resolution:

"Resolved, that the Missouri State Medical Association continue to support Medicaid medical benefit coverage for the treatment of dental conditions that complicate or exacerbate systemic medical disease."

2017 Resolution Actions

The Council reviewed the dispensation of the resolutions from the 2017 Annual Convention.

KaMMCO Health Solutions

Partnering with KaMMCO Health Solutions will allow MSMA to license a Health Information Exchange and clinical data analysis program to market to Missouri physicians and hospitals. This service will be a membership benefit with almost no financial risk to MSMA.

Membership

MSMA is ramping up for the 2018 renewal season, and has gained 207 new members for 2017. Ravi Johar, MD, Chair of the Membership Committee, asked that everyone reach out to the new members. MSMA's Membership department has postcards available for contacting those new members. The committee heard an update on student activities, and brain-stormed ideas for engaging residents. More than 120 physicians have signed up for a "White Coat Night" at the ballpark in St. Louis on Friday, August 11, when the Cardinals play the Atlanta Braves.

Report of the Physicians Health

The retirement of Charles Sincox, MD, as Medical Director of the Missouri Physicians Health Program, was announced. Lisa Thomas, MD, Columbia, assumed that role on July 1, 2017. Many thanks to Dr. Sincox for his long years of service. Dr. Thomas emphasized how vital the program is, and how the range of issues has broadened over the years. She introduced the MPHP's new gift acceptance

policy, and encouraged physicians to consider including the program in their will, estate, and trust planning.

Dr. Barbe reported that Bob Bondurant, the MPHP Executive Director, has connected with the Federation of State Physician Health Programs, and will participate in a forum or seminar at the AMA's Interim Meeting in November.

Continuing Education

In 2016 and 2017, the MSMA offered ABIM MOC Points for CME General Sessions during MSMA's Annual Convention. The number of physicians who received ABIM MOC doubled in 2017. In 2018, ABIM MOC points will again offered for the General Sessions. The MSMA's 2018 Annual Convention will be held March 23-25 at the St. Louis Renaissance Airport Hotel.

Accreditation/Activity Review/ Progress Report decisions included accreditations for both the Kansas City Southwest Clinical Society and the Missouri Baptist Medical Center.

The MSMA Insurance Conference is Thursday, July 20, at the St. Louis Renaissance Airport Hotel.

AMA

Edmond Cabbabe, MD, Chair of the Missouri Delegation to the AMA, reported Dr. Barbe is AMA President; David Fleming, MD, has been appointed to the AMA Council on Ethical and Judicial Affairs; Dr. Cabbabe has finished his third three-year term at the AMA Foundation, and has started a four-year appointment on the AMA Council on Long Range Planning and Development; and Jerry Kennett, MD, is on the AMA Council on Legislation. At the annual meeting, Rebecca Hierholzer, MD, chaired a reference committee, and Elie Azrak, MD, served as a reference committee member.

Dr. Barbe commented on the status of health care reform. He also encouraged members to sign up for "AMA Morning Rounds," a daily email push of information that is a synopsis of the day's activities. "Weekend Edition" is a members-only subscription, which summarizes the week's activities.

Alliance

Donna Corrado provided the report on behalf of MSMA Alliance President Marsha Conant, who has been traveling to various counties in Missouri. Barbara Hover has been appointed to the AMA Opioid Task Force and has helped coordinate an informational packet, as well as a DVD in which Missouri Alliance member Kelly O'Leary tells the story of losing her son to an opioid overdose. Mrs. Corrado and Mrs. O'Leary are now offering a 20-minute program for county groups discussing the opioid epidemic and the science of addiction. The Alliance Fall Conference will be October 4-5 in St. Joseph.

Announcements

Dr. Thomas will take the 5th District Councilor seat vacated by MSMA President Elect Joseph Corrado, MD.

Clark Andelin, MD, will take the 5th District Vice-Councilor seat vacated by Dr. Thomas.

Brian Curtis, MD, will take the 8th District Vice-Councilor seat vacated by the resignation of Ellen Nichols, MD.

Dr. Lovinger will take the AMA Delegate seat vacated by the retirement of Ted Groshong, MD.

Dr. Corrado will take the AMA Alternate Delegate seat vacated by the retirement of Nathaniel Murdock, MD.

Councilor District Reports (Selected)

The St. Louis Metropolitan Medical Society Physician Leadership Institute will begin September 16, and run through November 11, offering 21 CME credits. SLMMS and MSMA members receive a discount to participate. The annual Hippocrates Lecture is Wednesday, October 4, in St. Louis. There will be a cocktail hour, followed by dinner and a presentation by Dr. Barbe: "How the AMA Affects Everyday Practice – What Have You Done For Me Lately?" Contact the SLMMS office for more information on any of these programs.

Boone County Medical Society is inviting Cole County physicians to join. Work continues on local membership of residents and fellows, as well. An annual football tailgate will be held this fall in conjunction with the Alliance.

District #8 has been active producing CME programs on sports medicine, field management of heatstroke, and HPV prevention through vaccination and managing HPV. The Greene County Alliance sponsored Dr. Samantha Meltzer-Brody, a psychiatrist from North Carolina, dealing with physician burn-out.

Greene County Medical Society supports the adoption of the St. Louis County prescription drug monitoring program in Greene County and the city of Springfield.

In District #9, Lirong Zhu, MD, reported that the Mid-Missouri Medical Society has been re-activated, with Dr. Lovinger attending the May meeting.

Organized Medical Staff Section

Peggy Barjenbruch, MD, reported on educational sessions presented during the AMA-OMSS meeting,

which included emerging issues in medical staff affairs, individualizing by-laws, physician burn-out in relation to data entry, social media, and the liability involved in texting patients.

Medical Student Section

Efforts to improve recruitment include greater coordination among the chapters, more idea-sharing, and joint events. The focus of the 2017 Lobby Day was a PDMP, and 40-50 students came to discuss the issue with their representatives. The students are excited about promoting the physician mentorship program, and more than 75 physicians are already signed up to be mentors. MSMA will soon send out the first round of sign-ups. The students thank those participating in the program.

Meeting of October 15, 2017 – Jefferson City

The MSMA Council learned about the Show-Me Health Information Network of Missouri (SHINE), a statewide health information exchange set up in partnership with KaMMCO Health Solutions to develop a statewide health information network led by the physician community during the October Council Meeting held in Jefferson City. See complete article, above.

Advocacy

The Council discussed the ongoing battle with Anthem over a new policy that denies coverage for emergency department services if, after the fact, Anthem decides the services were not for a true emergency. This policy appears to violate the "prudent layperson" standard contained in both state and federal law. In recent weeks, Anthem has announced two additional policies that are causing concern. Effective November 15, Anthem will begin denying coverage for emergency department imaging services if it decides later that there was not a bona fide emergency. And Anthem is now denying certain out-patient imaging services provided in hospital-owned facilities, and using aggressive prior authorization to push patients to independent imaging facilities. MSMA has partnered with the Missouri Hospital Association, MAOPS, and Missouri College of Emergency Physicians to work on these issues, and is preparing remedial legislation for when the General Assembly reconvenes in January.

The Council heard an update on the activity with the Affordable Care Act. At the state level, issues include advance nurse practitioners scope of practice and licensure, comprehensive insurance packages, tanning bed prohibition for minors, and tort reform. Dates and sign –up processes for MSMA Physician of the Day program are on the MSMA website.

MSMA President, Warren Lovinger, Jr., MD, reported he has visited physicians in all 114 Missouri counties, the City of St. Louis, and several rural and urban hospitals, and learned of the financial challenges that they are facing. Dr. Lovinger also offered his thanks to societies in Lake Ozark, Washington, Hannibal, and Rolla. In West Central, he and Mrs. Lovinger hosted a barbecue at their home.

MSMA is educating physicians as to what they need to do in 2017 to avoid penalties in 2019 for the Medicare Quality Payment Program. Educational information/videos are on the MSMA website.

Membership

MSMA members are now renewing for 2018, with over 1,700 members already joined, including active physicians, residents, and students. The new MSMA Student Mentorship Program has more than 85 members signed up to be mentors, with the first wave of student/physician match-up underway. Dr. Lovinger applauded the enthusiasm of the new MSMA Resident and Fellow Section leaders, and introduced Joanne Loethen, MD, who is spearheading the resident membership effort. He also introduced Mr. Alex Goodson and Ms. Shannon Tai, Medical Student Section leaders, and thanked them for their excellent work.

Continuing Education

Betty Drees, MD, reported that planning for the CME portion of the Annual Convention is nearly complete. General session topics include Ethics/Palliative Care, Immunotherapy for Arthritis, Practice Management, Heart Failure Medications, and Finding Fulfillment as a Health Professional.

Physicians Health Committee

Lisa Thomas, MD, MPHP Medical Director, reported that the donor-dependent and highly regarded MPHP continues to assist physicians at all levels, and is considered to be a model program throughout the country.

Dr. Thomas reminded members that there are resources available for physicians who are impaired. Initial assessments, treatment referrals, and referrals to attorneys are provided by MPHP. Future developments utilizing teleconferencing to minimize travel, accomplishing initial assessments more quickly, and follow-up.

AMA Report

The Missouri Delegation to the AMA will hear a number of resolutions during the Interim AMA Meeting this month. Missouri will be well represented as the President of the AMA is MSMA's own David Barbe, MD, from Mountain Grove. Jerry Kennett, MD, serves as a member of the AMA Council on Legislation. Ed Cabbabe, MD, is a member of the AMA Council on Long-Range Planning and Development.

Councilor District Reports (selected)

AMA President Dr. Barbe was the guest speaker at the St. Louis Metropolitan Medical Society (SLMMS) Hippocrates Lecture on the topic "AMA – What Have You Done for Me Lately?" SLMMS wrote a letter to the St. Louis Post-Dispatch regarding the imaging issue with Anthem and the inappropriateness of the approach. In response to the opioid epidemic, SLMMS is joining with Clayton Behavioral Partners to present an opioid crisis symposium for practicing physicians early next year. It will be a half-day workshop focused on physician education and response to patients with opioid issues, and will promote St. Louis County's PDMP.

The Joplin medical school has opened with 162 medical students, and there has been a dean change. A Greene County presentation on physician burn-out was well received and attracted several new members. Dr. Barbe will speak to community physicians at the Jordan Valley Community Health Center regarding the opioid crisis.

Cape Girardeau County reported that it is developing a lecture series and applauded a recent successful campaign, which raised $16,000 for the American Cancer Society.

In Medical Student Section news, Mizzou recently hosted a residency panel for undergraduates in coordination with Boone County Medical Society. They received a small grant for the free clinic that they run at Mizzou. They also have an upcoming event, "Pints and Politics," that will focus on the opioid epidemic. Statewide, most schools of medicine have had their recruitment meetings; UMKC has been raising awareness about DACA; SLU has scheduled a roundtable discussion regarding DACA, to include a letter-writing campaign; and will also hold a resolution-writing workshop.

Alliance

The Council received the Alliance Holiday Sharing Card, which collects funds for the Missouri State Medical Foundation. In addition to representation at the North Central Alliance meeting in Novi, Michigan, the Missouri Alliance met for its Fall Conference in St. Joseph in October.

Meeting of January 14, 2018 – Jefferson City

The Council heard an overview on the new KaMMCO Health Solutions, dba SHINE (Show-Me Health Information Network), program, during MSMA's January 14, 2018, Council Meeting in Jefferson City.

The program is completely physician-directed; MSMA will have full control over data usage policies; and it will be a state-wide, MSMA effort. The SHINE program brings new capabilities in analytical reporting. There is a significant differential in member/non-member pricing, so it should provide an incentive for membership. A KaMMCO employee, Jonathan Smith, will start work in February, live in Kansas City, and travel statewide to promote SHINE.

Alexander Hover, MD, SHINE Technical Advisory Committee chair, stated the committee has continued to review the functionalities to be certain that this product is something that can be promoted to individual physicians and small practices. The additional clinical information that is brought by integration with EMRs is very helpful with the daily business of physicians (e.g. – immunization review). Another benefit is population analytics, and the ability to meet federal MIPS reporting requirements, as well as insurance contract requirements. This product is much more than simply a health information exchange. Implementing SHINE may bring a stronger relationship between MSMA and Missouri Hospital Association (MHA), as it has between KMS and KHA. Dr. Hover named the other members of the transition committee: Drs. Jim Schell, John Stanley, Charles Van Way, and Sharon Wallace.

Dr. Van Way shared his experience with the product and pointed out some of the ways in which care can be enhanced by utilizing the product, particularly avoiding duplication of efforts and ensuring that patients are receiving the necessary studies, tests, and procedures. Dr. Hover stated that the ability to access information necessary for quality reporting is a big selling point for the product, and it is not limited to those who are part of a big organization.

Advocacy

In other advocacy efforts, the Council was directed to copies of several letters that have been sent in an effort to oppose Anthem's policy of retrospectively denying emergency room services claims. A letter was also sent by Senator Claire McCaskill to Joe Swedish, the Chairman,

President and CEO of Anthem, wherein she requests specific items of information, including internal emails among senior management regarding their emergency department policies. MSMA, partnering with MHA, MAOPS, and MoCEP, has met with the Attorney General's Chief of Staff and Chief Counsel for Consumer Affairs, as well as the Director of the Department of Insurance (DOI), to discuss the Anthem emergency services claim denial issue. MSMA encourages anyone who knows of a patient who has been adversely affected by Anthem's policy to call MSMA, and they will be instructed on how to file a complaint on the DOI's website. There was discussion regarding whether the patient would be billed for the non-covered services, or the hospital would simply not be paid for those services. The latter would result in fewer complaints, as the patient may not know if the hospital did not get paid. Jeff Howell, MSMA Director of Governmental Affairs, stated that the hospital would have to bill the patient for the services. Peggy Barjenbruch, MD, stated that the patients know about this, as she has had patients come into her office with chest pain instead of going to the ER, for fear of the emergency services claim being denied.

The Council was referred to an example of an AMA sign-on letter, this one addressing the Prescription Drug Benefit Management Model Act. AMA has initiated the effort at the federal level, and then provided the letters to states and specialty societies.

An update on this year's legislative priorities was shared: workers' compensation fee schedules, Medicaid managed care expansion, APRNs, reeling in Anthem's ED denials and their modifier-25 clinical edits. The PDMP will be addressed again, as well as many other items. MSMA is part of a coalition with other groups, working on issues like tanning beds. The Council was encouraged to sign up for Physician of the Day and bring a friend along when serving.

A handout on the Missouri Medicaid ER Utilization Reduction Project reviewed what has happened in Washington with a software vendor that is trying to have early intervention with the "frequent flyers" of emergency rooms. MSMA is involved, so that Missouri Medicaid monies can be spent in the most appropriate fashion.

The Opioid Summit on March 2 in St. Louis is supported by MSMA, in addition to promoting a PDMP in every county in the state.

Warren Lovinger, Jr., MD, President, reported that he and his wife, Marilyn, have visited all 114 counties in Missouri and the City of St. Louis. He has also visited several component society meetings recently, including St. Charles, Pettis County, St. Joseph and the historic "Kansas Connection." They are looking forward to visiting Boone County, Greene County and St. Louis in the upcoming weeks, and thank all of the physicians who have shown them hospitality.

Assistant Physicians

Jim DiRenna, DO, spoke about the inception of the Assistant Physician licensing program in Missouri. Dr. Lovinger introduced Drs. Amanda Turner and Elizabeth Mukherjee of Nevada. Dr. Turner, of Nevada Medical Clinic, is sponsoring Dr. Mukherjee as an Assistant Physician. Each physician shared her perspective, along with details of how they are making the program work.

Membership

The Membership Committee reported that MSMA is developing marketing materials based on awareness, recruitment, and retention. MSMA is becoming more active in social media, with a YouTube channel featuring Dr. Lovinger as well as Facebook, LinkedIn, Instagram, Twitter, and the MSMA website.

AMA Report

Edmond Cabbabe, MD, reported that the AMA delegation, including Drs. Lovinger and Joe Corrado attended the interim meeting in Hawaii in November. AMA representatives were David Barbe, MD, AMA President; Jerry Kennett, MD, Council on Legislative Affairs; and Dr. Cabbabe, Council on Long-Range Planning and Development. Thank you to Drs. Lent Johnson and Ted Groshong for their past service on the delegation. Thanks also to Drs. Nathaniel Murdock and William Huffaker, who have also retired from the delegation. Dr. Barbe responded to several questions regarding AMA's position on different issues. He encouraged members to join the AMA and to contact their specialty representatives and delegates if they have concerns or questions.

Councilor District Reports (Selected)

Robert Corder, MD, reported that Mosaic has pulled out of North Kansas City, and will focus now on their regional area. Buchanan County Medical Society revised their bylaws last year, primarily to allow them to use their money for community action. Sandra Ahlum, MD,

reported that Hannibal Clinic, a private physician group, has sold all its shares to Blessing Hospital from Quincy. Physicians will still work at Hannibal Regional Hospital, and patients will not see any difference. They are very excited about the collaboration and new ownership.

Elie Azrak, MD, reported that the St. Louis Metropolitan Medical Society (SLMMS) is conducting a CME event regarding the opioid epidemic featuring an all-physician discussion panel on April 21 at St. Luke's in St. Louis. Lancer Gates, DO, reported that in Kansas City, a new clinically-integrated network has started as of January 1, 2018; it is a consolidation of the Shawnee Mission Medical Center, the University of Kansas Hospital, and the North Kansas City Hospital, combined with the Kansas City Metropolitan Physicians Association, which is an independent physician organization. The four organizations have come together for a Medicare shared savings program ACO. They have also made a deal with Blue Cross Blue Shield of Kansas City for a quality program that includes several measures, namely, decreased emergency department utilization, decreased readmissions, and colorectal screenings.

Dr. Hover reported that Dr. Barbe will be speaking on physician burnout, and there will be a night at the museum event in Springfield. Brian Curtis, MD, reported that the new Joplin medical school that started in July has 162 students enrolled. Representative Bill White, spouse of Ellen Nichols, MD, is running for a state Senate position (District #32), and is a good advocate for physicians' needs.

Organized Medical Staff Section

Dr. Barjenbruch reported that the OMSS has asked the AMA to urge all accrediting bodies to include the hospital medical staff in the accreditation process. They are working to change the nomenclature of "physician burnout," feeling that the term indicates that the problem is with the physician, when the problem is demoralization due to outside pressures. They also discussed hospital disaster plans, which no longer include physicians since becoming a system; they will push for involvement of physicians in hospital disaster plans. She encouraged members, particularly those from Kansas City, to join OMSS to further this effort. Lancer Gates, DO, spoke of a drill that was held in North Kansas City, with participation required. Dr. Corrado spoke of the "Stop the Bleed" program, a disaster response program in which the American College of Surgeons is very involved.

International Medical Graduate Section

Sri Kolli, MD, introduced Angeline Stanislaus, MD, the Chief Medical Officer for Adults of the Missouri Department of Mental Health. She encouraged members to contact her with any needs they may have in their counties, as the Department of Mental Health has many resources.

Medical Student Section

Shivani Singh reported that they are hosting naloxone trainings at medical schools across the state. They are also having student meetings across the state to discuss policy and regulations, and holding MSS Lobby Day on March 13. She thanked all physicians who have volunteered to be part of the mentoring program.

Appointments and Introductions

Brian Biggers, MD, will fill an open spot on the board of the MSMA Insurance Agency. Dr. Lovinger introduced new MSMA staff members Heidi Geisbuhler – Director of Legislative Affairs and Stephen Foutes – Director of Marketing, and Sarah Luebbert is now Director of Medical Specialty Societies. Ravi Johar, MD, was introduced as the Medical Director of United Health Care.

Reports

The Council heard reports from the Commission on Continuing Education, Missouri Physicians Health Program, Publications Committee, and Actions and Recommendations on 2017 Resolutions.

Alliance

County Alliances celebrated with holiday luncheons, "Student Santas," and adopting families. The Alliance recognized Barbara Hover for having articles published in Alliance in Motion and Physician Family magazines. The Alliance will have Advocacy Day at the Capitol on February 20 and 21, and planning the Alliance Annual Meeting on March 23 and 24 in St. Louis.

Gill Waltman gave an update on fundraisers to benefit the MSMA Alliance Scholarship fund and the MSMF. There will be two evening events during Annual Convention: a women's clothing direct-sale event on Thursday evening and a fundraiser dinner with the theme "Come Fly with Me" on Friday night. **MM**

Reports of the Delegate Handbook: 2017-2018

Secretary

The Missouri State Medical Association had 3,958 members as of December 2017. This was a net loss of 324 members from our membership of 4,282 as of December 2016. Following is a breakdown according to classification.

Year	Students	Residents	Active	Honor	Total
2016	986	154	2,705	437	4,282
2017	790	173	2,585	410	3,958
	-196	+19	-120	-27	-324

The number of member deaths reported during 2017 totaled 19.

The Committee on Nominations, which is appointed by the President, from the House of Delegates, must submit nominations for the following offices:

President-elect to fill the expired term of Joseph Corrado, MD, Mexico.

Three Vice Presidents to fill the expired terms of William Turner, MD, Nevada; Nathaniel Murdock, MD, St. Louis; and Kirby Turner, MD, Poplar Bluff.

A Speaker and Vice Speaker to fill the expired terms of Lancer Gates, DO, Kansas City, Speaker, and Sam Page, MD, Creve Coeur, Vice Speaker. Both are eligible for re-election to their current positions.

Two Delegates and Four Alternate Delegates to the AMA to fill the vacancies created by the expiration at the conclusion of the 2018 Annual Convention of the terms of Delegates: Edmond Cabbabe, MD, St. Louis; Warren Lovinger, Jr., MD, Nevada; and Alternate Delegates: Elie Azrak, MD, St. Louis; Michael O'Dell, MD, Kansas City; Charles Van Way III, MD, Kansas City; and Joseph Corrado, MD, Mexico. The new two-year terms will begin at the conclusion of the 2018 MSMA Annual Convention and end at the conclusion of the 2020 MSMA Annual Convention.

The terms of the following Councilors will expire in 2018: 3rd District – Elie Azrak, MD, St. Louis; George Hruza, MD, Chesterfield; 5th District – George Hubbell, MD, Lake Ozark; Lisa Thomas, MD, Columbia; 7th District – James DiRenna, DO, Gladstone; Lancer Gates, DO, Kansas City; 8th District – Matthew Stinson, MD, Springfield; 9th District – Lirong Zhu, MD, Clayton; Organized Medical Staff Section – Peggy Barjenbruch, MD, Mexico; International Medical Graduate Section – Sri Kolli, MD, Fenton; Resident & Fellow Section – Nathanial Nolan, MD, Columbia; Medical Student Section – Shivani Singh, Fenton.

The terms of the following Vice Councilors will expire in 2018: 3rd District – Inderjit Singh, MD, St. Louis; 5th District – Clark Andelin, MD, Mexico; 7th District – Marc Taormina, MD, Lee's Summit; 9th District – David Barbe, MD, Mountain Grove; Organized Medical Staff Section – James Conant, MD, St. Joseph; International Medical Graduate Section – Ramona Aitken, MD, St. Louis; Resident & Fellow Section – Mihir Brahmbhatt, MD, Columbia; and Medical Student Section – David Alex Goodson, Columbia.

Delegates shall meet during the Annual Convention to elect the Councilors and Vice-Councilors for their respective districts and sections. The election shall be certified to the House of Delegates on the prescribed form which will be furnished.

The entire session will be held at the Renaissance St. Louis Airport Hotel, St. Louis, Missouri. The House of Delegates will hold its First Session on Friday, March 23, 2018, at 8:00 a.m. and the Second Session on Sunday, March 25, 2018, at 8:15 a.m.

Registration facilities will be open on Thursday, March 22, at 3:30 p.m.; Friday, March 23, at 6:30 a.m. and Saturday, March 24, at 6:30 a.m. Registration will be in the Concourse Foyer.

Treasurer

The report of the Treasurer is covered in the Financial Statement which is published in the May/June issue of *Missouri Medicine* and appears on the following page in the Delegate's Handbook.

Executive Vice President

You should be proud that your Missouri State Medical Association is widely recognized as the voice of medicine in Missouri. Be it the Missouri General Assembly, the countless governmental bureaus and agencies, the business community, the insurance industry, hospitals, advocacy groups, or the media, MSMA is considered the leading

advocate for your profession and your patients. Following is just a sample of the many things your MSMA did for you in 2017.

State Legislative Activities

Your MSMA lobbyist team enjoyed a very good year in the state Capitol in 2017. They are quick to credit you and your MSMA colleagues with much of that success, not only for your active involvement in the political process, but also for the respect you command in your community. MSMA is involved in more legislative issues than any other organization in the state; everything from immunizations to scope of practice to tort reform and PDMP. Your lobbyists are among the first to arrive at the Capitol every morning, and among the last to leave at night. Their diligence and effectiveness are unsurpassed. Rather than overwhelm you with details on the myriad bills and issues they work on, I'll refer you to our weekly Legislative Report, which members receive during the legislative session. If you are not reading this publication, you're missing out. If you are reading it, please reach out to your local senator and representative to ensure they know which issues matter to you. Your personal contact amplifies your lobbyists' efforts.

Federal Activities

MSMA's advocacy work is not limited to Missouri's borders. We are involved in a wide range of federal government issues, year in and year out, both alone and with other organizations within the house of medicine. We lobbied federal authorities on such issues as the cost of pharmaceuticals, proposed Anthem/Cigna and Aetna/Humana mergers, brand and generic drug prices, MACRA, and Anthem's flagrant disregard of the "prudent layperson" statutory language. And those efforts weren't limited to letters, e-mails, and telephone calls to Washington, DC. Your MSMA leadership and staff traveled to Capitol Hill to lobby in person in the halls of Congress.

Other Notable Activities

Despite having only the resources and numbers of a medium-sized state medical association, your MSMA is one of the most diverse and active state organizations in the nation. Here are just a few of the activities undertaken on your behalf over the last year.

Your President and MSMA staff attended a number of local component society meetings across the state. From Rock Port to Caruthersville, and from Memphis to Pineville, your leadership is available to all parts of the state, no matter how large or small.

MSMA boasts an outstanding group of member physicians who, twice a year, give the better part of a week to represent you and your patients in the AMA House of Delegates. It is thankless work at times, but there is not a better AMA delegation than yours. Please thank them.

In AMA-related news, we are excited and extremely proud that one of our very own, David Barbe, MD, a past MSMA President, was inaugurated as AMA President in June 2017. In addition to his significant travels, Dr. Barbe has remained available to meet with Missouri physicians and students.

In addition to its regular duties, your MSMA staff also provides top-rate administrative services for several statewide medical specialty societies, and serves on or maintains liaison with many external governmental and private-sector committees, task forces, boards and commissions.

Membership Services and Benefits

Your MSMA staff and leadership are constantly striving to bring even more value to your membership. One constant priority is to improve communications with our members and respond more quickly to answer questions and resolve issues. In the autumn of 2015, we undertook a major overhaul of the MSMA website to make it more useful and user-friendly for our members. More content is constantly being added, with more timely information to help you and your office staff. Also, you can now pay membership dues online and access our membership database to search for your physician colleagues.

Missouri Medicine, MSMA's outstanding scientific journal, is free to you with your membership. It has won seven prestigious Ranly Awards, and now is published in digital format in addition to the paper copy you receive. The journal's scientific content is accessible in the renowned PubMed database, and it enjoys a unique partnership with MedHelp, the world's largest online health community, joining such other notable partners as Johns Hopkins, the Cleveland Clinic, and Cornell University. You can find current and archived electronic editions on our website.

Progress Notes, our monthly newsletter (free to members), is chock-full of timely news items, tips, and

information.

MSMA also offers you free CME credits at the Annual Convention, and numerous other opportunities to earn CME through our statewide CME recognition program. MSMA accredits 28 entities to offer CME, many of which participate in joint providerships across the state. Yet another membership benefit.

I would ask you to also be mindful of the more direct benefits your MSMA membership offers. For example, we are partners with Moneta, an outstanding financial services firm that provides MSMA members with expert financial planning and investment services. We also have a relationship with the Resolve Physician Agency, which offers a wide range of career services, including job placement, contract review and negotiation, practice evaluation, benefits analysis, debt management, and a lot more, all at a discount to MSMA members. We are partnered with the CCPA Purchasing Partners to give you access to up-front discounts on a variety of medical and office supplies, including some vaccines. We have an exclusive arrangement with DocbookMD, which offers you a secure, HIPAA-compliant tool to send messages, patient information, images, and more to your MSMA colleagues through an application on your smart phone or other hand-held device (free to MSMA members). Medical Waste Services offers MSMA members significant savings on medical and biohazard waste removal and treatment services. Our most recent partners include LifeLock, a leading provider of identity theft protection; Officite, a medical practice website development and internet marketing provider; and MedJet Assist, a medical transport service. All of these offer MSMA members a nice discount on their services. Other great offers include the Missouri Drug Card, coding and billing resources, and Go Next for your travel arrangements, all with special rates and savings for MSMA members. When put to good use, MSMA membership saves you far more than your membership dues.

MSMA's Affiliate Organizations

Your Missouri State Medical Foundation has loaned more than $11.8 million to Missouri medical students since its inception more than fifty years ago. The Foundation board made the decision in 2017 to cease its loan program due to the significant number of private lenders already in the market. The focus is now on scholarships for Missouri medical school students. The Foundation is currently funding ten $2,500 MSMA Scholarships at each of the six Missouri medical schools. The Foundation also offers $5,000 matching funds to component medical societies to create their own medical student scholarship fund.

Your Missouri Physicians Health Program is widely considered one of the most successful of its kind in the nation. Last year, the program served 108 physicians who were dealing with chemical, emotional, or behavioral issues. You can assist your colleagues by asking your hospital medical staff and administration to contribute funds to this exceptional and vitally important program.

Your Missouri Medical Political Action Committee is one of the most respected and effective PACs in the state. In the last election cycle, MMPAC contributed close to $120,000 to support physician-friendly candidates across the state. Membership begins at the $100 Sustaining Member level, but you can demonstrate your political savvy by upgrading to one of the Super levels: Super Silver ($250), Super Gold ($500), or Super Diamond ($1,000). Your participation is essential to our political effectiveness.

Your MSMA Insurance Agency was formed by MSMA and is directed by physicians to serve you and your practice. This trusted business provides you with access to all lines of insurance, and provides some financial support for MSMA. Please visit with the Agency's staff during this Convention. The MSMA Alliance has dedicated and enthusiastic physician spouses who work tirelessly to promote health education and support health-related charitable activities, all toward improving the health and welfare of all Missourians. And they are a force to be reckoned with when they march on the Capitol every year to advance medicine's legislative causes.

The Center for Patient Safety is a private, not-for-profit organization originally founded by MSMA, the Missouri Hospital Association, and Primaris. It is dedicated to being the leader in providing solutions and resources to reduce medical errors and improve patient safety, and was among the very first organizations in the nation to win federal designation as a Patient Safety Organization. We are very proud of the Center's work.

Your Organization

It is nearly impossible to list all of the duties and services MSMA provides for the physicians of Missouri. The advocacy and representation, the publications, the CME, the Foundation, the Physicians Health Program,

the Alliance, and your AMA Delegation all create an organization deeply rooted in service to its members and the patients they serve. The MSMA is YOUR organization, and your officers and staff welcome your thoughts on how best to serve you and your fellow members. Feel free to seek them out – at this convention or at any time – and share your ideas.

Staff

On behalf of the staff and the entire MSMA membership, I want to express gratitude for your officers, councilors, committee members, and other leaders who give so much of their time and resources for the betterment of the Association, the profession, and patient care in Missouri.

I also want to express my appreciation for allowing me to work with talented and dedicated MSMA employees whose creativity and diligence are unmatched anywhere. Tom Holloway, your recently retired Executive Vice President, who lobbied and then guided MSMA for more than 30 years. Liz Fleenor, the Director of Communications, is the Managing Editor of your award-winning *Missouri Medicine* and *Progress Notes*, designs all the MSMA member materials, oversees MSMA's website, and staffs the MSMA Alliance. Jeff Howell is the General Counsel and Director of Governmental Relations. In addition to handling legal affairs, he heads your extremely effective lobbying team and writes the *Legislative Report*. Heidi Geisbuhler is your new Director of Legislative Affairs and comes to MSMA with six years' experience working in the capitol. Haley Wansing, the Director of Membership, works tirelessly to maintain and grow the membership base, travels widely to liaison with the local societies, residents, and students, and serves as Executive Director of the Missouri-Kansas Neurological Society Sarah Luebbert is the Director of Specialty Society Services (Missouri College of Emergency Physicians, Missouri College of Obstetricians and Gynecologists, and Missouri Chapter – American College of Physicians), in addition to helping to oversee the SHINE program. Stephen Foutes, your new Director of Marketing, travels the state to personally interact with local societies and members on a first-hand, face-to-face basis and directs MSMA member engagement plans. Benita Stennis, the Director of Scientific Affairs, does all of our meeting planning – including the Annual Convention – and also directs CME credentialing in programming. Cheri Martin, the Office Manager, keeps the office running like a well-oiled machine, day in and day out. She also manages MMPAC's day-to-day activities. Lisa Cassmeyer, the Finance Manager, not only minds the books and the human resources, but keeps a watchful eye on our investments, our taxes, our vendors, and the auditors. Cassie Williams, the Membership Data Manager, tends to our complicated member database and coordinates all the membership billing and mailing for MSMA, and most of our local component societies. Carol Meyer, the Administrative Assistant, is an invaluable team member who helps a great deal with CME and convention details. And Fran Draper is our cheerful and irrepressible receptionist. When she's not answering your call, she's happily helping other staff members with their projects.

And finally, please allow me to thank you, the physicians of Missouri, for the opportunity to serve you in this outstanding organization.

Alliance

I would first like to thank all those individuals who with their talents and time made my year survivable. MSMA staff, particularly Liz Fleenor, have been invaluable. My board, officers, and committee chairs have worked diligently to make this year a success. Again, thank you all, because YOU are the HEART of the Alliance!

My whirlwind year as MSMA Alliance President began surrounded by family and wonderful friends. The invocation was given by my sister; and my best friend, Kathy Weigand, performed my installation. My husband and all of my children were there to support me. And I was honored to have my Senator and close friend, Dr. Robert Schaaf, in attendance.

Our MSMA Alliance mission is "Physician families: Advocating for a healthy Missouri since 1924." Donna Corrado, VP of Health from Mexico, Missouri, educated about the opioid epidemic and encouraged safe disposal of medication. Shweta Agarwal, VP of Membership from Springfield, updated our membership database and worked to increase our numbers. Kirk Doan, VP of legislation from Kansas City, planned and hosted a successful Advocacy Day with our legislators in Jefferson City. Julia Norregaard, VP of Foundation from Columbia, has been busy collecting donations for Medical School scholarships. She has organized a fun evening Friday, March 23 in St. Louis. So plan to "Come fly with her."

I very much enjoyed meeting with Alliance members

around the state. It was an honor to install the officers for the St. Louis, Springfield, Kansas City, and Cape Girardeau County Alliances. In June, I was part of a large delegation from Missouri at the AMA Alliance Meeting in Chicago. I was privileged to be present at the inauguration of our own Dr. David Barbe to the office of President of the AMA. In September, Kathy Weigand and I attended the North Central Regional Alliance Meeting in Novi, Michigan. Our MSMA Alliance Fall Conference was held in October in St. Joseph. I was able to showcase some highlights of my hometown. We toured the Glore Psychiatric Museum and the Walter Cronkite Memorial Museum.

It has been an honor to represent our Alliance members across the state, and what a diverse, talented group of men and women! Just my executive board includes a teacher and part-time Rabbi, a CPA, an attorney, an amateur chef, a county medical society executive officer, an investment advisor, and a Neuro Orthoptist and Professor of Ophthalmology.

One focus I chose for my year was family. Alliance members were recognized at happy occasions and consoled during sad ones. I also chose to make kindness a priority this year. Just a smile, a thank you, or a gift of one's time can touch someone and make this world just a little bit better.

Commission on Continuing Education

The Commission reviewed and approved the following accreditation actions:

Reaccreditations:

- Capital Region Medical Center-Jefferson City, MO
- Esse Health-St. Louis, MO
- Kansas City Southwest Clinical Society-Kansas City, MO
- Mosaic Life Care-St. Joseph, MO
- St. Francis Medical Center-Cape Girardeau, MO

Progress Reports:

The following entities submitted Progress Reports that were approve by Commission:

- Missouri Baptist Medical Center
- Mosaic Life Care

The Commission planned and approved the 2018 Annual Convention CME Program for 17.75 hours of AMA PRA Category 1 CreditsTM. Additionally, the program was approved for 9 American Board of Internal Medicine Maintenance of Certification Points. Following the Annual Convention, attendees were able to participate in an online survey that measured outcomes based on questions designed by the Commission.

In 2017 the following entities withdrew from accreditation:

- SSM Health Care St. Louis (Now nationally accredited by the ACCME)
- Mercy Hospital Washington

The Missouri State Medical Association currently accredits twenty-six entities statewide. MSMA staff submitted the Self-Study and activity files. On November 1, 2017, MSMA staff and Dr. Drees participated in the accreditation conference call. MSMA will receive an accreditation decision in March of 2018.

MSMA staff hosted new staff training at MSMA headquarters in 2017. Additionally, MSMA and Kansas Medical Society hosted a joint provider training in Overland Park, KS, on June 16, 2017.

Membership

MSMA closed out the 2017 membership year with 2,585 active physician members, 724 medical student members, 169 resident/fellow members and 408 retired physician members. AMA reported a total of 2,184 active members from Missouri in 2017. On the state level, MSMA recruited 245 new members in 2017, 104 of which took advantage of the half-price offer in July 2017.

As of January 30, 2018, MSMA counted 1,896 active members for 2018. We've picked up 93 new members, with nine of them being in their first three years of practice. Newly-licensed physicians receive a "Greetings from Your MSMA Council" postcard, congratulating them on their achievements. This includes a link to www.msma.org/big-wins, highlighting our success in the legislature and introducing MSMA's preferred partners.

When physicians join MSMA, they get a personal phone call from MSMA staff and a series of introductory welcome e-mails. Member certificates are mailed upon request. We encourage existing members to embrace those who are new to organized medicine and extend your own welcome to them. If you need help recruiting a physician to MSMA, there are tools on our website at www.msma.org/recruitment-tools.

In addition to the long-standing benefits and resources MSMA provides to our members, we are optimistic about bringing a new statewide health

information exchange, Show-Me Health Information Network (SHINE of Missouri) to members at a discount. SHINE will allow connected physicians to share patient information while employing powerful analytic reports designed to help improve clinical outcomes, reduce inefficiencies, and positively impact patient safety.

The local component medical societies statewide have appreciated their visits from MSMA President Warren Lovinger, MD, this past year. MSMA staff is coordinating with members from inactive local component medical societies who want to revitalize their societies, as well. We've also added a page on our website for assistant physicians to consider affiliate membership in MSMA.

Physicians have the option to sponsor the membership of a medical student when they renew their own membership dues. In addition to that, MSMA is currently launching a new student mentorship program. We encourage Councilors, Delegates, physician leaders, and members to volunteer as a mentor through Haley Wansing, hwansing@msma.org.

MSMA is proud to have such amazing leadership and members. Please read about them, acknowledge their accomplishments in each issue of Missouri Medicine, tune in to our Facebook page at www.facebook.com/momedical, follow us on LinkedIn, check us out on Instagram, and tweet with us @MOMedicalAssn. Share our successes with your non-member colleagues as often as you can. Thank you for your help in making MSMA membership the one membership every physician needs.

Missouri Physicians Health Program

This has been a busy year as indicated by the number of referrals and the numerous Missouri physicians that were assisted. The MPHP provides a variety of services. This includes consultation, intervention, referral for treatment, monitoring and advocacy. The consultive service is especially active. Hospital administrators, physicians, colleagues and family members call the Program Coordinator or Clinical Coordinator to make a referral, discuss a potential referral or brainstorm about the necessity of making a referral. Information is often requested about how to identify problems, what services are available and how to handle issues of impairment should they occur. Many hours are required to meet their needs. The MPHP provides a safe and knowledgeable venue for any question or concern about physician health.

MSMA Insurance Agency

Your MSMA Insurance Agency is an independent insurance agency that offers professional insurance consultation to all Missouri physicians. The Agency offers policies primarily for professional liability and health, but also covers workers' compensation, business office coverage, disability, and life.

The board of the Insurance Agency reviews the budget and financial statements at each quarterly meeting. Agency financial statements are audited and consolidated into the MSMA financial statements.

The board is supportive of the Agency and encourages all MSMA members to contact the Agency for a competitive health insurance or professional liability insurance bid.

Missouri State Medical Foundation

The Foundation has made more than 3,000 medical school student loans over 56 years totaling almost $12 million. In 2017, the Foundation board closed the medical school loan program due to the large number of non-governmental lenders already making medical school loans and the compliance efforts required to sustain a loan program.

The ongoing focus of the Foundation will be medical school scholarships and support of scholarship funds. The board budgeted ten $2,500 MSMA Scholarships at each of the 6 medical schools for a total of $150,000. This gives us a cumulative scholarship total of more than $900,000 awarded to Missouri students attending a Missouri medical school.

The Foundation has also matched funding up to $5,000 for local medical societies and the MSMA Alliance, which have initiated their own scholarship funds. The MSMA Alliance has been and remains an important partner to the Foundation through generous fundraising activities.

Committee on Publication

Volume Number 114 of *Missouri Medicine* showcased national authors and featured ground-breaking scientific articles. This volume published four issues featuring "theme" articles and two issues featuring a variety of

scientific topics and micro-series. It contained 476 pages and 58 scientific articles. The Journal received a record number of scientific manuscripts for peer-review and continued regular departments. We received a satisfactory number of unsolicited articles; acceptance rate is about 75%.

The University of Missouri Press published our near-death experiences articles in book form that was introduced at the MSMA Annual Convention in late March 2017. It is also available on msma.org and the University of Missouri Press website. The title is "The Science of Near-Death Experiences." The response to the Death/Near-Death Experiences series has been exceptional and papers have been cited or reprinted in several books. *Missouri Medicine* continues to receive reprint requests from around the world, the most recent being Spain and China.

In 2017, our Journal presented its third Arthur Gale Freedom of Expression Award to physician John Holds, MD, St. Louis. It is presented annually to the author of the best commentary article published in *Missouri Medicine*, in honor of Arthur Gale, MD, one of the Journal's Contributing Editors and MSMA member since 1976.

Missouri Medicine has been indexed by MEDLINE/Pubmed since 1966. Several years ago, PubMED Central also reviewed *Missouri Medicine* and accepted our Journal for linking. Indexing and world-wide distribution and availability are essential to all medical journals that aspire to national recognition. In June 2017 both MEDLINE/Pubmed and PubMED Central required all of our content to be submitted in XML format. Complying with this critical new requirement has proved difficult and time-consuming. The Publication Committee has expressed to MSMA that having the Journal indexed is critically important to the well-being and viability of *Missouri Medicine*. MSMA Council has emphasized that all resources be directed to meeting the new technical requirements of the indexing services and that Pat Mills assume a direct role in prompt completion of this long-overdue compliance problem. Once successful linking using XML is complete, the plan is to upload back issues to MEDLINE/Pubmed so that the indexed articles there have complete continuity from 1966. Going forward we hope to link all 2018 content on PubMED Central.

Our thanks to the Editorial Board for their good work: Drs. David Fleming, Art Gale, William Reynolds, Charles Van Way, III, Justin Albani, Jeffrey G. Copeland, and Betty Drees. Added experts in 2017: John Holds, MD, Ophthalmology; Kan N. Huang, MD, Hematology/Medical Oncology; and Christopher Carpenter, MD, Statistics/Methodology.

Missouri Medicine provides reprinted papers for several prestigious medical specialty magazines and journals, and also selectively reprints articles from the medical component societies in Missouri and from national publications appropriate for our audience.

The Publication Committee Chair and Editor, John C. Hagan, III, MD, and Managing Editor, Lizabeth Fleenor, appreciate the many contributions of the MSMA, Alliance members, and others who have contributed to *Missouri Medicine*. The Committee appreciates the Association's continued support of the Journal. By any objective criteria *Missouri Medicine* is among the top 5 state medical society journals in the United States.

Young Physicians Section Report

The Young Physician Section (YPS) is meeting again at the 2018 Annual Convention. This will be the fourth consecutive year for a YPS meeting and the third consecutive year for an educational presentation. The 2017 presentation was entitled "Fundamentals of a Malpractice Lawsuit." Two attorneys from Boyle Brasher were the presenters. The presentation was excellent, and a request was made to have the same speakers for 2018.

YPS has developed web pages within the MSMA website to provide more information about the section, and to use as a resource to store the handouts and recordings from educational sessions.

International Medical Graduate Section

Last year has been an exciting year for the International Medical Graduate community in the US, since the physician shortage crisis has been addressed by the state of Missouri through the introduction of the Assistant Physician Bill in 2014. Our state has been first in the nation to address this concern. Since 2014, the bill has been expanded and applications are being accepted to these positions, beginning in 2017.

One in four physicians in the US is trained abroad. This includes American citizens who could not get into a school in the US or those abroad like the Caribbean. Every year the Educational Commission for Foreign

Medical Graduates clears about 8,000 IMGs, not including American citizens who go to schools abroad, and only around 3,000 match. Whereas American graduates, who match in the National Match System at 93.9 %. IMGs only match on average of 42.1% leaving a great majority of unmatched people waiting to work in their chosen profession but doing other jobs to get by.

Due to the predicted shortage of physicians after the implementation of the Affordable Care Act, there has been an increase in the number of accredited medical schools and increase in American medical graduates, but not enough to keep up with the health care needs of our country. International Medical Graduates continue to be a large and consistent part of the American health care system.

AAPI (American Association of Physicians of Indian Origin), under the presidency of Dr. Gautam Samaddar M.D., had its Leadership Seminar in New York in August of 2017, a cultural and media event. They have signed a memorandum of understanding with the AMA to have a "common goal and voice for the physician community" as per Dr. Samaddar's address at the seminar. In addition to the annual meeting, Hurricane Harvey Relief Drive, they made efforts to facilitate teaching, patient-related activities, and research toward Malaysia, Singapore and Thailand, countries that have been attracting patients from around the world for medical tourism. Of note, the local St. Louis chapter, the Indian Medical Council of St. Louis, has named Dr. Annu Terkonda, M.D., as its President for 2017.

The Association of Physicians of Pakistani Descent of North America, under the presidency of Dr. Sajid Chaudhary M.D., hosted the National Health Care Day, where 32 sites all over US served various chapters. This provided free flu shots; eye exams; blood pressure, glucose and cholesterol screenings; and health care presentations. There continue to be other charitable activities, as in food banks and relief missions.

The National Arab American Medical Association, under the presidency of Dr. Rouba Ali- Fehmi M.D., held its 39th National Convention in Chicago in September 2017, and Dr. David Barbe, M.D., was the keynote speaker. The international convention was in Amman, Jordan. They have made plans with the Atlantic Humanitarian Relief to support medical missions in Jordan for the aid of Syrian refugees, among other charitable activities.

Closer to home, Dr. Angeline Stanislaus M.D., has agreed to serve on the MSMA Council in the IMG section. She is a graduate of Tirunelveli Medical College in India, and completed her residency and fellowship in Forensic Psychiatry at Southern Illinois University in Springfield, Ill. She serves as the CMO of Adult Services for the Missouri Department of Mental Health and has private practice in Forensic Psychiatry in St. Louis, Mo. Dr. Stanislaus has extensive expertise in the field of psychiatry, in particularly the legal aspect, and has presented extensively in the past.

Resident and Fellow Section

The Resident and Fellow Section (RFS) continues to engage as an active MSMA section. RFS remains a diligent voice in representing the interests and concerns of our members. Primary objectives over the past year included enhancing the presence and influence of residents and fellows within MSMA, growing awareness of MSMA among non-member colleagues, and solidifying a RFS-specific leadership structure. We have made significant progress on each of these fronts and continue to show growth as a section.

The RFS showed a 30 percent membership increase from 2016 to 2017 and continues to show steady growth into 2018. Though we have much room to improve and better engage our colleagues, the steady growth of our section is encouraging, as similar sections across the nation are experiencing membership declines. We have implemented several strategies to enhance awareness about MSMA and better reach residents and fellows. The RFS now has an established presence on MSMA's website where potential members can access information and quickly link to membership enrollment. We have implemented a Resident Ambassador Program, which represents a core group of MSMA-RFS members at various institutions across the state. These individuals serve as local liaisons of the MSMA mission to their respective training programs. We are pursuing expanded membership options to ease the burden of annual renewal for RFS members. Efforts to enhance relations with residency program directors are underway, so as to better lead on policy issues affecting graduate medical education in Missouri. Additionally, we continue to look for partnership opportunities with our medical student and young physician counterparts, including shared programming at this year's Annual Convention.

At the national level, MSMA-RFS continued to have strong representation at AMA Annual and Interim meetings. Most recently, the AMA-RFS convened their House of Delegates at AMA Interim to vote on RFS policy. Adopted resolutions included requesting ACGME investigation into student and resident suicide events; supporting better critique of requirements to residency and fellowship application processes; advocating for a uniform residency match system and timeline; and reducing requirements for unnecessary components of clinical documentation.

Medical Student Section

A.T. Still University – KCOM

The A.T. Still KCOM MSMA-MSS Chapter successfully held three recruiting events at the beginning of the year. The incoming class of 2021 was welcomed and encouraged to join MSMA-MSS at the annual Taste of Kirksville organization fair, followed by a more in-depth presentation regarding the benefits of being a member with opportunities to be involved on local, state, and national levels. This year, we were also very excited and grateful to have Dr. Warren Lovinger, MD, MSMA President, and his wife Marilyn Lovinger, visit our school and speak with first- and second-year students about the importance of being involved in organized medicine and the impact students can have on issues that will directly affect them as practicing physicians. We are greatly appreciative of the support Haley Wansing, MSMA Membership Director, has provided in helping to recruit students and organize Dr. Lovinger's talk, and she has helped ignite student interest to explore all that MSMA-MSS has to offer.

Our chapter is devoted to service, as demonstrated by our bi-annual Red Cross Blood Drive that our chapter hosts. The MSMA-MSS blood drive is one of the largest school-wide events on our campus, bringing together students and faculty to volunteer as donors and to help run the event. We exceeded our goal for the fall donations and are looking forward to hosting the spring blood drive in two months.

We are currently in the process of planning a Naloxone Training Workshop to be held this spring. A large number of first- and second-year students, both members and non-members, have shown strong interest in the event and we are looking forward to hosting this informative and interactive workshop.

We are proud to continue the success of our organization at KCOM and eagerly look forward to an exciting year ahead.

Kansas City University of Medicine & Biosciences

The Kansas City University of Medicine and Biosciences (KCU) MSMA-AMA Chapter started this academic year by continuing the highly successful "How To Survive Medical School" event for the incoming Class of 2021. We were the first student group to host such a meeting, so attendance was exceptional, and we registered 50+ new members as the first years were eager to get involved. This year, our organization has focused on empowering the communities we serve while bettering ourselves academically and professionally.

We hosted Dr. James Dockins, former healthcare executive and now faculty for the MBA program at Rockhurst University, to discuss with us an often-absent aspect of medical education...health insurance. Further, Dr. Schoen Kruse, associate dean and professor of pharmacology here at KCU, discussed with us his personal health story and the necessity of eating clean and finding space amongst our busy schedules to include exercise. Finally, Dr. Larry Segars of KCU shared with us a very personal and intimate reflection of his battle with cancer, the current state of the opioid epidemic, and an increasing risk of under-treatment within the highly stigmatizing practice of pain management.

KCU's AMA-MSS chapter was immensely service-oriented and focused on giving back to the people of Kansas City and around the country. We volunteered at multiple locations around the city, such as the Ronald McDonald House and American Cancer Society's Hope Lodge, where food products were donated and then used to prepare delicious snacks and meals for the resident families and cancer patients during these trying times in their lives. We also served at the Kansas City Community Kitchen, where volunteers go beyond the norms of other soup kitchens in order to allow the hungry passersby to dine with dignity.

Lastly, our student group members remain ever interested and excited to build upon the successes of those that came before them. While at the National Interim Meeting in Honolulu in late 2017, members were trained in Naloxone administration and learned

more about the governmental arm of the AMA, voting on policy matters that were important to our constituent medical students here at KCU, across the state of Missouri, and even nationally. We look forward to implementing the information learned into amendment writing sessions with our group members, as well as playing host to a community event, training our peers on Naloxone administration, tabling for local treatment programs to share the work they're doing, as well as offering a prescription drug take-back booth.

Saint Louis University

The Saint Louis University Chapter welcomed the Class of 2021 during orientation week with a chapter lunch presentation on AMA, MSMA and SLMMS. At that time, immediate MSMA Past President Dr. Johar spoke to us about the role of organized medicine in health policy and his experiences with MSMA. We again introduced students to MSMA with tables at the Student Interest Group Fair during the first few weeks of school.

This year, our chapter continued its strong commitment to serve the St. Louis community. Chapter leaders Chyleigh Harmon (MS2) and Amanda Khouri (MS2) coordinated student involvement in the Health Protection and Education Services Clinic at the University City Public Library, providing free screenings to 50 patients on the third Saturday of each month.

Beyond SLU, our chapter participated in the larger SLMMS, MSMA and AMA organizations. Shannon Tai (MS2) served as the AMA Missouri Alternate Delegate and will complete her two-year term this upcoming year. Shivani Singh (MS4) served as MSMA-MSS Councilor. Ellen Kim (MS2) served as the MSMA-MSS Secretary/Treasurer. George Kung (MS1) was recently appointed as the SLMMS Student Board Member for 2018. Four of our members attended the 2017 MSMA Annual Convention. Nationally, our chapter sent delegates to AMA Annual in June and AMA Interim in November.

We are dedicated to changing healthcare policy for the better. Shannon Tai (MS2) submitted a resolution regarding myopia and outdoor activity that was advanced through SLMMS, MSMA, and the AMA House of Delegates during the Annual Meeting 2017. Shivani Singh (MS4) also passed a resolution regarding medical student mental health that advanced through the AMA Medical Student Section and AMA House of Delegates Annual Meeting 2017. Dr. Johar and Dr. Cabbabe were kind enough to host a resolution writing workshop for the medical students of SLU and WashU at the beginning of the school year. We hope to produce resolutions and propose legislation in the future.

SLU and WashU partnered again in November 2017 to host a Naloxone training event, sponsored by the MO-HOPE Project, to inform students of the current legal landscape in Missouri for Naloxone, risk compensation and common fears patients have about Naloxone, and how to have a conversation with a patient who might be at risk for opioid abuse and overdose. Our chapter also hosted a round-table discussion about DACA to engage SLU medical students in current national events. AMA President Dr. Barbe spoke to us about the importance of organized medicine as well as the AMA agenda for the coming year. We are grateful for last year's success and hopeful of our chapter going forward.

University of Missouri - Columbia

The MSMA-MSS at University of Missouri-Columbia started off the year with a recruitment table at the orientation week activities fair. We continued this effort with a luncheon meeting to provide information on the benefits of organized medicine. We were able to recruit many new students to join and get excited about opportunities within the MSMA and AMA.

Also within the recruiting process, Mizzou was the first school to have MSMA physician and student mentorships. To date, nearly 50 students and physicians have been connected through this successful inaugural year.

In September, we partnered with the Boone County Medical Society (BCMS) to co-host a Q&A Panel with Mizzou Residency Directors. Furthermore, we hosted an event to educate students and faculty about DACA recipients, and time to call legislators to emphasize the importance of the DREAM act. In October, at our annual Halloween party fundraiser led by Meghna Srinath, we raised and donated $1,000 to MedZou, the free student-run clinic at Mizzou.

During our Advocacy Week, Mizzou focused on raising awareness about the national opioid epidemic. Several of our chapter officers tabled over lunch to encourage students and faculty to call legislators emphasizing the importance of combating this epidemic. In January, Mizzou hosted a Naloxone Training

Workshop. During the workshop, students learned about the current legal landscape in MO for Naloxone, fears about Naloxone, how to identify the signs of an overdose, and how to administer naloxone. This event was a large success.

We were also awarded a Section Involvement Grant from the AMA, in which we help fund a MedZou event, Project Homeless Connect, which helps connect the homeless of Columbia with resources around the city.

As in the past, Mizzou has continued to have strong attendance at national conferences and representation in state leadership. At the AMA Interim Meeting in November, Ariel Carpenter and Jared Lammert represented the medical student section within the AMA House of Delegates, while Junaid Yasin and Scott Berndt represented Mizzou at the Medical Student Section Meeting. For the State MSS, Alex Goodson is currently serving as Vice-Councilor and Sonia Boodram is serving as Vice-Chairperson.

University of Missouri – Kansas City

This has been an excellent year for the UMKC chapter of the MSMA-MSS. We kicked off the year in August with a recruitment event for our first year BA/MD students, for which Haley Wansing, our MSMA-MSS Liaison, kindly travelled to attend. We had such a successful recruitment event that our recruiter, Andrew Williams, was named one of the top 6 AMA recruiters in the country.

Since August, we have had 1-2 meetings each month, including our District Representative speaking about current issues, a DACA Awareness event, resolutions meetings, and more. We also participated in the National Advocacy Week for the first time and held events daily; this was possible thanks in large part to Amudha Porchezhian, our Advocacy Chair, and Nick Yeisley, MSS member. We are so grateful for all the effort they put in to make sure the week went off without a hitch.

Our winter recruitment event targets the third year BA/MD class and students who are joining the UMKC SOM solely for medical school. In the spring, we look forward to one of our most popular events each year, "Differential Diagnosis." At this event, all the attendees are split into groups and compete to determine the best differential diagnosis for a given case. The winning team receives a restaurant gift card and Contigo coffee mugs.

Outside of UMKC, our chapter members continue to be involved on the Regional and National Level. Manna Varghese, our President, is the Region 2 Community Service Chair, a Region 2 Alternate Delegate, and a AMA-MSS Committee on Long Range Planning member. Nick Yeisley is a member of the AMA-MSS Minority Issues Committee. Akash Jani, our Delegate, Priya Jain, our Alternate Delegate, and Amudha Porchezhian are all involved in Region 2 subcommittees. We have had good UMKC representation at national conferences (Interim, MARC, and Annual) in recent years, and we look forward to continuing that in the coming year. We are extremely grateful to the MSMA for all of their assistance in helping us travel to these conferences, which are often far (e.g. Hawaii, Washington, D.C.), and look forward to another wonderful year.

Washington University

The Washington University chapter continued our success in training physician-advocates and healthcare leaders. Last spring, we hosted then-president-elect of the AMA, Dr. Barbe. He gave a well-attended lunch talk, was given a tour of the medical campus, and attended various meetings with administrators and student-leaders. We began the school year with a very successful recruiting event during the First Year activities fair. Our introductory lunch talk featured an update on the current state of healthcare reform from the chair of the Brown School of Public Health, Tim McBride, PhD. We also had a meeting where students were given the opportunity to learn more about SLMMS from SLMMS Executive Vice President Dave Novak and through a discussion with Dr. Cabbabe, Dr. Behshad, and Dr. Corder about medical training.

We have continued to focus on giving future physicians the skills to advocate for their patients. Our advocacy chairs organized a Lobby Day in the spring, and we have facilitated transportation reimbursement for students to testify in Jefferson City. Students also participate in letter writing and phone calling sessions. Last year, we sent 20 students to attend MSMA Lobby Day in Jefferson City, and we are continuing to plan our own additional Lobby Days for April and May.

We hosted a Naloxone training through the organization MOHope, in conjunction with SLU, which was attended by nearly 100 students. State Representative Stacey Newman recently came to campus to give one of her GOV101 training sessions specifically

for medical students looking to become stronger patient advocates.

Individual student leaders are continuing their involvement. Samantha Lund, one of the incoming chapter leaders was recently appointed as the SLMMS Student Board Member for 2018. Craig Yugawa currently serves as the MSMA-MSS chair. WUSM sent 7 students to the AMA Annual Meeting, and 3 students to the AMA Interim Meeting. Several WUSM members continue to serve on AMA standing committees and in Region 2 positions.

As we transition our leadership roles to the next class of medical students, we are excited to continue working to improve healthcare on a local, state, and national basis in 2018. **MM**



Medical Students attend the Second House of Delegates.

Missouri State Medical Association Financial Statement

Statement of Financial Position
December 31, 2017

ASSETS

CURRENT ASSETS:	
Cash and Cash Equivalents	$ 428,219
Short-Term Investments	11,238,775
Accounts Receivable	8,350
Prepaid Expenses	487
Total Current Assets	11,675,831
FIXED ASSETS:	
Land	83,000
Building and Improvements	605,078
Furniture and Equipment	274,966
Less: Accumulated Depreciation	(847,128)
Total Net Fixed Assets	115,916
OTHER ASSETS:	
Note Receivable - MSMA Ins. Agency	209,610
Investment in Subsidiary - MSMA Insurance Agency	(32,018)
Long-Term Investments	2,627,650
Total Other Assets	2,805,242
TOTAL ASSETS	$ 14,596,989

LIABILITIES AND NET ASSETS

CURRENT LIABILITIES:	
Accounts Payable and Accrued Expenses	$ 11,541
Accrued Vacation	71,738
Funds Held for Others	18,709
Deferred Revenue	31,904
Deferred Dues	629,981
Total Current Liabilities	763,873
NON-CURRENT LIABILITIES:	
Non-Qualified Deferred Compensation Agreement	560,128
Pension Benefit Liability	4,590,177
Total Non-Current Liabilities	5,150,305
Total Liabilities	5,914,178
NET ASSETS:	
Unrestricted	8,682,811
Total Net Assets	8,682,811
TOTAL LIABILITIES AND NET ASSETS	$14,596,989

Missouri State Medical Foundation Financial Statement

Statement of Financial Position
December 31, 2017

ASSETS		LIABILITIES AND NET ASSETS	
CURRENT ASSETS:		**LIABILITIES:**	
Cash	$ 492,743	Funds Held for Others	$ 200,469
Investments	294,977		
Notes Receivable - Current	322,345	**TOTAL LIABILITIES**	200,469
Accrued Interest	101,209		
Total Current Assets	1,211,274		
EQUIPMENT:			
Office Equipment	1,091		
Software	10,692		
Less: Accumulated Depreciation	(11,492)		
Total Net Fixed Assets	291		
NON-CURRENT ASSETS:			
Investments	4,555,069		
Total Non-Current Investments	4,555,069		
Notes Receivable - Long Term	1,317,503	**NET ASSETS:**	
Allowance for Doubtful Accounts	(218,880)	Unrestricted	6,664,788
Notes Receivable - Long Term (Net)	1,098,623		
TOTAL ASSETS	$ 6,865,257	**TOTAL LIABILITIES AND NET ASSETS**	$ 6,865,257

Missouri Physicians Health Program Financial Statement

Statement of Financial Position
December 31, 2017

ASSETS		LIABILITIES AND NET ASSETS	
CURRENT ASSETS:		**CURRENT LIABILITIES:**	
Cash and Cash Equivalents		Accounts Payable	$ 6,649
Cash - Checking	$ 86,177	Accrued Payroll Tax	-
Cash - McIntosh Fund	67,972	Accrued Vacation	21,884
Mutual Funds - McIntosh Fund	15,467	Total Current Liabilities	28,533
Certficates of Deposit	135,000		
Accounts Receivable	179,131	**NET ASSETS:**	
Allowance for Doubtful Accounts	(10,200)	Unrestricted	458,787
Accrued Interst	37		
Total Current Assets	473,584	**Total Liabilities and Net Assets**	$ 487,320
NON-CURRENT ASSETS:			
Investments - McIntosh Fund	8,112		
Property and Equipment			
Office Furniture and Equipment	48,077		
Less: Accumulated Depreciation	(42,453)		
Net Property and Equipment	5,624		
Total Non-Current Assets	13,736		
TOTAL ASSETS	$ 487,320		

2018 Annual Convention Attendance

Delegates	*102*
Members	*112*
Exhibitors	*47*
Staff	*21*
Guests	*141*
Officers	*8*
Councilors/Vice	*30*
Alliance	*23*
Total	*446*

(Actual numbers will not balance due to overlaps in positions served.)

Officers
Biggers, Brian, MD
Corrado, Joseph, MD
Johar, Ravi, MD
Lovinger, Jr., Warren, MD
Murdock, Nathaniel, MD
Page, Sam, MD
Pohl, David, MD
Turner, William, MD

Councilors
Azrak, Elie, MD
Barjenbruch, Peggy, MD
Behshad, Ramona, MD
Brennan, Jr., Robert, MD
Corder, Robert MD
DiRenna, Jr., James, DO
Drees, Betty, MD
Gates, Lancer, DO
Hover, Alexander, MD
Hruza, George, MD
Hubbell, George, MD
Kuhlmann, David, MD
Memken, John, MD
Nolan, Nathaniel, MD
Singh, Shivani
Stinson, Matthew, MD
Thomas, Lisa, MD
Weikart, Kevin, MD
Zhu, Lirong, MD

Vice Councilors
Ahlum, Sandra, MD
Andelin, Clark, MD
Barbe, David, MD
Conant, James, MD
Curtis, Brian, MD
Florio, Sarah, MD
Goodson, David Alex
Ratcliff, Keith, MD
Singh, Inderjit, MD
Taormina, Marc, MD
Weigand, Robert, MD

Delegates

District 1
Buchanan County Medical Society
Conant, James, MD
Weigand, Robert, MD

District 2
Northeast Missouri Medical Society
Ahlum, Sandra, MD
Behniaye, Hossein, MD
Bukstein, Michael, MD
Hassien, Joel, MD
Johnson, Lent, MD

District 3
St. Louis Metropolitan Medical Society
Amon, Erol, MD
Best, Michael, MD
Butler, David, MD
Cabbabe, Edmond, MD
Cabbabe, Samer, MD
Dehner, Jonathan, MD
Gale, Arthur, MD
Giuffra, Luis, MD
Goodhope, Karen, MD
Greco, Thomas, MD
Gunby, Mark, DO
Huffaker, William, MD
Johar, Ravi, MD
Lund, Jr., Herluf, MD
Meyer, Jay, MD
Murdock, Nathaniel, MD
Page, Sam, MD
Page, Jenny, MD
Pohl, David, MD
Ryall, Jo-Ellyn, MD
Shariff, Anjum, MD
Singh, Inderjit, MD
Singh, Toniya, MD
Slocum, Stephen, MD
Swingle, Christopher, DO
Thomasson, Jeffrey, MD
Vickar, Garry, MD
Wild, Alan, MD

District 4
St. Charles-Lincoln Medical Society
Andrews, Brian, MD
Copeland, Jeffrey, MD
Moeller, F. Delbert, MD
Sill, William, DO
Tyree, Thomas, MD
Willman, Martin, MD

Tri-County Medical Society
Chalk, David, MD
Raney, Michael, MD
Ratcliff, Keith, MD

District 5
Audrain County Medical Society
Audrain County Medical Society
Taylor, Steve, MD

Boone County Medical Society
Cunningham, Milamari, MD
Groshong, Ted, MD
Hillard, Alan, MD
Hsu, Albert, MD
Kennett, Jerry, MD
Murrell, H. Jerry, MD
Rajcher, Wilma, MD

District 6
West Central Medical Society
Lovinger, Jr., Warren, MD
Turner, William, MD

District 7
Kansas City Medical Society
Allen, Thomas, MD
Collins, John, MD
Florio, Sarah, MD
Hahn, Jr., Frederick, MD
Hierholzer, Rebecca, MD
O'Dell, Michael, MD
Perryman, John, MD
Potts, Donald, MD
Sarma, Subbu, MD
Taormina, Marc, MD
Van Way, III, Charles, MD

District 8
Greene County Medical Society
Biggers, Brian, MD
Blaine, Jim, MD
Knowlton, III, Norman, MD
Reynolds, William, MD
Ridpath, Carlin, MD
Swearengin, Tim, DO
Wolfe, James, MD
Wright, Andy, MD

Southwest Medical Society
Curtis, Brian, MD
Kahraman, Levent, MD

District 9
Mid-Missouri Medical Society
Fasuyi, Omofolarin, MD

South Central Counties Medical Society
Barbe, David, MD

District 10
Cape Girardeau County Area Medical Society
Jung, Chris, MD
Jung, J. Marshall, MD
Pjura, George, MD
Talbert, Clifford, MD

Mineral Area Medical Society
Terpstra, Gregory, DO

Medical Schools
A.T Still Osteopathic School of Medicine
Drake, Lauren
Roberts, Bryan

Kansas City University of Medicine
Hrebec, William
Smutz, Kellen

St. Louis University
Baugnon, Koh (Second Session)
Kung, George (Opening Session)
Tian, Amy

University of Missouri-Columbia
Berndt, Scott
Morris, Calli

University of Missouri-Kansas City
Jain, Priya
Williams, Andrew

Washington University
Lund, Samantha
Yugawa, Craig

International Medical Graduate Section
DelCampo, Louis, MD

Resident and Fellow Section
Barbe, Nathaniel, DO
Loethen, Joanne, MD
Umstattd, Lauren, MD
Young, Daniel, MD

Young Physician Section
Dunn, Kirsten, MD

Delegates-At-Large
Past Presidents
Barbe, David, MD
Cabbabe, Edmond, MD
Copeland, Jeffrey, MD
Hahn, Jr., Frederick, MD
Johar, Ravi, MD
Johnson, Lent, MD
Kennett, Jerry, MD
Knowlton, III, Norman, MD
Murrell, H. Jerry, MD
Thomasson, Jeffrey, MD
Van Way, III, Charles, MD
Wolfe, James, MD

Vice Speaker
Page, Sam, MD

Members
Ahmed, Humza
Andelin, Clark, MD
Aubuchon, Mira, MD
Azrak, Elie, MD
Baber, William, MD
Banton, Milagros, MD
Barjenbruch, Peggy, MD
Barnes, Alicia, DO
Beal, Catherine, MD
Beal, Jr., Eugene, MD
Behshad, Ramona, MD
Berkowitz, Wallace, MD
Boodram, Mitra, MD
Boodram, Sonia
Brasington, Richard, MD
Brennan, Jr., Robert, MD
Calhoun, Joshua, MD
Chang, David, MD
Colbert, Stephen, MD
Corder, Robert, MD
Corrado, Joseph, MD
Corry, Frank, MD
Daus, Arthur Steven, MD
Devineni, V. R., MD
DiRenna, Jr., James, DO
Dombrowski, John, MD
Drees, Betty, MD
Eisenbeis, Jack, MD
Ekunno, Josiah, MD
Ettelson, Charles, MD
Faubion, Matt
Fischer, Keith, MD
Fleming, James, MD
Frederick, Keith, DO
Gardner, Erin, MD
Gardner, Joe, MD
Gates, Lancer, DO
Gibbons, Jr., Robert, MD
Goodson, David Alex
Gover Havener, Myrna, MD
Hardy, David, MD
Hazan, Joseph, MD
Heimburger, Richard, MD
Herzog, Jacques, MD
Hoeman, Michael, MD
Hollocher, Richard, MD
Hover, Alexander, MD
Howard, Barbara, MD
Hruza, George, MD
Hubbell, George, MD
Iqbal, Sherifa, MD
Johnson, L. Mark, MD
Kim, Chul, MD
Kiyanclar, Mehmet, MD
Klatt-Cromwell, Christine, MD
Kraft, Shannon, MD
Kranker, David, MD
Krojanker, David, MD
Kuhlmann, David, MD
Lammert, Jared
Larsen, Christopher, MD
Lester, Lauren
Maitz, Carlos, MD
Mammen, Joshua, MD
McJunkin, Jonathan, MD
Memken, John, MD
Metlis, Schuyler, MD
Montes, Arturo, MD
Moore, John, MD
Nolan, Nathaniel, MD
Oliver, Malcolm, MD
Pamaong, Arturo, MD
Patel, Indu, MD
Patterson, Jonathan, MD
Peterson, Jay, MD
Poggemeier, David, MD
Porchezhian, Amudha
Powell, Jennifer, MD
Rigg, Lee, MD
Rollo, John, MD
Schell, James, MD
Schwarz, Evan, MD
Serota, Pearl, MD
Sincox, Charles, MD
Singh, Shivani
Smith, Stephen, MD
Spencer, Chris, MD
Srinath, Meghna
Stewart, Larry, MD
Stinson, Matthew, MD
Stith, John, MD
Tariq, Manzoor, MD
Taylor, Marsha, MD
Tedrow, Jeff, MD
Thomas, Lisa, MD
Threlkeld, Kevin, MD
Torontow, John, MD
Tuhlei, Breanna
Turner, Amanda, MD
Waheed, Shahid, MD
Wahl, Richard, MD
Wallace, Douglas, MD
Wankum, Robert, MD
Weikart, Kevin, MD
Westerman, Robert, MD
Wilbers, Raymond, MD
Williams, Randall, MD
Winn, Hung, MD
Woods, William, MD
Zacharias, Kulangara, MD
Zacharias, Sara, MD
Zhu, Lirong, MD

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573-634-3415

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312-464-5000

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MO Dept of Health & Senior Services
www.dhss.mo.gov
573-751-6400

MO Dept of Social Services
www.dss.mo.gov
573-751-2086

MO Dept of Insurance
www.insurance.mo.gov
573-751-4126

MO Board of Registration
www.pr.mo.gov/healingarts.asp
573-751-0098

MO Bureau of Narcotics & Dangerous drugs
www.dhss.mo.gov/bndd
573-751-6321

MO HealthNet
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573-751-3425

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National Medicare Helpline
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CLAIM Helpline
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Provider Hotline
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