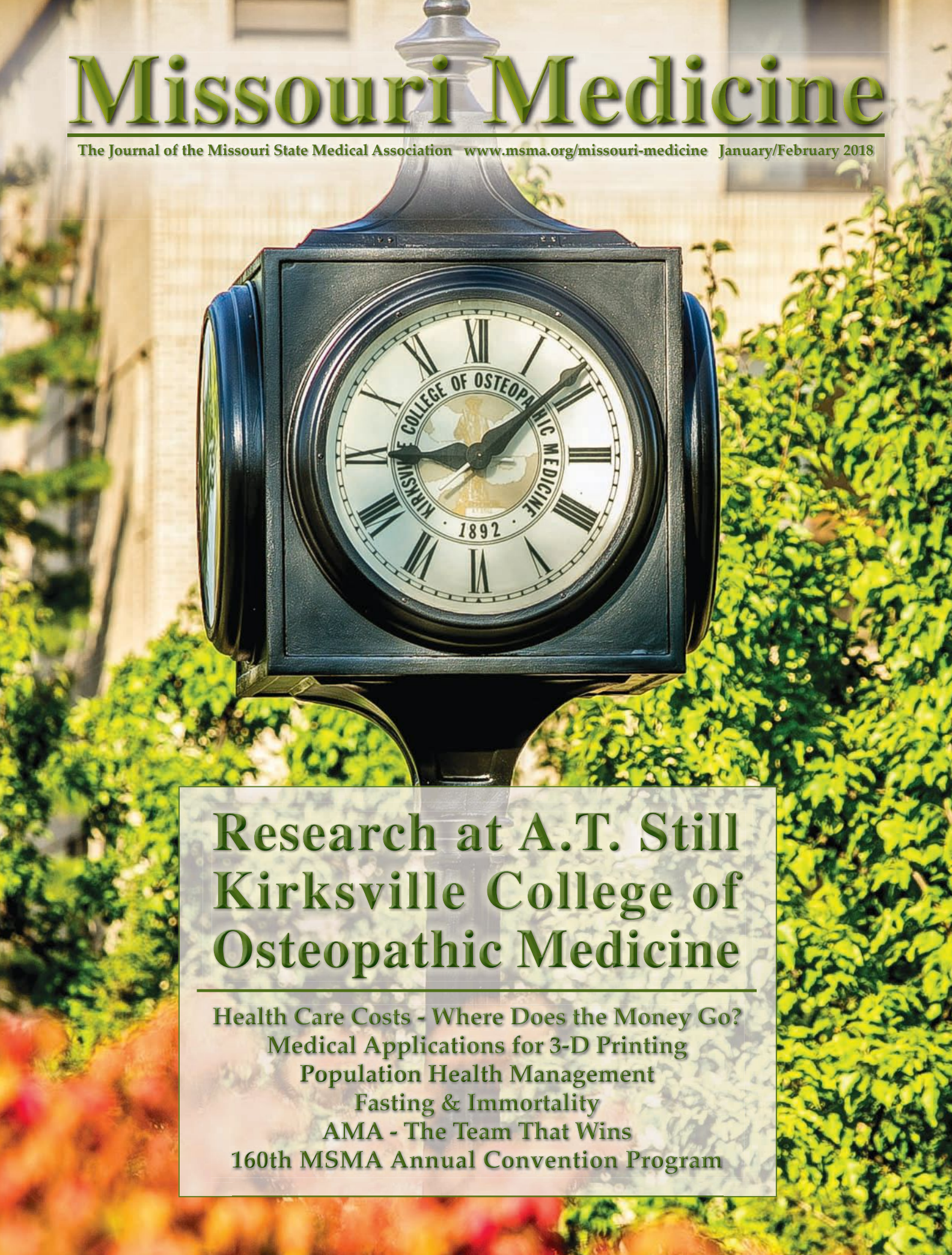
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GUEST EDITOR

Where Does the Money Go?

by Charles W. Van Way, III, MD

"We have met the enemy, and he is us."

-Pogo (Walt Kelley)



The whole country seems to be intensely concerned about just how to lower the cost of health care. It's a little uncertain exactly why that should be so. After all, few people want to lower the cost of, say, the auto industry. Or the electronics industry. Folks want to grow those, don't they? But the health care industry ... 18% of the US economy, most of the new jobs, largest employer in America's small towns, one of the fastest-growing economic segments.

What's not to like? Wanting to cut it back seems counterproductive. Of course, what people really want is to lower the cost of their health care. Health insurance for a family of four is now well up into five figures, which gets the attention of nearly everyone. Many people just don't make enough to pay for that, or have it paid by their employers. Then too, despite Medicare for the old and Medicaid for the poor, a whole lot of Americans can't get insurance, and can't pay for their care. They still get care, but unreliably. Even then, hospitals and docs have to soak up the cost.

You know, putting it this way makes it look as if we don't have a problem with health care costs. We have a problem with health care economics. Or to put it more simply, we have not been smart enough to figure out how to pay for our collective health care. It's very refreshing to see a recent piece in the *Journal of the American Medical Association* (*JAMA*) by a group of researchers from Seattle[1,2], who have actually looked at health care spending over the last 15-20 years.

From 1996 through 2013, total spending increased from $1.2 to $2.1 trillion. The authors analyzed five fundamental factors which contribute to the increase. About 23% of the increase was due to simple population growth. Another 12% was due to aging of the population. So, about a third was due to inherent population factors. Changes in disease prevalence overall were associated with a small spending reduction of around 2.4%. Naturally, some diseases increased (diabetes) and some decreased (cardiovascular disease), but the overall effect was close to nil. Changes in service utilization, interestingly, did not cause increased spending. But changes in service price and intensity accounted for 50% of the increase.

No, they don't add up to 100%. There are other factors, and the analysis was not designed to explain everything.



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What was the money spent on? The biggest increase was in ambulatory care, with hospital care second, and pharmaceuticals third. We've been trying to shift more care from hospitals to the ambulatory setting, but it seems that we've succeeded in increasing both. Other contributors, nursing facility care, emergency departments, and dental care, also showed increases, the amounts were smaller. Although, percentage-wise, emergency departments increased the most of any of the six sites of care. This supports the general perception that emergency department use is increasing dramatically. ED spending rose 6.4% per year over the entire period, the highest of any component. Over the study period, spending rose 3.5% per year, over and above inflation.

Starting sometime before the passage of the Affordable Care Act, most of the Big Thinkers in health care began talking about "bending the cost curve." I should define the group. Big Thinkers are located in major universities, usually have PhDs in economics, are never practicing physicians, and (most importantly) are politically well-connected. Few of them know anything about health care delivery to actual patients. Why we should pay attention to these amateurs is beyond me, but we do. It's sort of like picking Army generals from a group of conscientious objectors. But I digress.

"Bending the cost curve" is one of those phrases which seems to mean something, but is sufficiently vague as to mean pretty much anything. The generally accepted meaning is slowing the rise in health care spending. Given that a third of the rise in health spending is due to population growth and aging, and is pretty much unavoidable, slowing the increase is pretty much all we should be able to hope for.

If we look at the five fundamental factors, we can't do much about disease incidence. Or more accurately, we're already doing as much as we can. Surprisingly, service utilization didn't factor in to the spending increases. Price and intensity appear to be the major areas in which spending might be cut. But this introduces some uncomfortable questions. Just how do we go about doing that? What are our options?

Rationing? Perhaps each hospital should have a cap on ICU days. Or hospitals should have a fixed budget for expensive items, like artificial joints or pacemakers. "Sorry, Mr. Baker, we've used up our quota. You'll just have limp for a while. We'll see about a new hip joint next January." Actually, hospitals in Canada and Great Britain do have these kinds of limits. It's doubtful whether Americans would support such a system. Canadians, at least, can always head south.

What about incentives? Let's pay doctors less, and they'll order fewer tests, and do fewer procedures. Well, we've tried that. It didn't work. Partly as a result, more and more doctors now work for health systems. And surprise! Health systems aren't getting paid less. They're being paid more. Even Medicaid is fairly decent reimbursement for hospitals. Health systems and hospitals have been more effective in lobbying Congress than physicians.

Centralization? We're fairly far along that road, and it hasn't lowered health care spending. If anything, forming larger and larger health care systems over the last 20 years has been associated with increased costs. Things like steel, and automobiles, and computers all have economies of scale. Unit costs get less as organizations get bigger. That's not true in health care. Taking out someone's gall bladder requires a surgeon, an anesthesiologist, nurses, an operating room, and an hour or so of time. That doesn't change for a health system which does a thousand cholecystectomies per day. But the health system puts layers of management and bureaucracy on top of the surgeon and the operating room, so that costs may actually be higher in a large system. That's a very politically incorrect thing to say, but political correctness and truth have a very uneasy relationship with one another. Especially in health care.

What about Medicaid? It's a very important program, but it has major problems. Another politically incorrect truth is that poor people are more expensive to care for than most other people. They have more diseases, are more often disabled, and have fewer resources to care for themselves. If we were to recognize that caring for the poor is an expensive thing to do, perhaps we could design our systems, including Medicaid, to do a better job of it. But we are committed to the proposition that the poor are like everyone else, just with less money and no insurance.



Competition? We have a very competitive medical market place, but it doesn't seem to have lowered expenditures. Of course, that's because much of the competition is in the form of new buildings, or shiny new treatment programs. "Come to our heart center!" "Look at our cancer center!" "Our stroke center is the best in the state." And so on. Folks, all of these things cost money. That's exactly what is meant by "service intensity." And all of those buildings, and new programs, tend to produce a rise in price in order to pay off the bond issues and pay the salaries of the new clinical workers.

Maybe we could close more hospitals. There actually have been a fair number of hospital closures over the years, as hospitals become unable to attract patients and go out of business. But each one has produced great public distress. Certainly, closing non-productive facilities is a legitimate and effective way to cut costs. But the reason hospitals close is that patients are already going somewhere else. And that means that the spending is simply happening somewhere else.

What about limiting the supply of physicians? We did that 20 years ago, when Congress capped the number of resident shots. The result? We have a physician shortage right now, and people are trying to find advanced practice nurses and physician assistants to stretch the existing physician supply, and otherwise fill the gap. We're actively trying to increase the number of physicians. In truth, we have several thousand more physicians than we have training positions, if you count US citizens who are trained in other countries. Rather than cutting the supply, we actually need to increase it. In particular, we need to increase the number of residency positions.

Better organization? Accountable Care Organizations are the current cure-all being pushed by the Big Thinkers. Previous ones included managed care, group practice, managed competition, and capitated payment schemes. While all of these things had at least a few virtues, none of them succeeded in lowering costs. Do we think that ACOs will succeed where managed care failed? Sure, we do. We always prefer hope to experience. The reason history repeats itself, as someone once said, is that nobody listens the first time. Big Thinkers rarely look back.

Pharmaceutical costs? Well, yes. These affect hospital care, ambulatory care, and pretty much all other aspects of the health system. There seems to be a consensus that drug prices are out of control. For example, doxycycline has been around for decades. It's off-patent and generic. But the current price has been raised from $0.03 to $5.00 per dose over the last few years. Wholesale prices rose 8,000%. The polite term for this sort of thing is "market failure." The less polite is "price gouging." Getting drug prices under better control would seem to be an effective way to control spending. Just how to do that is another question. Controlling drug prices is currently being debated in Congress. Anything may happen.

Speaking of Congress, it's clear by now that the Affordable Care Act has not really made health care more affordable. Not only has spending continued to rise, its rate hasn't slowed since, briefly, during the so-called Great Recession. Some fine tuning is in order. Improving Medicaid would be an obvious first step. But with one party wanting to repeal the whole thing, and the other party defending every line of it, "fine tuning" is not going to happen.

While the study by Dieleman, et al,[1] ended in 2013, total annual spending has since risen to $3.2 trillion, 18% of the economy, in 2015.[3] Note that this figure includes some things which were not included in the study. In any case, there has actually been a modest acceleration in the rise in spending.

Paradoxically, as we wring our collective hands about health care spending, an increasingly large number of us actually make our living in the system. It will probably reach 20% of the US economy sometime in the next decade. It's futile to ask whether health care "should" be that large a part of the economy. The real question to ask is, why is it not more affordable for the average citizen? As the food industry has centralized and grown, food has become less expensive. The computer and electronics industries are the same. Health care, like education, professional sports, and other people-intensive industries, has become more expensive.

One major factor, oversimplified though it may be, is that we require a large number of well-educated people to run the health care system. Such people are very expensive. Including, I should point out, doctors. Yes, indeed, we are part of the problem. Will it be hard for us to be part of the solution? Perhaps so. But if we are not heard on this issue, we won't like the results.

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MM

Population Health Management and ACOs: Will They Achieve Their Goals of Better Health and Lower Costs?

by J. Collins Corder, MD

What are the elements of a successful population health management program? What results have been reported for ACOs to date?

Having been in practice for over 36 years, I have seen many technological advances in the diagnosis and management of diseases; much has been taken for granted. We have seen the dissolving of a code of medical ethics that opposed advertising and solicitation of patients, replaced by a system of so-called free-market competition, clinical integration, and the right of insurers and hospital systems to choose their own providers. During this managed care revolution, we have seen reforms that have actually increased costs and are responsible for much of the frustration and anxiety that is so prevalent today among practicing physicians and many patients as well. One thing that remains constant is the patient in need of a competent and compassionate physician who can spend the time to listen to their complaints.

We are entering another era of change in medicine reimbursement as the concepts of population management and Accountable Care Organizations (ACOs) enter the picture. Many feel this is a continuum of what started with the HMOs in the 1990s failing to control costs. The U.S. has by far the highest health care cost of any Western industrialized nation without any discernible improvement in life expectancy or other measures of health care. Many say this is the result under managed care with the formation of hospital and insurance company monopolies, which like all monopolies, bring increased costs.[1]

Whether we like it or not, we are entering this phase and must attempt to improve the quality of care and reduce cost at the same time. I will define what population management is and the desired role of ACOs in trying to achieve the goal of delivering "value-based payment (VBP)."

Value-based care (VBC) or VBP has been broadly adopted in the private market by both commercial insurance payers and employers. According to the Catalyst for Payment Reform's 2014 National Scorecard on Payment Reform,[2] about 40% of payments by private plans to health care providers were based on quality and performance measures. This represented a significant increase in adoption from 2013, when a scorecard found that only 11% of payments were value-based. Assuming that regulations under the Medicare and CHIP Reauthorization Act (MACRA) regulations continue unchanged, VBP will soon be implemented in some form for nearly all Medicare reimbursement, regardless of what happens to the Affordable Care Act.

MACRA has two payment tracks, MIPS and the advanced alternative payment models (APMs). Both tracks meet the broad definition of VBP. This means that by the end of 2017—absent regulatory changes due to administration or congressional action—all Medicare Part B services will be reimbursed through value-based payment of some sort. By the end of 2018, the Department of Health & Human Services has a goal of devoting 50% of Medicare spending toward value-based reimbursement. However, Kaiser reports most physicians are not participating in risk-based contracts, but I suspect this will increase as the number of ACOs grows. Medicare payment reform gives preferential treatment to the APMs created by the ACA Innovation Center and the Centers for Medicare and Medicaid Services (CMS), who have made changes to allow more participants to qualify as advanced APMs.



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The development of ACOs in response to the transition of payments to the VBP model is the central piece necessary for population health management to be implemented. The Medicare Shared Savings Program (MSSP) was established by the ACA to facilitate improved care and reduce unnecessary costs.

There are three types of ACOs: physician-led, hospital-led, and hybrids, which include both physician and hospitals. A study published in the New England Journal of Medicine, as well as one from KPMG, found that ACOs led by independent primary care groups typically saw greater savings than hospital-led ACOs.[3] "ACOs have shown an ability to reduce hospital admissions and health care spending, which is why Congress specified ACOs to be part of MACRA and why CMS has given them a prominent role in achieving its overall goals," says Tim Gronniger, deputy chief of staff at CMS.

The ACO program has evolved in the last five years, and all the changes have been based on feedback resulting in moving from 6 models to 10 in MACRA-proposed rules for 2018.

Defining Population Health Management

Health care reform is feeling the shift away from fee-for-service models toward pay-for-performance, VBP paradigms. And in order for health care organizations to successfully transition, there is an acute need for actionable analysis of data from individual patients and populations.

Multiple definitions for population health management abound. Some feel population health management should be defined the same way public health was defined years ago by C.E. Winslow, founder of the Yale Department of Public Health, as "the science and art of preventing disease, prolonging life, and promoting health through the organized efforts and informed choices of society, organizations, public and private communities, and individuals."[4]

Eighty percent of what affects health outcomes is associated with factors outside the traditional boundaries of health care delivery—health behaviors (tobacco use, sexual activity), social and economic factors (employment, education, income), and physical environment (air quality, water quality).[4] When health care delivery systems expand their interactions with patients to these territories—now the purview of the public health system—outcomes will improve.

Population health management (PHM) is the aggregation of patient data across multiple health information technology resources, the analysis of that data into a single, actionable patient record, and the actions through which care providers can improve both clinical and financial outcomes. The ultimate goal is to improve the health outcomes of the group by monitoring and identifying individual patients within that group, using a business intelligence tool to aggregate data and provide a comprehensive clinical picture of each patient. This allows the tracking of these patients and focusing on the sickest (such as those with diabetes, vascular disease, COPD, hypertension, heart failure or coronary disease), which hopefully will improve the clinical outcomes of these patients while lowering the cost.

EMR systems currently on the market are designed for a fee-for-service world, running entirely on encounter-based medicine. This makes it difficult to manage the health of populations of patients—and difficult to understand the cost of care. Fundamentally, in a population health environment, a health system is managing to margins on a per-member, per-month (PMPM) basis. And in this environment, everyone has to be aware of the cost of care at the point of care. This is not possible without major changes to current EMR software.

Elements of a Successful Population Health Management Program

A successful and well-developed PHM program will give real-time insights to both clinicians and administrators that allow them to identify care gaps within the patient population. This is the key to better outcomes in cost savings, especially in the population with chronic disease. A critical component of PHM is care management; while the objectives of care management can vary from organization to organization, they tend to revolve around improving patient self-management, improving medication management, and reducing the cost of care—such as admission rates to hospitals. In VBP, there is greater financial reward in preventing illness than there is in treating disease. Reducing expenditures can be accomplished by identifying preventable hospitalizations, ED visits, and preventable readmissions. This idea was recently put to the test in the Pioneer ACO program, which scored high for preventative health care measures, generating $147 million in total savings for these initiatives.

All of this leads to population health management in new form. To get there, the industry has to be smart about accelerating development of the right areas and manage expectations about what can be achieved.

For one, the industry needs to do a better job of collecting true patient outcomes data, rather than proxies for care. For example, it inherently does not matter if a

patient with diabetes has had a foot exam—but it matters very much if that foot exam discovers an open wound that will not heal or a severe neurovascular deficit identified to work on ways to prevent the ulcer from developing.

Additionally, organizations must also understand cost at a granular, patient level instead of guessing at costs by looking at the average cost for all patients. That approach is almost meaningless when managing margins.

The Population Health Equation and Return on Engagement

The fundamental, traditional Health Care Value (HV) equation is defined by the Quality of Care (QoC) plus Experience (E) divided by the Cost of Care (CoC), or HV = (QoC+E)/CoC. The fundamental equation of population health is the calculation of Return on Engagement (ROE): the Clinical Outcome Achieved (COA) divided by the Total Patient Investment in a Patient's Health by the Health Care System (TPI), or ROE = COA/TPI.[4]

Described otherwise, "How much does it cost our population health management system to increase a patient's clinical outcome by one unit of measure?" This is why the understanding of costs and patient outcomes is so fundamentally critical to the success of population health.

The motive behind a care management system—services and software—is to reduce the investment (TPI) necessary by the health care system to achieve a unit of improvement in clinical outcomes (COA) by engaging patients in both the numerator and denominator of their own health.

As provider groups assume more financial risks, there are ACO constraints by the Medicare legislation which limit the ability for patients to choose to exclusively use an ACO, as well as what can be done with regard to benefit redesign. A rogue patient that smokes and eats whatever one wants and does not care about BMI or blood sugar basically ties the physician's hands when it comes to quality measures. Since a Medicare ACO beneficiary is "not captive" as in private insurance, they can choose to seek care anywhere outside their assigned ACOs. This places that ACO at the mercy of overspending at another facility not involved in the ACO. Until patients have a monetary stake in their health or penalties if they go outside the ACO system, ACOs will be unable to maximize their results in quality and cost savings.

Evaluating ACO Success

Whether ACOs are living up to the lofty expectations of health care executives and federal policymakers is a matter of rising debate. Saving money while raising the quality of health care has been the central focus of the health care industry—from providers to health insurance carriers—since the arrival of the ACA. Yet, the initial costs of these programs were substantially more than the government anticipated. Kaiser Health News reported that 45% of ACOs cost more than anticipated, and in 2014, MSSP had a net loss of $2.6 million.[5] Some 40% of the participating sites ended their involvement in the program after the first year, they said.

Proponents contend that the early evidence points to increased care quality. But detractors counter that ACOs have failed to produce adequate cost savings and efficiencies, according to commentaries published in the Journal of the American Medical Association.

Kevin Schulman, MD, of Duke University School of Medicine and Harvard Business School, and Barak Richman, of Duke University School of Law, said they aren't impressed with the early findings, pointing to a trio of published evaluations that suggest less-than-ideal efficiencies generated by ACOs.[6]

The first, a comprehensive evaluation of Pioneer ACOs, showed savings in the cost of care to the CMS in 2012 of 1.2%. But after accounting for bonus payments, net savings to CMS were a paltry 0.4%, and 40% of the participating sites ended their involvement in the program after the first year, they said.

A second analysis by CMS showed smaller increases in total Medicare expenditures for ACO-aligned beneficiaries, but the result was substantially reduced by the second year of the program and didn't include incentive costs to ACO participants.

The third report, an evaluation of the CMS Medicare Shared Savings Program, found that the 2012 ACO cohort showed a lower cost of care but triggered CMS bonus payments that exceeded those savings. Then, the 2013 cohort didn't save money at all.

Furthermore, none of those evaluations, Schulman and Richman said, considered the costs to implement the ACO. They concluded that of the several iterations of ACOs, none have meaningfully reduced the cost of care, which begs the question whether the ACO concept itself is sound. This is an important consideration, they said, because ACOs carry a substantial cost to those outside Medicare.

Since this results in a lack of negotiating power on the part of private health plans, Schulman and Richman said that two strategies have emerged to maintain affordability in the health insurance market: high-deductible health plans, and narrow-network health plans with significant cost sharing. Co-payments

for care under these offerings are often unaffordable, leading the authors to conclude that the ACO model may have weakened the financial protection that is the core purpose of health insurance, while undermining the ACA's goal of expanding coverage.

Schulman and Richman suggested paying physicians and physician-led groups to keep patients away from and out of hospitals, away from costly facilities and tests, and use inpatient services only when other low-cost mechanisms are not effective.

In their view, the ACO model has also accelerated the trend of hospitals acquiring physician practices, enhancing their market power. Consolidation is responsible for sharp price increases across markets within states, they argue, with monopoly hospitals, those that dominate a local market with no real competition, showing 15.3% higher prices than hospitals in competitive markets.

Seeing the matter differently are Zirui Song, MD, of the Department of Medicine at Massachusetts General Hospital, and Elliott Fisher, MD, of the Dartmouth Institute for Health Policy and Clinical Practice. With limited evidence of the effects of ACO contracts, and most studies containing fewer than two years of follow-up, they said, reversing course so early in ACOs' lifespans would be a mistake—particularly since evidence on quality has been promising.[7]

Quality improved in both process and outcomes in the Blue Cross Blue Shield of Massachusetts Alternative Quality Contract, they said, with similar gains for Medicare beneficiaries in ACOs. For example, process measures included adherence with guidelines for screening for colorectal or breast cancer, and follow-up testing for patients with diabetes or coronary artery disease; outcome measures included the proportion of patients with diabetes achieving target blood pressure, lipid levels, or hemoglobin A levels. In both populations, bonuses for ACOs were highly contingent on achieving gains in quality.

Medicare beneficiaries also reported better access to care, and for those with multiple chronic conditions, much higher subjective ratings of the overall quality of care. That evidence, Song and Fisher contend, is grounds for "cautious optimism."

What's Next?

CMS is developing "refinements" to overcome these ACO early failures, culminating with the new APM models of higher levels of financial risk and reward to the providers. They maintain that opportunities for making the model more attractive involve supporting a gradual transition to reasonable risk-bearing that offers greater financial rewards for physicians. I would advocate a transition to enterprise liability, wherein the ACO, not the individual physician, would be liable for malpractice claims.

More clarity is needed to determine ACOs' efficacy, be it failure or success, and the only thing that can deliver that clarity is time.

These models focus not on historic performance but more on current performance efficiency at managing care, not for "picking low-hanging cost-cutting fruit." Physician behavior must change in this approach to care, and hopefully not physician practice to deliver the best of care.

Will these "modern" pay-for-performance models support previous failed studies in England and the U.S. that cost, efficiency, and quality are not improved? Are they the same old wine in new bottles? Will they be rejected again as the "gatekeeper" perception was in the 1990s? Will the Medicare Advantage Plans continue to be more costly and more cuts to providers occur in the future as the insurance companies continue to take their 15% cut? Should the patient be part of "cost responsibility" when they do not lose weight, continue to smoke, fail to take medication, ignore ACO guidelines in utilization of the ACOs services, or utilize their PCP first before needless ER visits?

The Physician's Foundation survey[8] continues to show physicians are demoralized and dispirited in a dysfunctional health care delivery system. Policymakers might benefit from consulting and listening to those who actually treat the patient, the practicing physician, and not solely to those like the Dartmouth Group.

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Don't Blame Doctors for Medication Nonadherence

by Skeptical Scalpel, MD

The *New York Times* says nonadherence* to prescribed medications is "an out-of-control epidemic" in the U.S. and quotes a review in *Annals of Internal Medicine*, which found "20-30% of medication prescriptions are never filled, and approximately 50% of medications for chronic illness are not taken as prescribed."

For example, "a third of kidney transplant patients don't take their anti-rejection medications, 41% of heart attack patients don't take their blood pressure medications, and half of children with asthma either don't use their inhalers at all or use them inconsistently."

Many reasons for nonadherence were discussed — aversion to chemicals, a desire to do things "naturally," pills represent reminders of sickness, self-experimentation with stopping medications and noticing no change in perceived health, and drug costs.

Another *Times* piece discussed a study showing that Medicare patients fail to adhere to prescriptions for high-intensity statins. At six months after discharge, 58.9% were taking their high-intensity statins as prescribed, and at two years, the percentage had fallen to 41.6%.

The study involved almost 30,000 Medicare beneficiaries who all had Medicare fee-for-service and pharmacy benefits coverage.

In addition to the reasons listed above, some say the problem must be because doctors are not to educating their patients about the importance of taking their medications.

From the *Times*: the senior author of the statin study, Dr. Robert S. Rosenson, a professor of medicine at the Icahn School of Medicine at Mt. Sinai, said, "Health care providers have an obligation to educate the patient. We need to stress the evidence that supports the therapy. People who continue the medicine have progressively fewer adverse outcomes over time. Once you have a heart attack, this is prevention for the rest of your life."

Skeptical Scalpel is a retired surgeon and was a surgical department chairman and residency program director for many years. He is board-certified in general surgery and critical care and has re-certified in both several times. He blogs at SkepticalScalpel.blogspot.com and tweets as @SkepticScalpel.
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Figure 1. Health in the U.S., Causes of Death for 2014

All causes	2,626,418
Diseases of heart	614,348
Malignant neoplasms	591,700
Chronic lower respiratory diseases	147,101
Unintentional injuries	135,928
Cerebrovascular diseases	133,103
Patient nonadherence	**125,000**
Alzheimer's disease	93,541
Diabetes mellitus	76,488
Influenza and pneumonia	55,227
Nephritis, nephrotic syndrome and nephrosis	48,146
Suicide	42,773

Adopted and amended from Centers for Disease Control, Table 19, Leading causes of death and numbers of deaths, 2014

However, the full text of the paper does not mention the words "educate" or "education." What the paper says is this: "Reasons for statin down-titration or discontinuation were not analyzed because these data are not available in Medicare claims. Lower medication costs, cardiologist visits, and cardiac rehabilitation may [emphasis mine] contribute to improving high-intensity statin use and adherence after myocardial infarction."

The *Annals* review estimated that nonadherence leads to 125,000 deaths and as many as 10% of hospitalizations every year at a cost of at least $100 billion—possibly as high as $289 billion.

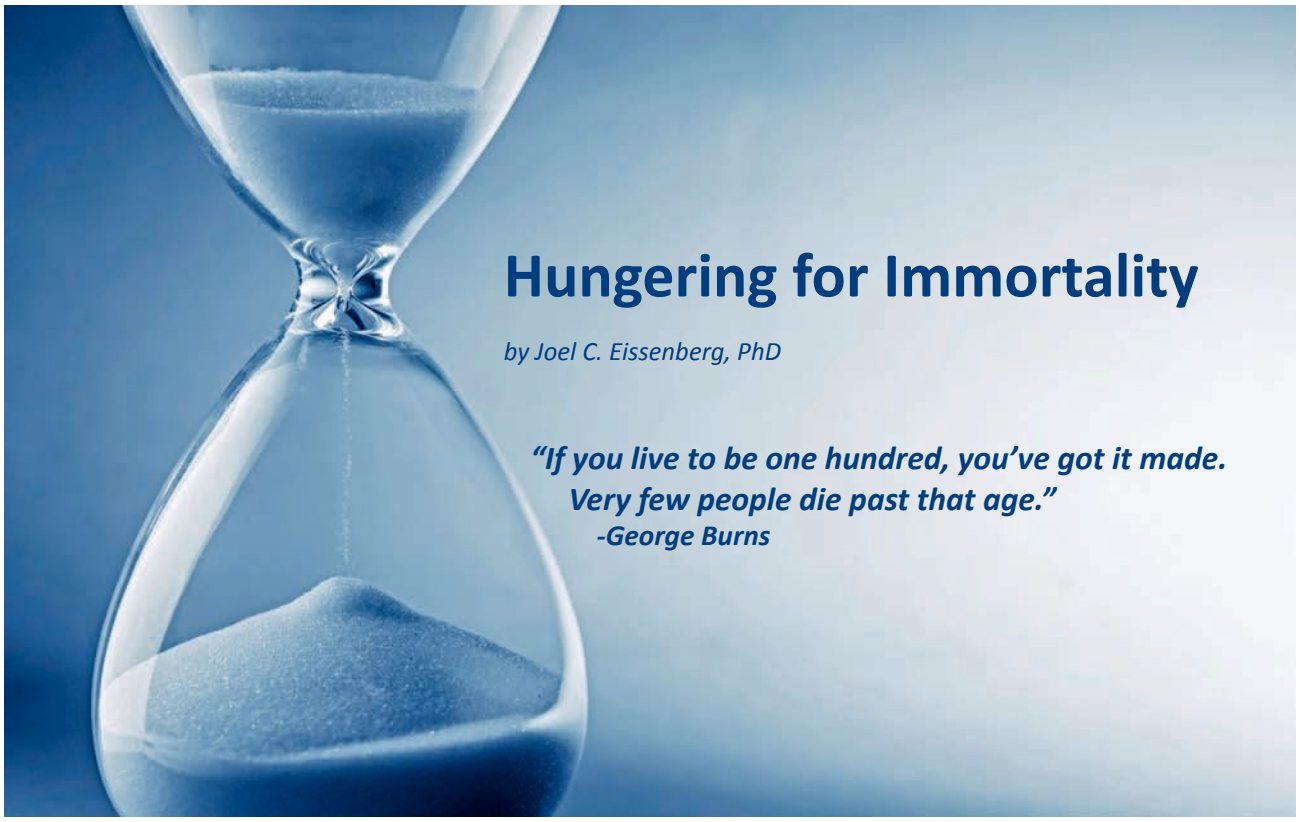
Consider this. If the Centers for Disease Control and Prevention tracked medication nonadherence, it would rank as the sixth leading cause of death in this country. The most current data are from the CDC's report, Health in the U.S., Table 19. See Figure 1 with medication adherence added.

Let's look at another issue — cigarette smoking. Despite extensive educational and other measures, it has taken more than 50 years to reduce the percentage of US adults who smoke cigarettes from >42% to about 15% which means 36 million people still smoke.

Rather than blaming doctors for the problem of medication nonadherence, let's focus on ways to enlighten the patients. No foundations or patient advocate groups are promoting awareness of nonadherence. There are no colored ribbons, no fundraising walks, runs, jogs, trots, or swims.

For starters, I suggest this slogan, "If you want to make it, you've got to take it.

Editor's Note: Many physicians, including myself, continue to use the word 'noncompliant' for this problem. That is now deemed politically incorrect by the word police.* **MM



Hungering for Immortality

by Joel C. Eissenberg, PhD

"If you live to be one hundred, you've got it made. Very few people die past that age."
-George Burns

Abstract

Beyond avoiding risky behavior—smoking, substance abuse, obesity—and embracing healthy habits like exercise, a balanced diet, and non-obese body weight, are there things we each do today to significantly extend our lifespan? Caloric restriction is the only behavioral intervention consistently shown to extend both mean and maximal lifespan across a wide range of species. In most cases, the lifespan extension is accompanied by a marked delay in the onset of age-associated disease and infirmity.



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Introduction

Public health measures like sanitary sewers and water purification, together with the discovery of antibiotics and vaccines, have greatly extended human lifespan. An American born today can expect to live an average of 78.7 years, although significant regional and racial disparities exist. Have humans living in western societies in the 21st century achieved maximum lifespan, or are there additional interventions that could extend lifespan further?

There are many things everyone can still do to increase their likelihood of a long life: don't smoke, wear sunscreen, engage in regular exercise, maintain a healthy body weight, don't drive while texting. Some factors are beyond our control, such as genetics. But which of us would not eat or drink a magic elixir that would make us live longer? The best medical evidence suggests that it's not what we eat, but what we don't eat, that could add years to our lives.

Aging is the confluence of age-associate conditions ranging from wrinkles and baldness to cardiovascular disease and cancer. Aging-associated diseases can and do occur in young patients with either genetic predisposition or due to environmental insults. However, these diseases will eventually develop in aging individuals even without any specific genetic or environmental etiology if they live long

enough. The result is an age-dependent increase in personal suffering and a substantial societal burden imposed by the aging demographic. Increased lifespan free of chronic illness is a highly desirable goal.

In a previous issue of *Missouri Medicine,* I discussed the theory that progressive loss of DNA from the ends of our chromosomes could be mechanistically associated with aging.[1] As I pointed out then, "[t]he most consistent predictor of longevity in every organism tested is caloric restriction." Here, I summarize some of the evidence that caloric restriction can extend healthy lifespan.

Caloric Restriction and Longevity

Caloric restriction refers to reduction in caloric intake short of malnutrition, typically a reduction of 20-50% compared to *ad libidum*. The association between caloric restriction and longevity has been known for over eighty years.[2] Studies in yeast, protozoa, nematodes, insects, fish and mammals have so far shown that caloric restriction is the only known intervention consistently and reproducibly associated with prolonging lifespan.[3,4] In some experiments, the lifespan extension can be 1.5-3 fold! The longevity benefit of caloric restriction follows a U-shaped curve; modest-to-significant caloric restriction can significantly extend lifespan, but when caloric restriction becomes frank starvation, the longevity benefit is reversed (Figure 1).

But how relevant are the data in model organisms, which tend to be genetically homogeneous and are tested under highly constrained environmental conditions, to genetically diverse, free-living humans? Various large- and small-scale studies over the past 60 years suggest that caloric restriction can slow age-related degeneration in metabolic regulation, muscloskeletal systems and cognition (Figure 2).[5] The most complete study on the effect of caloric restriction in humans was the CALERIE (Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy) study, which ran from 2007 to 2015. The goal of the CALERIE study was to test the hypothesis that two years of sustained 25% caloric restriction in men age 21-50 and women age 21-47 can slow aging and protect against age-related cardiovascular disease risk, insulin sensitivity and secretion, immune function, neuroendocrine function, cognition and quality of life.[6] Two hundred and thirty-eight volunteers were enrolled, 220 were randomized, and 218 started the assigned intervention. The results demonstrated some of the caloric restriction-dependent effects reported for mammalian models, such as improving cardiovascular biomarkers and insulin sensitivity.[7,8] It seems likely that at least some of the exceptions are due to the more modest

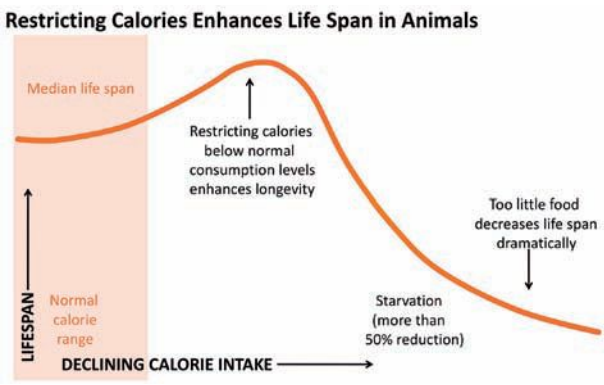


Figure 1. The benefits of caloric restriction follow a U-shaped curve.
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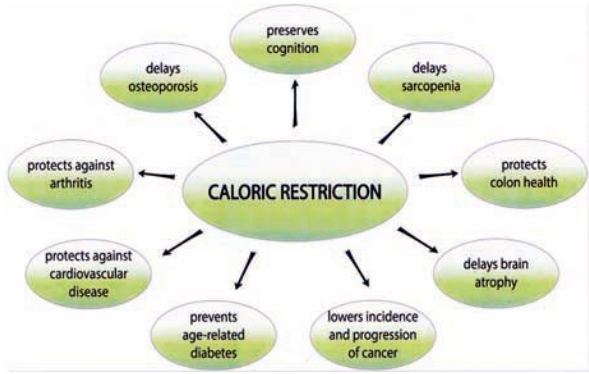


Figure 2. Proposed benefits from long-term caloric restriction.
From Reference 5.

caloric restriction achieved by participants in the CALERIE study, compared to the enforced restriction imposed in the animal studies.[7]

All Calories Are Not Equal

A standard human diet contains various classes of macronutrients (carbohydrates, proteins, fats) and micronutrients (vitamins, minerals). Recent studies in performed on the macronutrients involved in caloric restriction indicate that the ratio of protein to carbohydrates is important.[9-11] Specifically, Simpson et al.[11] conclude that enhanced longevity is associated with an optimum ratio of protein to carbohydrates of about 1:10, with the protein content of the diet as low as 10%. Within the category of dietary protein, there is evidence that reducing the intake of the essential amino acids methionine and tryptophan, as well as branched chain amino acids, can delay aging in several animal models.[10,12] The typical American diet consists of 15% protein, 50% carbohydrate and 35% fat,[13] so even without caloric restriction, this would entail a 33% reduction in average calories from protein.

Better Living Through Geroprotective Chemistry?

Let's face it: caloric restriction is uncomfortable. Sure, you get to live longer, but is that really "living?" If we could take a pill that mimicked the anti-aging effects of caloric restriction without the discomfort of eating less, lots of folks would be on board. Not surprisingly, there is considerable interest in research and development of caloric restriction mimetics. Also called "geroprotectors," these compounds have been shown to prolong lifespan in model systems, making them candidates for geroprotecting drugs in humans. Some examples that have attracted recent attention.

Resveritrol

Resveritrol is a naturally occurring polyphenol and secondary plant metabolite enriched in peanuts, pistachios, grapes, red and white wine, blueberries, cranberries, cocoa and dark chocolate. In cells, resveritrol enhances the activity of Sirt1, an enzyme that removes acetyl groups from selected proteins, thereby changing cell metabolism and increasing mitochondrial function.[14] Evidence that resveritrol is geroprotective comes from a number of model organism studies, although results have been inconsistent.[15] Some human studies showed promising improvements in markers associated with longevity using controlled dosages of resveritrol.[15] However, field studies using dietary resveritrol are not so promising. For example, a cohort of 283 men and women over the age of 65 in the Chianti region of Italy were followed from 1998-2009, and total urinary resveritrol metabolites and all-cause mortality, as well as markers for inflammation, were recorded.[16] No significant association was found between total urinary resveritrol metabolites and inflammatory markers, cardiovascular disease or cancer, nor were they predictive of all-cause mortality. This suggests that dietary levels of resveritrol may not have the lifespan-extending effects in humans that were found in studies of superdietary levels of resveritrol in laboratory studies of model organisms.[15]

Rapamycin

Rapamycin was initially isolated as an antibiotic secreted by the soil bacterium *Streptomyces hygroscopicus* found on Easter Island (known locally as Rapa Nui).[17] Rapamycin has long been used clinically as an immunosuppressant to prevent organ transplant rejection. Several studies found that rapamycin can extend lifespan in mice.[18-22] One report describes the use of rapamycin to improve immune parameters in aged humans.[23] However, adverse metabolic side effects such as insulin resistance and dyslipidemia make chronic rapamycin use as a lifespan-extending drug in humans untenable.[24] Alternatives, such as combinations of low-dose rapamycin with other drugs, as well as rapamycin analogs that lack the side effects, are the subject of active research.[25,26]

Metformin

The oral drug metformin is a safe frontline therapy for prevention and treatment of type 2 diabetes. Compared to alternative anti-diabetics, it is also reported to decrease cardiovascular disease risk, cancer incidence, and overall mortality.[27,28] The association of metformin with longevity has been extensively documented in nematodes[29] and rodent models.[30-32] In mice, metformin causes similar changes in liver gene expression profiles as caloric restriction.[33]

Can Metformin extend longevity in humans? An interdisciplinary consortium is currently pursuing a large-scale clinical trial called the "Targeting Aging with MEtformin (TAME)" project, sponsored by the American Federation for Aging Research.[34] TAME is a double-blind, placebo-control study to test whether metformin can delay the onset of diseases such as cancer, cardiovascular disease and cognitive decline, as well as delay mortality. If so, it will catalyze the development of additional drugs aimed at treating human aging and improving resiliency in older adults.[35]

For cancer and HIV drugs, the current approach is to use combination therapy with multiple drugs that target different pathways. Among its advantages, combination therapies can mean reduced dosages compared to using a single drug. Thus, the future of geroprotectives may lie in the compounding of several molecules, perhaps tailored to the specific physiology of each patient.[36]

Caloric Restriction vs. Intermittent Fasting

For free-living animals in the wild (including our ancestors at the time *Homo sapiens* first appeared), intermittent aperiodic feeding and fasting based on food availability is a constant reality. Given the chronic discomfort that most people experience from caloric restriction, considerable interest has focused on whether the benefits associated with chronic caloric restriction can be achieved through intermittent fasting. Intermittent fasting entails going for ca. 16-48 hours without energy intake, alternating with periods of normal feeding.[37]

In rodents, lifespan can increase by up to 30% as a result of a 24-hour fast every other day or twice a week and can slow or reverse cancer, cardiovascular disease, diabetes, and neurodegenerative disorders in animal models.[38,39] Reliable data on the effects of intermittent fasting and longevity in humans would require large numbers of fasting and matched control individuals followed over several

decades. But somewhat more limited studies using biological markers of age-related decline have shown promising results. In a study of 107 overweight or obese women aged 30-45 years, the effects on various biomarkers was compared for 25% energy restriction over a six month period using either continuous energy restriction (~6276 kJ/d, 7d/wk) or intermittent energy restriction (~2710 kJ/d, 2 d/wk).[40] Both groups showed similar weight loss, reductions in C-reactive protein, total and LDL cholesterol, triglycerides, insulin, insulin resistance and blood pressure, suggesting that intermittent fasting is an plausible alternative to chronic caloric restriction in reducing markers of aging. Whether similar benefits accrue to people with healthy body mass is still an open question.

Caloric Restriction and Exercise

The typical consequence of caloric restriction is a loss of lean body mass. Does this imply a loss of robustness as a necessary consequence? In humans, physical activity has been shown to lower mortality rates.[41,42] The benefits of moderate exercise, like the benefits of caloric restriction or intermittent fasting, are thought to be examples of "hormesis," the chronic or intermittent exposure to low-grade negative stress that leads to long-term enhanced resilience.[43,44] As such, the lifespan-extending benefit of exercise may lie primarily in opposing the negative stress of obesity and metabolic disorders such as diabetes and cardiovascular disease. Still, exercise is proven treatment to reverse or prevent age-dependent muscle wasting.[45] A randomized control study of 48 non-obese individuals found that both caloric restriction and exercise-induced negative energy balance results in similar and substantial reduction in risk factors for coronary heart disease.[46] Interestingly, a literature survey of 44 observational studies concluded that there is an inverse linear dose-response relation between volume of physical activity and all-cause mortality rates in humans.[47] Thus, like in many things, moderation in the dose and duration of exercise is likely to provide the optimal benefit.

Inflammaging

Normally, inflammation is a protective response our bodies mount to infection and tissue injury. This response is self-limiting, abating after a period of hours or days. Dysregulation of inflammation, however, can lead to pathological conditions. Acute dysregulation of the inflammatory response can lead to septic shock. Chronic dysregulation of the normal inflammatory response during aging, called "inflammaging," results in a low-grade inflammatory state that can drive such age-associated conditions as rheumatoid arthritis, atherosclerosis, asthma and various autoimmune syndromes, cancer and Alzheimer disease.[48]

A general decline in immune function accompanies aging, a phenomenon called immunosenescence. Immunosensence leads to a general decline in immune function with a higher risk of infection and of cancer. But paradoxically, immunosenescence also leads to immune hyper-responsiveness, with increased risk of autoimmune and inflammatory diseases.[49]

Inflammaging is mediated primarily by small molecules called cytokines that trigger the recruitment and activation of immune cells (T cells, B cells, macrophages) to respond to the infection. Secretion of cytokines is in turn triggered by the innate immune system. It appears that aging may be accompanied by age-associated reprogramming of cells of the adaptive immune system to innate immune responsiveness.[50] Age-associated increase in adiposity and the recruitment of macrophages in inflamed tissues contribute to chronic insulin resistance and metabolic dysregulation by increasing levels of pro-inflammatory cytokines.[51]

Recent evidence suggests that caloric restriction can attenuate the cellular markers of inflammaging.[52] Although the mechanisms are still being defined, they may include the elevation of anti-inflammatory glucocorticoids, reduction of blood glucose levels (reducing oxidation and oxidative stress) and activation of the nuclear hormone superfamily of peroxisome proliferator-activated receptors.[52]

"Lifespan" vs. "Healthspan"

In the Greek myth of Eos (goddess of the dawn) and her lover, Tithonus, Eos asks Zeus to grant Tithonus immortality, but forgets to ask also for eternal youth. Accordingly, Tithonus ages like all mortals, gradually shrivelling and shrinking with age and begins to babble continuously. Eventually he is transformed into a cicada. None of us wants to spend an extended lifespan shriveling through those extra years. The goal of geroscience is to increase "healthspan" as well as lifespan. Healthspan is the length of time during a person's life when they are in optimal health/functional capacity (Figure 3). Put another way, geroscience seeks to add life to years and not just years to life. The promise of caloric restriction and intermittent fasting is a delay in the decline in physical and cognitive functions that accompany aging. Based on the current evidence, continued regular exercise should contribute to improved healthspan.

Conclusion

Taken together, the weight of evidence supports the conclusion that if you want to increase your lifespan and maintain good health into old age, watch what you eat and

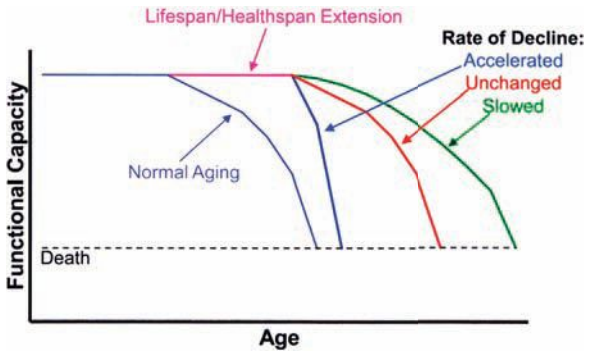


Figure 3. The goal of lifespan/healthspan extension is to extend both the age before death and to maintain functional capacity while increasing lifespan. This may also be accompanied by a slowing of the age-related decline in functional capacity.
From Reference 56.

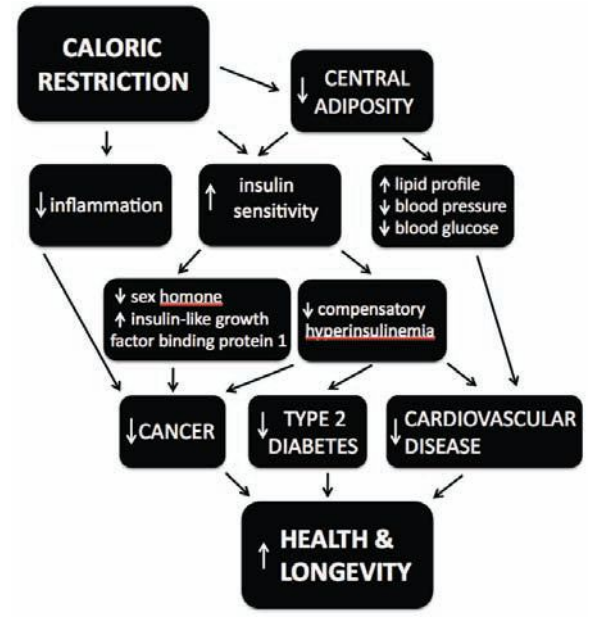


Figure 4. Hierarchical model for the effects of caloric restriction on health and longevity.
Modified from Reference 8.

how much of it. Caloric restriction acts through multiple pathways and mechanisms to attenuate the primary causes of age-related disease (Figure 4). It remains unclear to what extent the effects on longevity and healthspan reported for caloric restriction in humans are due primarily to decreased caloric intake versus a high quality diet.[53] However, the data suggest that reduced caloric intake in humans prior to the onset of old age improves healthspan[54] and delays cardiovascular aging, one of the main causes of death in humans.[55] Whether there is any longevity benefit for caloric restriction begun after the age of 60 is unknown; indeed, weight loss may increase mortality in this demographic.

The appeal of increasing lifespan through caloric restriction is balanced by the reality that caloric restriction is unpleasant; it may or may not extend your life, but it will certainly make your life feel longer. This difficulty is compounded by the fact that in western cultures, three meals a day with between-meal snacks are a cultural norm. Extending healthspan is a goal worth striving for, in the face of habit, discomfort, and peer pressure. With or without caloric restriction, healthy diet, regular exercise, and positive social engagement are proven strategies to attain that goal.

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MM

The MSMA Headquarters Staff: Exceptional Service and Professionalism

by Warren C. Lovinger, Jr., MD

To be successful, any large organization, such as the Missouri State Medical Association, must have effective professional leadership. While MSMA has a long tradition of dedicated physician officers, elected from our membership, the complexity of issues and constituencies for which MSMA is responsible makes the task too big for part time leaders to manage. This was recognized in 1944, when Mr. Tom O'Brien was hired as MSMA's first professional executive, soon assisted by Mr. Ray McIntyre. Though the Missouri State Medical Association was based in St. Louis for its first 100 years, its Headquarters was moved to Jefferson City in 1965. This provided a central location close to the legislative process. In 1973, the MSMA staff moved into an historic building at 113 Madison Street, directly across from the Missouri Governor's mansion.

The senior position at MSMA is the Executive Vice President. On December 31, 2017, Tom Holloway retired from this position after 30 years of distinguished service, including seven years as EVP. He handed the reins to Patrick Mills, who is a 26-year MSMA veteran. Patrick is well equipped to continue the tradition of dedicated leadership and long range planning for our organization. He is assisted by two very capable front office persons: Fran Draper and Cheri Martin.



From left, Joe Corrado, MD, MSMA President Elect, Tom Holloway, MSMA Executive Vice President 2011-2017, Warren Lovinger, MD, MSMA President, and Patrick Mills, Executive Vice President 2018-current.



Thirteen staff at 113 Madison Street, MSMA Headquarters. Top, from left: Jeff Howell, Cheri Martin, Lizabeth Fleenor, Fran Draper, Cassie Williams, Benita Stennis, Patrick Mills, Stephen Foutes, Sarah Luebbert, Lisa Cassmeyer, Heidi Geisbuhler, Carol Meyer, and Haley Wansing.



Warren C. Lovinger, Jr., MD, MACP, MSMA member since 1979, and President for 2017-2018, is an Internal Medicine physician, Nevada, Missouri.
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Another key position is Director of Communication. Lizabeth Fleenor, a 25-year MSMA veteran, does a great job overseeing *Missouri Medicine, Progress Notes,* and *Legislative Report*, as well as several other sources of information that keep us all updated and connected.



Communications: Lizabeth Fleenor

Legislative advocacy is an important and highly visible role of MSMA. Almost 700 bills are presented annually in the state legislature that somehow impact our profession and the health of Missouri citizens. Monitoring these proposals and presenting MSMA's position on them is the job of 11 year veteran lobbyist and attorney-Jeff Howell. He is now assisted by Heidi Geisbuhler, who came to MSMA after several years staff experience in the Missouri Senate.



Advocacy: Heidi Geisbuhler, Jeff Howell

Because the Missouri State Medical Association is committed to promoting the science and art of medicine, we strive to provide excellent continuing medical education across the state and at our annual MSMA meeting, which rotates between Kansas City and St. Louis. Coordination of these events is the task of Benita Stennis (Scientific Director) and Carol Meyer, who collectively have over 35 years of experience with MSMA.



Medical Specialties: Sarah Luebbert

Promoting membership in, and awareness of, the Missouri State Medical Association to the 20,000 medical students, residents/fellows, and graduate physicians in our state requires the energy of Membership Director Haley Wansing. She is assisted by our new Director of Marketing, Stephen Foutes, who is also developing new ways to showcase MSMA's many services.

Several of Missouri's medical specialty organizations, such as the Missouri Chapter of the American College of Physicians, have long benefited from the capable management services of MSMA. Sarah Luebbert has recently assumed the role of Specialty Services Director.

For medical and osteopathic students in our state, MSMA's Missouri State Medical Foundation gives more than 60 $2,500 scholarships annually to Missourians who are attending one of our six professional schools. Assisting Patrick Mills in this process is Lisa Cassmeyer and Cassie Williams. They are also responsible for the financial and information technology services at MSMA.

As members of the Missouri State Medical Association, we can be very proud of the 13 professionals who staff our Headquarters in Jefferson City. They work hard for us to promote the medical profession and issues that advance the health and well being of Missouri's citizens. **MM**



CME & Meeting Planning: Carol Meyer, Benita Stennis



Membership: Stephen Foutes, Haley Wansing



Finance & Data: Lisa Cassmeyer, Cassie Williams



Administration: Fran Draper, Cheri Martin

The Team That Wins

by David O. Barbe, MD

At the AMA Annual Meeting in June, I talked about physician leadership. I talked about how we are all leaders in a variety of contexts: in our practices, in our communities, and as members of organized medicine. Our patients, our colleagues and our communities look to us for leadership. And I challenged all of us to ask ourselves, continually: What kind of leaders will we be?

Now, I'd like to take that concept a bit further and talk about what it takes to put together . . . the team that wins.

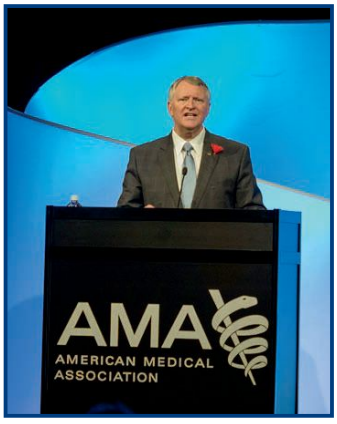
What is the formula for a winning team?

Winning teams recognize that the greatest success comes not from the effort of one or more individuals but from a team effort. One of the greatest individual talents in baseball, George Herman "Babe" Ruth put it this way, "The way a team plays as a whole determines its success. You may have the greatest bunch of individual stars in the world, but if they don't play together, the club won't be worth a dime."

Each physician is a physician leader . . . and I hope each of us is committed to our professional mission of promoting the art and science of medicine and the betterment of public health. However, our success will be determined by how well we play – or work together, as a team, to achieve our common goals.

So, the team that wins . . . shares a common vision, and works aggressively to achieve it.

The AMA has worked relentlessly to WIN, not only for our members, but for all physicians, for practice sustainability, and for patients . . . achieving a direct, positive impact as we move medicine forward.



David O. Barbe, MD, MHA, MSMA member since 1985, is the American Medical Association President and a Family Physician from Mountain Grove, Missouri.
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When physicians ask, 'What has AMA done for me lately?" which they often do, I can tell them, "plenty." It's almost hard to know where to start.

1) The AMA fought back against insurance mergers that would have decreased competition, weakened our negotiating power, and in the case of the Anthem-Cigna merger alone, would have cost physicians an estimated $500 million in reduced payments . . . every year. And we won.

2) Some of our most significant wins have come through our advocacy on behalf of physicians as we transition to a new Medicare payment system, the MACRA-Quality Payment Program.

- We fought for a simple way for physicians to avoid a four percent payment cut in 2019 . . . and won.
- We fought for—and won—retroactive policy changes to align Medicare's old reporting programs with the new MIPS program, helping clinicians avoid millions of dollars in penalties under prior law.
- In the 2018 MACRA rule, we fought for greater flexibility for small physician practices . . .and we won

3) We are working to make sure every physician—in every practice setting and every specialty—is prepared to make the successful transition to the MACRA-QPP, and we've posted multiple resources on our website including: tools, tutorials, podcasts and education modules.

4) The AMA continues to fight against burdens imposed by government and private insurers . . . and we are winning some battles:

- We fought to allow physicians to refuse virtual credit card payments from insurers, because they carry fees that reduce our reimbursements . . . and we won.
- We are fighting to reform the prior authorization process, and starting to see results … some insurers are beginning to reduce or eliminate their prior authorization requirements.
- We are fighting physician burnout and the time crunch by working to improve EHRs, mobile devices, and interoperability . . . and again, there are signs of success.

- Our work to improve physician satisfaction by reducing these headaches and making the practice environment more satisfying is at the heart of the AMA's strategic vision.

5) In addition to the above, we are fighting high drug prices through our Truth in Rx campaign. More than 150,000 people have signed our online petition calling for increased drug pricing transparency. We are encouraged to see Members of Congress now also calling for transparency.

At the AMA, we are not only advocating aggressively for physicians, we are advocating aggressively for patients. Nowhere is this more evident that in the renewed debate over health system reform.

From the beginning, we have fought for nine key principles – including affordability, accessibility, protecting safety net programs and patient protections, and one overarching goal: maintaining and expanding health care coverage for Americans.

Throughout this debate, the AMA has been a voice of reason . . . asking Congress to put Patients Before Politics, and urging Congress to work on bipartisan, sustainable solutions.

In fact, the AMA has been the leading voice among non-partisan organizations in this debate. An independent analysis showed that we achieved a 48 percent "share of voice" in the media for leading the national conversation. That's more than AARP, the American Hospital Association and the insurance industry lobby (AHIP) combined.

The team that wins . . . also creates partnerships that make us stronger. The AMA is working with outside organizations to strengthen and increase the momentum behind our patient facing strategic focus – reducing the burden of chronic disease.

We know the AMA alone, cannot solve the burden of chronic diseases that affects half of American adults and consumes more than 75 percent of the more than $3 trillion per year in health care spending. But, working with partners like the Centers for Disease Control and Prevention, the American Diabetes Association, and the American Heart Association, we can have a meaningful impact.

- More than 500,000 people have completed our online prediabetes test at DoIHavePrediabetes.org.
- We are also pleased to report more insurers are moving to cover the proven Diabetes Prevention Program; and
- Medicare has announced it will begin covering the Diabetes Prevention Program for seniors beginning next spring;
- That campaign has been so successful that the Improving Health Outcomes team is again working with the Ad Council and the American Heart Association on another public awareness campaign, this time focusing on hypertension. The campaign targets adults who have been diagnosed with high blood pressure but are not following their treatment plans.

If, working in partnership with patients and outside organizations, we can slow the progress of these chronic diseases or prevent them altogether, that will be a significant victory for public health, and will mean a much brighter future for our patients.

Which brings me to my next point.

The team that wins . . . prepares for the future. Here at the AMA, we are not just concerned about our patients and our professional lives. We are working hard to be sure the physicians of the future are prepared to care for the patients of the future.

Our Accelerating Change in Medical Education (ACE) Initiative has made amazing progress just in the four years since its creation. Among the most promising developments: schools are not just focusing on helping students become excellent clinicians . . . they are helping them understand the health system and training them to become physician leaders and innovators. Future physicians will be called on to lead the way in solving countless health care challenges. Thanks to the ACE initiative, they will have the skills they need to do that.

So, we've talked about the importance of 1) commitment to shared goals and working aggressively to achieve those goals, 2) partnerships to make the team stronger; and 3) preparing for the future.

In the past few months, I've had the opportunity to interact with physicians across the country to update them on all the AMA is doing. In every instance the response has been extremely positive. Members are encouraged, and many non-members tell me they are going to join based on what the AMA is doing for them and for their patients.

I opened with a quote by Babe Ruth on the importance of working together as a team. He made another observation that I think is equally important: "It's hard to beat a person who never gives up." Your AMA leadership will never give up in our efforts to advance our policies, achieve our common goals, and get our message out.

We know that Membership Moves Medicine. I invite you to be part of a winning team… part of our AMA. **MM**

Annual Grant to a Missouri Physicians-led Free Clinic is now available from the AMA Foundation

by Edmond B. Cabbabe, MD

After several years of fund raising from Missouri physicians and friends, the Missouri Honor Fund at the AMA Foundation reached its $250,000 mark, and is now set to start granting an annual grant to a physicians-led free clinic in our State.

This great milestone for our Honor Fund which was reached, before several other larger States' Honor Funds, is a testimony to the generosity of our donors.

The Honor Funds are restricted perpetual Funds at the AMA Foundation. They are established after ten donors pledge/donate $10,000 each. Once the $100,000 is collected, the Honor Fund starts earning revenue from the Foundation's investment revenue. When the collected donations reach $250,000 the fund starts granting an annual grant under the Foundation's Community Health Program. Part of the revenue derived by the Fund is used for the grants.

Other States Funds are designated for scholarships and some are for health care as is the case with ours. Because our Missouri State Medical Foundation loans and grants annual scholarships to our allopathic and osteopathic medical schools' students, therefor the founding 10 donors to the Missouri Honor Fund chose to grant the proceeds of our Fund to physicians' led free clinic in our State.

Our Fund is distinguished for having the largest number of contributors. Our generous donors contributed between $100 and $30,000.



Edmond B. Cabbabe, MD, MSMA member since 1979, is Chair of the Missouri Delegation to the AMA and Member of the AMA Council on Long Range Planning and Development.
Contact: ebcsl.aol.com

For the sake of brevity, I am listing, in alphabetical order, the names of the ten founding members who made an initial $10,000 contribution. A couple of them made substantial additional contributions. They are:

- Dr. Daniel A. and Mrs. Ruth Abodeely, St. Louis
- Dr. Elie C. and Mrs. Carine Azrak, St. Louis
- Dr. David O. and Mrs. Debbie Barbe, Mt. Grove
- Dr. Edmond B. and Mrs. Rima Cabbabe, St. Louis
- Dr. Rebecca Hierholzer, Kansas City
- Dr. Jerry and Mrs. Michelle Kennett, Columbia
- Dr. Vickie Massey, Kansas City
- Mr. John and Mrs. Denise O'Rourke, St. Louis
- Dr. John L. and Mrs. Anne Rollo, St. Louis
- Dr. Robert W. Smith, St. Louis

Additional $10,000 donors are:

- Pro Assurance Insurance Co.
- St. Anthony's Medical Center Medical Staff, St. Louis
- Drs. Samer and Amy Cabbabe
- Missouri Physicians Health Foundation

In order for a clinic to apply for Healthy Community Health Grants, the following conditions must be met:

1. The clinic meets the National Association of Free Clinics' definition of a free clinic:

"Free clinics are volunteer-based, safety-net health care organizations that provide a range of medical, dental, pharmacy, and/or behavioral health services to economically disadvantaged individuals who are predominately uninsured. Free clinics are 501(c)(3) tax-exempt organizations, or operate as a program component or affiliate of a 501(c)(3) organization. Entities that otherwise meet the above definition, but charge a nominal fee to patients, may still be considered free clinics

provided essential services are delivered regardless of the patient's ability to pay."

2. Currently have 501(c)(3) status and have held that status for at least three years at the time of application.

3. Provide essential services to patients regardless of their ability to pay.

4. Provide at least 20 or more hours of medical care a week, defined as physicians providing direct patient care.

5. Not have received an AMA Foundation Healthy Communities/Healthy America grant in the past five years.

6. Ensure that the project is led by a physician.

7. Complete the CDC's Capacity Assessment to determine whether or not this program is appropriate for their organization.

8. Have electronic medical record (EMR) or other practice software to allow for reporting.

The usual application acceptance period extends from October to December each year with the exact dates outlined on the Foundation website at https://amaf.smapply.io/. The grants for the next three years are $10,000 annually.

I encourage our colleagues and friends in Missouri to contribute to the AMA Foundation Missouri Honor Fund to grow the principal so we may be able to grant more and larger grants. Any donation is accepted and appreciated. Please consider honoring your parents, spouses, colleagues with a tax deductible donation to the Fund, your honoree(s) will receive an acknowledgement from the Foundation.

I want to personally thank all those who donated to this great cause, no matter how small or big was the donation. We in the "Show Me State" proved to others that when we set a goal, we not only achieve it but we surpass it.

To give, visit https://www.ama-assn.org/about/ama-foundation. **MM**

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Calendar for Continuing Medical Education

Jan. 20	Hematology and ASH Abstract
Feb. 3	Breast Cancer Update
Feb. 3	Rheumatology Update and Highlights from ACR
Feb. 21-24	Annual Refresher Course and Update in General Surgery
March 23-24	11th Annual Sports Medicine Update
March 24	Nephrology Update
April 7	Melanoma Update
April 13-14	Fetal Cardiac Symposium
April 14	Update on Osteoporosis and Fracture Prevention
April 28	Care of the Hospitalized Patient
May 31	9th International Pediatric Antimicrobial Stewardship
June 2	Cardiology Update

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These activities have been approved for *AMA PRA Category 1 Credits*™.

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A "Thank You" to the American Medical Association

by Robert Bondurant, RN

On November 12, 2017, I had the privilege of speaking at the AMA Convention in Honolulu, Hawaii. This opportunity was arranged by the President, David Barbe, MD, the first Missouri physician to hold this office in 90 years. Dr. Barbe is a friend and supporter of the Missouri Physicians Health Program.

This educational event provided 25 minutes for my presentation with additional time for questions and answers. The attendance was small, but I have always been willing to speak to any audience about physician health, no matter how large or small. I was able to describe how the physician health concept came to Missouri and has been implemented.

The Missouri Physicians Health Program (MPHP) was brought to Missouri in the mid-70s by Dr. Don McIntosh, a Kansas City anesthesiologist. He had a strong desire to help his distressed colleagues. He assisted fellow physicians in Kansas City until the Missouri State Medical Association (MSMA) adopted the physician health concept and formed an official program in 1985.

The Missouri model is a true reflection of what the AMA and Federation of State Medical Boards envisioned. The MPHP remains under the auspices of the MSMA.



Robert Bondurant, RN, LCSW, is Executive Director of the Missouri Physicians Health Program. Shown above his presentation at the AMA Interim Meeting in November 2017.
Contact: rbondurant@themphp.org

No funding is received from Missouri physician licensure fees. This is truly a statewide program with staff located in the major communities in Missouri. MPHP is a 501c3, not-for-profit organization, which permits tax deductible contributions.

When the physician health concept was developed, the main issues were substance abuse and physician suicide. Substance abuse interventions have been very successful. Unfortunately, physician suicide remains a serious concern and is responsible for the loss of many physicians.

MSMA has taken the basic framework that Dr. McIntosh imported to Missouri and expanded it. In addition to substance abuse and suicide, the program accepts referrals for mental health, behavior and sexual boundary issues. In fact, we will attempt to assist any physician who requests help. These requests may include marital issues, burnout issues, legal matters and personal health issues.

There are other services that in many ways set us apart. The MPHP assists medical students, residents, practicing physicians and even physicians who may not currently be licensed. We serve medical students because they can exhibit the same problems as licensed physicians, but earlier. We would rather resolve these issues before being licensed. Once the student is licensed, these unresolved problems if not dealt with will have more serious ramifications.

Another important service is our educational outreach. Our staff travels the state to speak with medical students, residents and practicing physicians. We especially like to be on a revolving schedule with medical schools and residency programs so that we appear each year.

It is amazing how many of our referrals never heard about us before they got into trouble. We strive to change this through our presentations, website, newsletters and the outreach by MSMA.

Organized medicine is responsible for the physician health programs. However, many newer physicians are not becoming involved in their professional organizations. They, therefore, do not hear about the services available to them through the MPHP. We encourage medical schools and residency programs to provide information about the benefits of organized medicine and the 24/7 help available

through this first responder for Missouri physicians, the MPHP.

Education is a very critical aspect of our program. I really appreciate the cooperation of the Deans of the Medical Schools, Residency Program Chairs and Directors, VPMAs and medical staff leadership, who give us the opportunity and time to introduce our program.

While I appreciated my opportunity to speak at the AMA Convention, it also brought with it a sobering reality. This came outside the scheduled meetings when I met physicians from around the country. Physicians would notice that my title indicated I was a speaker but not a physician. They gave me the opportunity to introduce myself and the MPHP. Many of them I spoke with did not have much knowledge about the physician health programs created by the AMA and especially their local program.

This made me appreciate the physician leadership of the MSMA and the St. Louis Metropolitan Medical Society (SLMMS). They have often allowed opportunities for our staff to meet with their members and leadership. They have greatly contributed to our visibility. This is very necessary.

The collaboration of the AMA with the Federation of State Medical Boards has given a great gift to physicians. The nursing profession did not develop a similar service until the mid-80's. Many professional groups have yet to develop similar services for their members.

As a parent organization, the AMA is positioned nationally to give the local physician health programs more exposure. This should go beyond information on stress and burnout. The AMA could also encourage medical societies to more actively support their local physician health programs and advertise their existence and services. The AMA and state medical societies may contribute by taking a more active role in supporting program development and expansion of services.

I have often been asked if our program prevents or reduces the occurrence of physician suicide. We rarely get the opportunity to stop an active suicide attempt, but our services can provide the means to resolve an issue that could lead to suicide as the only alternative.

Physician health programs are in the trenches with troubled physicians. We are the first responders experiencing the fear, pain and confusion that these physicians often face alone. We need the training, tools and the voice to better engage and stand with these physicians.

To the American Medical Association, I say again, "Thank You." There are thousands of physicians, family members, colleagues and patients who could stand and echo this. Your efforts have made a difference.

As a non-physician, I have a deep respect for what the AMA has done for its physicians. As a first responder to these physicians, I now ask the AMA to re-commit with their child that they brought into the world. I share the compassion that caused the AMA to champion physician health, but the work is not over; it is ongoing. Please reaffirm the value of your physician health program and help us to be more effective by teaching more physicians about this vital source of help. **MM**

☑ **Yes! I want to help physicians through MPHP's Spirit of Compassion Campaign.**

Please accept my tax-deductible gift of:

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Contributors to the MPHP 2017 Fund Raising Campaign

The Missouri Physicians Health Program is proud to recognize the following organizations and individuals who contributed to our annual fund drive. We are truly grateful for their generosity which helps provide crucial support as we strive to provide high quality physician health care services and meet the demand for our services statewide. Many of our participants are physicians in training who are unable to pay for services rendered. Your contribution helps us to defray those costs. We encourage you to generously contribute to our 2018 campaign. Thank you for your compassionate support.

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2017 Contributors, continued

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St. Mary's Medical Center, Blue Springs
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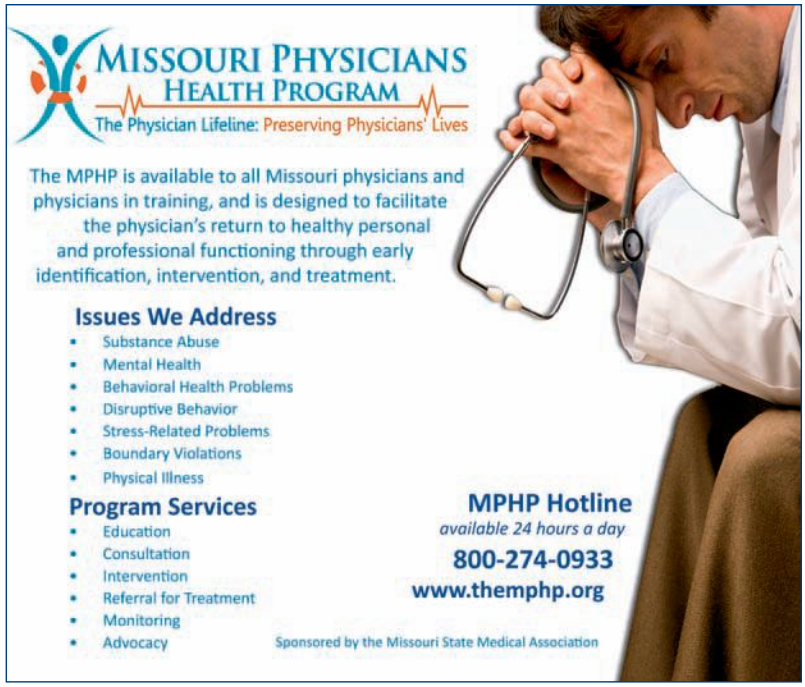
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Foundations

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MSMA Members in the News

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

Missouri Medicine announces new members of our Editorial Board. Board members are selected on the basis of exceptional professional accomplishment and expertise in their specialty.



Christopher R. Carpenter, MD, MSc, MSMA member since 2016, is Associate Professor in the Divison of emergency Medicine at Washington University School of Medicine in St. Louis. He has accepted a new Editorial Board Member position in Statistics/Methodology.



David Bean, DO, (left) MSMA member since 1998, accepted the St. Louis Metropolitan Medical Society (SLMMS) President's Award from J. Collins Corder, MD, MSMA member since 1980 at the Annual SLMMS Gala and Installation Ceremony.



Edmond Cabbabe, MD, MSMA member since 1979 (left) accepts the Robert Schlueter Leadership Award from his son Samer Cabbabe, MD, MSMA member since 2010, at the SLMMS Gala and Installation Ceremony.



Arthur Gale, MD, (right) presented the Arthur Gale Writing Award to Samer Cabbabe, MD, at the SLMMS Gala and Installation Ceremony.



Steven Eldenburg, DO, has been a valued MSMA member since 1992, and recently moved his practice in Sedalia to service patients at American Family Care.



Richard Hellman, MD, MSMA member since 1976, was honored with the Lifetime Achievement Award by Kansas City Medical Society at its Annual Meeting.

Joanne Loethen, MD, MSMA RFS Chair, was honored at the Annual Meeting of KCMS with a Member Recognition Award.





MSMA member since 1976, William Sasser, MD, was recognized at the Annual Meeting of KCMS with a certificate for his 50 years of membership in KCMS.

Karen Yates, MD, has expanded her practice from Cape Girardeau to include patients at Cameron Regional Medical Center. MSMA is grateful for her membership support since 1985.



Student members of UMC-MSS raised $1,000 for their student-run free clinic, called MedZou, which serves the local uninsured.



Customized MDpocket-WhiteCoat Clipboards were mailed to six new MSMA student members whose names were drawn in a raffle, along with $150 cash from MSMA. Martha Bissing, SLU; Kevin FitzGerald, KCU; Danielle Kinsey, UMC; Lavanya Kolluru, UMKC; Matthew D. Murphy, ATSU; and Alexander Scott, Wash U are all new MSMA members who joined MSMA for the duration of their medical education.

Errata

The article "Medical Education" by Charles Van Way, III, MD, published in the November/December 2017 issue was published with permission from Kansas City Medicine.

The book review "From Cuba with a Vision" by Felix Sabates, MD, published in the November/December 2017 issue was written by John C. Hagan, III, MD. **MM**

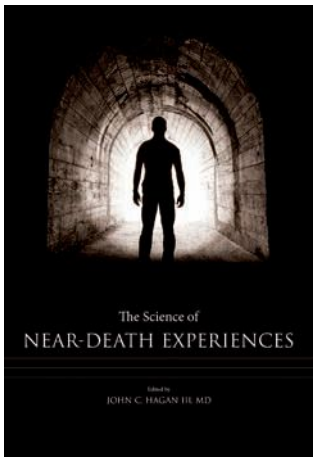
BOOK REVIEW

The Science of Near-Death Experiences

by John C Hagan III, MD, Editor

University of Missouri Press
Hardcover. 169 pp. ISBN 978-0-8262-2103-2
Available on Amazon, University of Missouri Press and msma.org

Submitted by Charles W. Van Way, III, MD



Men and women who have died and been successfully resuscitated sometimes undergo what is called "near-death experiences" (NDEs). They recall being detached from their dying body, often seeing their body from the outside. They pass to a bright light, sometimes through a dark tunnel, and feel the light is welcoming them. The whole experience is usually characterized by a feeling of detachment and peace. Such experiences have been recorded in about 15% of patients undergoing cardiac arrest with successful resuscitation, as well as in other circumstances. Patients have had NDEs even when under general anesthesia.

Between 2013 and 2015, *Missouri Medicine* published a series of articles on near-death experiences. John Hagan, MD, the long-time editor-in-chief of *Missouri Medicine*, has compiled these into a slim but highly informative volume. I should point out that any proceeds from the book will go to the Missouri State Medical Association. The 13 chapters range from a scholarly review of the published evidence to discussions of the theory of consciousness to personal accounts by physicians of their own near-death experiences. All of the authors in the book, save one co-author, are physicians and scientists. This brings the objectivity of scientifically-trained observers even to the personal accounts. I found that reading the account of a NDE by someone I know and respect was a very convincing experience.

Modern interest in NDEs dates back only about 50 years, to the 1970s. But descriptions can be found as long ago as the ancient Greeks. Heraclitus, Democritus, and Plato all wrote on "revenants," people who apparently died, and then recovered. There have been published studies in the recent literature. Pim Van Lommel, MD, describes a prospective multi-hospital study from the Netherlands of cardiac arrest patients.[1] Of 344 patients who were entered into the study because they had cardiac arrest, 62 (18%) had some sort of NDE. His chapter cites other, smaller studies with similar results.

But while the existence of NDEs is generally recognized, they are not understood. Kevin Nelson, MD, a neurologist, presents a strong argument for placing NDEs into modern neuroscience. Other authors deny this. Eben Alexander, III, MD, a neurosurgeon, makes an equally compelling argument for NDEs being outside the current framework. Most of the other chapters touch on this issue in one way or another. Basically, the argument revolves around the theory of consciousness. Is consciousness produced by the brain, as some sort of epiphenomenon? Or is consciousness separate, existing alongside but separate from the physical nervous system? This question is far beyond the scope of the present review.

Several of the contributors urge strongly that physicians should recognize NDEs as being part of the life experience of at least some of our patients. Many people who have had such experiences feel a need to talk about them. Most are affected by their NDE. Such an experience may be life-altering. Further, while "classic" NDEs are generally positive experiences, some may be negative or threatening. PDSD has been reported following NDEs. As physicians, we need to be sensitive to the existence of NDEs. We must be able and willing to talk about the subject, especially if and when a patient wants us to help them understand their experience.

Lastly, this book should induce a certain feeling of humility in all of us. For all our knowledge, and skill, there are things which we do not yet understand. Let Shakespeare have the last word:

There are more things in heaven and earth, Horatio,
Than are dreamt of in your philosophy.
- Hamlet (1.5.167-8), Hamlet to Horatio

Reference

1. Van Lommel P, van Wees R, Meyers V, and Efferich I. Near-death experiences in survivors of cardiac arrest: A prospective study in the Netherlands. 2001, Lancet 358:2039-45.

MM



Missouri State Medical Association
160th Annual Convention
March 23-25, 2018 | Renaissance St. Louis Airport Hotel

www.msma.org/annual-convention

Pre-Convention Meetings

Thursday, March 22

2:30 pm	MSMA Insurance Agency Board Meeting
3:30 pm	MSMA Executive Committee
3:30-6:00 pm	Convention Registration
3:30-6:00 pm	Exhibitor Setup & Registration
5:00 pm	**MSMA Council Meeting**
6:30 pm	Alliance Dutch Treat Dinner
6:30 pm	**MSMA Council Reception & Dinner**

Convention Meetings

Friday, March 23

6:30 am-4:00 pm	Convention Registration
6:45 am	Moneta Group Investment Advisors Breakfast
7:00 am	**Exhibit Hall Opens/Continental Breakfast for all Conferees**
8:00 am	**Opening Session MSMA House of Delegates**
8:30 am	Alliance Board Meeting
10:00 am	Alliance General Assembly - Session I
10:00 am	**Reference Committee A**
10:30 am	**Reference Committee B**
11:00 am	Missouri Physicians Health Luncheon & Meeting
11:30 am	"Spirit of the Alliance" Awards Luncheon
Noon	SLMMS Caucus & Luncheon
Noon	KCMS Caucus & Luncheon
1:30 pm	**MSMA General Session**
2:00 pm	Million Hearts Meeting
3:30 pm	**MSMA General Session**
4:00 pm	Medical Student Section Business Meeting
4:30 pm	Alliance Past President's Reception
5:00 pm	Organized Medical Staff Section Business Meeting
5:30 pm	Medical School Alumni Receptions
7:00 pm	Alliance Foundation Fundraiser/Dinner
7:00 pm	Resident and Medical Student Mixer

Program subject to Change. Refer to Convention Official Program for times and meeting locations. For more information, contact MSMA's Benita Stennis, at 800-869-6762 or bstennis@msma.org.

Saturday, March 24

6:30 am-4:00 pm	Convention Registration
7:00 am	**Exhibit Hall Opens/Continental Breakfast for all Conferees**
All Day	CME Programs, Lectures & Meal Functions
7:00 am	International Medical Graduate Section Meeting
8:00 am	**MSMA General Session**
8:30 am	Alliance General Assembly - Session II
10:00 am	**MSMA General Session**
10:00 am	MMPAC Meeting
10:30 am	Exhibit Hall Closes
Noon	SHINE of Missouri Product Theater
12:30 pm	Alliance Installation Luncheon
1:00 pm	AMA Issues
1:00 pm	Resident and Fellow Section/ Young Physicians Section Program
1:30 pm	**MSMA General Session**
2:00 pm	Resident and Fellow Section Business Meeting
2:00 pm	Young Physician Section Business Meeting
2:30 pm	Missouri State Medical Foundation Meeting
2:30 pm	Alliance Board Meeting
3:00 pm	Component/Specialty Society Leaders Meeting
3:30 pm	OMSS Educational Session
5:15 pm	Reception: 50-Year Pin Recipients & MSMA Past Presidents
6:30 pm	**MSMA Presidential Inauguration**
7:30 pm	**MSMA Presidential Reception**
	Entertainment, Hors d'oeuvres & Cash Bar

Sunday, March 25

7:00 am	District Breakfasts & Caucuses
8:15 am	**Second MSMA House of Delegates**
Immediately Following Closure of the HOD	MSMA Council Meeting

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General Sessions & Events



Friday, March 23 | 1:30 pm

Ten Practical Techniques for Improving Care for Patients with Life-Limiting Illnesses

Patrick White, MD
Chief Medical Officer
BJC Home Care
Washington University
School of Medicine
St. Louis, Missouri



Friday, March 23 | 3:30 pm

Immunotherapy for Disease Management

Richard D. Brasington, MD
Professor of Medicine
Division of Rheumatology
Washington University
School of Medicine
St. Louis, Missouri



Saturday, March 24 | 8:00 am

Hospitalists: What You Need To Know

Hiral Choksi, MD
Section Chief of Hospital Medicine
Saint Louis University Hospital
St. Louis, Missouri

FREE CME TO MEMBERS

CME procedures, sessions available for MOC points, how to obtain CME credit, disclosures, and evaluations will be described in the Official Program. For more information, contact Benita Stennis at 800-869-6762 or email bstennis@msma.org.



Saturday, March 24 | 10:00 am

Advances in Heart Failure Management

Justin Vader, MD
Assistant Professor of Medicine
Division of Cardiovascular Medicine
Washington University
School of Medicine
St. Louis, Missouri



Saturday, March 24 | 1:30 pm

Burning Out or Burning Bright?

Richard Gunderman, MD
Chancellor's Professor
John A. Campbell Professor Radiology
Indiana University
School of Medicine
Indianapolis, Indiana



Saturday, March 24 | 3:30 pm

OMSS PRESENTATION Hospital Medical Staffs 2018: Protect Your Practice & Profession

Elizabeth "Libby" Snelson, Esq.
Legal Counsel to Hospital Medical Staffs
St. Paul, Minnesota

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Research at A.T. Still University's Kirksville College of Osteopathic Medicine

by Margaret A. Wilson, DO

To this day, KCOM strives to educate osteopathic physicians who focus on evidence-based, whole-person patient care.



Margaret A. Wilson, DO, MSMA member since 2012, is Dean, Kirksville College of Osteopathic Medicine, and Professor, Department of Family Medicine, Preventive Medicine, and Community Health, A.T. Still University—Kirksville College of Osteopathic Medicine, Kirksville, Missouri.
Contact: mwilson@atsu.edu

Background and Overview

The Kirksville College of Osteopathic Medicine (KCOM) was established in 1892 by Dr. Andrew Taylor Still, MD, DO, in the rural Missouri town of Kirksville. As the first of six health professions schools within A.T. Still University (ATSU), KCOM is currently celebrating its 125th year of excellence in osteopathic education, patient care, and research; and it is proud to be the founding college of the osteopathic medical profession. To date, KCOM has graduated an estimated 17,634 osteopathic physicians, approximately 6,487 of whom are currently in practice across all 50 states and in several foreign countries. At present, KCOM has 701 students enrolled in its four-year osteopathic medical education program.

Nationwide, approximately 20% of all students who attend medical schools enroll in Doctor of Osteopathic Medicine (DO) programs. According to the American Association of Colleges of Osteopathic Medicine, 33 colleges of osteopathic medicine are accredited in 48 teaching locales across 31 states. Six schools are state sponsored, 27 are private—including KCOM, and more than 27,000 students are enrolled in total.[1]

In 2016, the American Osteopathic Association reported that osteopathic medicine was one of the fastest growing healthcare professions in the nation with 102,137 DOs in the United States (US) and 129,649 total DOs and osteopathic medical students in training.[2]

To this day, KCOM strives to educate osteopathic physicians who focus on evidence-based, whole-person patient care.

KCOM students spend their first two years studying integrated basic and clinical sciences in a rural campus setting. In the third and fourth years, students are educated through clinical rotations in one of KCOM's national rotation regions, which include sites in Arizona, Illinois, Iowa, Michigan, Missouri, New Jersey, Ohio, Pennsylvania, and Utah. KCOM graduates are selected to many prestigious residency programs across the nation, including Yale, Johns Hopkins University, the Mayo Clinic, and the Cleveland Clinic Foundation. With an emphasis in primary care and rural health, KCOM graduates enter primary care as well as a variety of specialties such as anesthesiology, dermatology, emergency medicine, diagnostic radiology, and surgery.

KCOM faculty members have developed a stellar anatomical and clinical ultrasound curriculum. Students learn living human anatomy with the use of bedside ultrasound technology that will ultimately enhance their ability to diagnose at the point of care.

Research Perspectives - Past, Present and Future

Both KCOM and ATSU recognize the importance of research and scholarly activity in their strategic plans, and these current plans align because both specify a strategic goal to expand student and faculty scholarship. At ATSU and KCOM, scholarship is defined as being engaged in discipline-based research, clinical studies of illness and treatment, current and future trends in healthcare, and/or the scholarship of teaching and learning. In essence, it is the plan and the practice of KCOM faculty and students to vigorously engage in research and scholarly activity.

KCOM's clinical and basic science faculty have a long and rich history of engaging in scientific research, including a notable era in the late 1940s and 1950s with the pioneering work of John Stedman Denslow, DO, class of 1929, who studied the osteopathic lesion using electromyographical methods,[3] and Irvin M. Korr, PhD, who collaborated with Dr. Denslow and pursued his own line of research into the role of the peripheral nervous system in health and disease.[4]

In the 1970s, Richard J. Cenedella, PhD, former chair and now emeritus professor, KCOM's Department of Biochemistry, began investigating molecular mechanisms of cataract formation, among other research topics. Throughout his distinguished teaching and research career, he received 35 years of National Institutes of Health (NIH) grant support, published more than 100 research papers, and was the first person at KCOM to be named a Fulbright Scholar (in 2008). Dr. Cenedella has inspired an entire generation of KCOM students and faculty.[5]

In more recent years, KCOM has had active research programs in cancer biology, osteopathic manipulative medicine, medical education, cardiovascular disease, muscle biology, bone and joint disease, neuroscience, and infectious disease.

Given that the specialty of osteopathic manipulative medicine (OMM) originated at KCOM, the A.T. Still Research Institute (ATSRI) was created by ATSU in 2001 to advance and coordinate research into the evidence base of OMM. In 2010, DO-Touch.NET—which focuses on OMM research—was created as the ATSRI's inaugural practice-based research network. This growing OMM research network is comprised of more than 200 members from 30 states and 11 countries.[6] The ATSRI and DO-Touch.NET are headed by one of ATSU's leading OMM researchers, Brian F. Degenhardt, DO, associate professor and director, ATSRI. Dr. Degenhardt and team work alongside Karen T. Snider, DO, professor, Department of Osteopathic Manipulative Medicine, and assistant dean, Osteopathic Principles and Practices Integration, and many of the OMM faculty to pursue osteopathic research.

The ATSRI, along with ATSU and Sigma Xi, hosts an annual Interdisciplinary Biomedical Research Symposium each fall on ATSU's Missouri campus to promote knowledge and collaboration in biomedical research. This event provides faculty, students, residents, and external researchers the opportunity to hear a keynote presentation with a research focus and to present their own biomedical research studies as oral or poster presentations. More information about this symposium, the ATSRI, and DO-Touch.NET is available at atsu.edu/research.

In 2006, KCOM was the first osteopathic medical school to win a multiyear NIH R25 research education grant from the National Center for Complementary and Integrative Health (formerly the National Center for Complementary and Alternative Medicine). From 2011-2015, KCOM's R25 grant award focused on the enhancement of evidence-based medicine (EBM) coverage in the college's clinical training and affiliated residency programs and worked to more deeply entrench preclinical, campus-based advancements in EBM. All of this was accomplished with KCOM's R25 research-intensive partnering institution, Penn State College of Medicine, located in Hershey, Pennsylvania.

During the past three decades, KCOM has received more than $28 million in federal funding from the Health Resources and Services Administration (HRSA), a division of the US Department of Health and Human Services. The majority of these grant awards supported the infusion of scholarly teaching and learning initiatives at KCOM. Currently, KCOM holds a HRSA Primary Care Training and Enhancement (PCTE) award that focuses on preparing students to reduce health disparities and barriers to care for vulnerable populations, improve patient engagement, and become leaders in the nation's primary care workforce. In addition, KCOM was recently awarded a PCTE supplement grant to expand medication-assisted treatment training in response to the nation's current opioid crisis.

In terms of NIH research funding, KCOM has received $11.9 million in recent decades, including more than $4 million for Dr. Cenedella's research and more than $1.5 million for the R25 research education grant mentioned above.

Today, our broad view of a "research laboratory" at KCOM includes traditional basic science and biomedical laboratories, osteopathic manipulation teaching laboratories, clinical patient examination rooms, human simulation laboratories, electronic and virtual learning environments, and so on. At KCOM, the medical school classroom itself is also considered an important teaching and learning laboratory.

As highlighted in this edition of *Missouri Medicine*, KCOM investigators are currently engaged in various studies focused on the scholarship of teaching and learning, including maintaining balance through medical humanities electives, integrating ultrasonography into the curriculum, infusing 3-dimensional and 4-dimenstional ultrasound technology into didactics, and assessing human patient simulation as a teaching tool. Each of these medical education studies adds depth to the overall body of knowledge of each topic plus serves to inform and enhance KCOM's academic program offerings.

In 2001, KCOM added a master of science (MS) degree in biomedical sciences, which is a thesis-based research degree that provides an opportunity for students aspiring to health science careers. Graduate student research projects typically involve the fields of anatomy, biochemistry, cell biology, histology, immunology, microbiology, molecular biology, neuroscience, pharmacology, or physiology. Successful MS graduates often earn subsequent admission into ATSU's osteopathic medical, dental, or other health professions programs, creating a more research-proficient applicant pool for KCOM and all ATSU schools. Other MS graduates elect to pursue active research careers or matriculate into external PhD training programs.[7] Without question, the MS research degree program amps up the research culture and atmosphere on KCOM's rural campus.

Moving forward, KCOM's biggest challenges include the need for more experienced research mentors to support early career faculty and encourage our ever-growing student interest in research and scholarly studies. Also, dedicated time for faculty research and scholarly activity is always a challenge and must constantly be balanced with other faculty responsibilities (ie, teaching, advising, serving on committees, professional practice, and community service outreach).

KCOM faculty and students welcome the opportunity to share the various studies herein, while aspiring to build stronger research collaborations with internal investigators and external partners and mentors—especially those at more research-intensive universities.

Acknowledgments



We at KCOM extend our heartfelt gratitude to the late Neil J. Sargentini, PhD, former professor and chair, Department of Microbiology and Immunology, for initiating and coordinating KCOM's contributions to this edition of *Missouri Medicine*. Dr. Sargentini's leadership, commitment, and selflessness in advancing KCOM's research culture will serve as his legacy. We dedicate KCOM's contributions in this edition to him.

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Maintaining Balance in Medical School through Medical Humanities Electives

by Patricia Sexton, DHEd

"A gentle and humane temper, so far from being inconsistent with vigor of mind, is its usual attendant; rough and blustering manners generally accompany a weak understanding and a mean soul…" [1]
-John Gregory (1724-1773)



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Abstract

The amount of scientific and medical information students are expected to master is ever increasing. This may draw attention away from the human aspect of medicine – the reason most enter medical school in the first place. Medical humanities may help students remain empathetic, self-aware and reflective as they work to become excellent physicians.

A Holistic View of Medical Education

It is well-recognized that medicine is both art and science. Osteopathic medicine prides itself on attending to the whole person: body, mind, and spirit. However, the ever-increasing amount of medical knowledge to be mastered in the undergraduate medical curriculum leaves little time to explore the mind and spirit – the humanistic side of patients or physicians-in training. Although the numbers vary by source, news reports of depression and suicidal ideation in medical students and practicing physicians have reached the mainstream media and are concerning to medical educators.[2] Likewise, disruptive unprofessional behavior has increased.[3] While medical education is rigorous and fraught with difficult topics such as illness and death, some have posited helping medical students learn about themselves, about human relationships, and reflecting on their calling to serve may assist in creating compassionate, healthy physicians.

Medical humanities as a field is not well defined but is broadly defined as "the stories, the ideas, and the words that help us make sense of our lives and our world."[4] Example topics include history, literature, art, spirituality, servant-leadership, bioethics and professionalism, among others. The call for increased humanistic focus in medical school matriculants is reflected in the revision of the Medical College Admissions Test (MCAT) in 2015 to include testing in "psychological, social, and biological foundations of behavior."[5] Medical schools, take differing approaches to including these topics in the core or elective curriculum.

At the Kirksville College of Osteopathic Medicine (KCOM), the founding college of osteopathic medicine, our approach is multi-pronged. Our Complete DOctor course spans the first two years and includes not only history-taking and physical exam skill development but also emphasizes communication skills, patient engagement, spirituality and death and dying as well as many public health and health systems topics. The department of Student Affairs promotes complete student wellness with the inclusion of spiritual, emotional, occupational, social, environmental and intellectual wellness in addition to the physical.[6] Recently, a "mindfulness and gratitude" initiative has begun at KCOM and has garnered student interest and involvement. One area that encompasses social, spiritual, emotional and intellectual wellness is the study of medical humanities topics. We believe that students who avail themselves to study topics in the medical humanities will retain their own humanity, balance, and compassionate spirit while in school.

Humanities Elective Coursework

In 2009 the first medical humanities elective course, Spirituality in Medicine, was introduced at KCOM.

At that time there were three elective courses offered at KCOM in other specialty topics such as Cranial Osteopathy. The Spirituality in Medicine elective attracted a student cohort of 20 students. This success led to creation of elective courses in Medical Letters (literature in medicine), Vulnerable Populations, and Cultural Awareness in Medicine, among many other research and specialty oriented elective courses. At this time, there are more than 20 elective courses for first and second year medical student enrichment. Although no elective coursework is required for graduation, greater than 40 percent of KCOM students take one or more course during their time on campus.

The humanities' topics are literature- or film-based and reflection-discussion oriented. Students borrow books from the humanities' library, created with generous donations from alumni and others, thus the student incurs no additional expense. Bi-monthly or monthly meetings allow students to discuss their readings, submit reflective writings, report on assigned topics and generally share thoughts and feelings about the topics for review. Patient, caregiver, societal, and physician points of view are all considered. We emphasize cultural humility and expect each participant to enter discussions respectfully and with an open mind. Over an eight-month period, these students are exposed to patient stories and explore their own reactions, as well as discuss self-care plans for their futures. At the close of the medical humanities electives, we hold a school-wide Capstone Exhibit to share with the greater KCOM community, the displays, writings and projects produced by the students in the course.

Student Reflections

Student enrollment has stayed strong over the past several years of offering these electives but the true assessment of their value comes in student comments about the roles these courses have played in their lives. We asked students three questions: Did taking humanities elective(s) enrich your academic experience and /or help you maintain balance in your life? What did you gain from taking humanities elective(s)? Would you take this type of elective again? Students passionately expressed their regard for the electives with 100% stating they would take them again. One student summed up the feelings of many stating:

"We memorize algorithms and commit flowcharts to memory without giving much thought to the fact that these figures describe actions we will undertake on real people, with sometimes profound consequences for their lives and the lives of those around them. In other words, it's easy to lose the forest for the trees and forget that, at the end of the day, medicine is a human-driven science. This elective helped remind me that empathy is the essential ingredient for a successful medical practice and that only by understanding my patients, and the worlds that they inhabit, could I begin to effectively treat them. I felt the elective helped enrich my academic experience and foster more equilibrium in my life. It got me reading for pleasure again, a hobby (if not passion) I forgot in the scramble to cram as much medically-related information into my brain as is humanly possible. Regarding my academic experience, if not my performance as well, enrolling in an elective rejuvenated me and reminded me that the end-goal of my time in medical school is not to nurture self-importance but instead refine my ability to render care in service to others."

Another student noted: "I believe humanities electives in medical school are imperative. The volume of scientific information that students are required to learn in the first two years of training can be overwhelming and it is easy to lose sight of why you're putting yourself through the demanding rigors of medical school. It is without a doubt that these courses not only increased and strengthened the critical thinking skills but also re-centered my focus on people, to let me see beyond the ill patient."

Yet other students wrote about the safety to discuss topics such as physician-assisted suicide or end-of-life, which are difficult and emotionally charged, in the safety of a small group. Students stated that these discussions allowed them to carefully evaluate their own core values and express themselves more clearly – ultimately helping them to become more compassionate and non-judgmental.

Conclusion

We believe that in medical education and, later, in the practice of medicine, the ability to truly listen, to be open to the viewpoint of another person, and to remain cognizant of the reasons for entering a profession of service will create the resilience required of tomorrow's doctor. We select the best and the brightest students. Opportunities such as the medical humanities electives at KCOM ensure that we produce physicians to care for humanity by not only mastering the science of medicine but by being healthy and compassionate humans.

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Disclosure

None reported.

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Integration of Ultrasonography into the Undergraduate Medical Curriculum: Seven Years of Experience

by Tatyana Kondrashova, MD & Peter Kondrashov, PhD

Our published research shows that integration of dissection-based Gross Anatomy and ultrasound imaging resulted in better retention of anatomical knowledge, significantly enhanced student learning of the human body's structure and function, and helped students to better understand correlations with the clinical applications of anatomy and imaging.





Tatyana Kondrashova, MD, PhD, (left), Department of Family Medicine, Preventive Medicine, and Community Health, and Peter Kondrashov, PhD, (right), Anatomy Department, are at A.T. Still University—Kirksville College of Osteopathic Medicine, Kirksville, Missouri.
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Abstract

Ultrasound education has been part of the curriculum at A.T. Still University's Kirksville College of Osteopathic Medicine for over seven years (since 2011), and has been successfully integrated into the first two years of the four-year medical school curriculum. Students master ultrasound techniques through hands-on laboratories covering all body regions and systems. Ultrasound training has the potential to enhance the medical school learning experience for students and improve the quality of their future patient care.

Introduction

Ultrasound education is becoming an important component of the undergraduate medical school curricula. Early ultrasound education has a positive effect on student clinical decision-making skills and results in a higher level of comfort and better ability when using ultrasonography during clinical rotations.[1, 2] Such training reinforces the anatomical knowledge of students,[3-9] solidifies understanding of physiological processes in the human body,[10, 11] and fosters development of clinical skills.[12] Early ultrasound training for medical students may prevent future diagnostic mistakes by maximizing the ability of students to obtain accurate ultrasound images.[13] Further, research suggests that medical students can attain a sufficient degree of proficiency in ultrasonography techniques in the early stages of their medical education.[1] Its growing influence and importance in medical practice makes ultrasound education an increasingly popular addition to medical school curricula.[14-16] Even though several medical schools in the United States have incorporated ultrasound imaging into medical education,[13, 15, 17-20] there has been no standardization in the ultrasound training programs.

Ultrasound education has been part of the curriculum at A.T. Still University's Kirksville College of Osteopathic Medicine (ATSU-KCOM) for over seven years and is now fully integrated into the first two years of the four-year medical school curriculum. At ATSU-KCOM, the first two years of the curriculum are didactic and taught on campus; the last two years are clinically based in various hospital systems across the United States.

In 2011, the first few ultrasound laboratories were integrated into the KCOM Gross Anatomy I and II courses and were followed by a Clinical Ultrasound Elective course offered to second-year students.

Ultrasound as Part of Gross Anatomy

Initially, the ultrasound curriculum consisted of five ultrasound laboratories for first-year osteopathic medical students that were aligned with the gross anatomy laboratories:

- Ultrasound Laboratory 1. Introductory, neck
- Ultrasound Laboratory 2. Heart
- Ultrasound Laboratory 3. Abdomen
- Ultrasound Laboratory 4. Pelvis
- Ultrasound Laboratory 5. Lower extremities

Students received an opportunity to learn and visualize "living anatomy" with the use of ultrasound technology through correlations with cadaveric dissection. Our efforts resulted in the implementation of a successful hybrid of a dissection-based Gross Anatomy course with embedded ultrasound imaging. Our published research[5] shows that such integration resulted in better retention of anatomical knowledge, significantly enhanced student learning of the human body's structure and function, and helped students to better understand correlations with the clinical applications of anatomy and imaging. These benefits will hopefully be reflected in quantitative outcomes (board subscores) and qualitative outcomes (student satisfaction surveys).

Initially, the first class of 172 students had to be divided into three teams to provide the best hands-on experience to students because ATSU-KCOM only had 10 ultrasound machines. Within two years, the number of ultrasound machines at KCOM was increased to 25 machines comprised of 10 SonoSite-MSK (Fujifilm SonoSite, Inc.) and 15 MindRay M5 (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.) units. The class was then split into two groups so that every ultrasound laboratory had a maximum of 3-4 students per ultrasound machine to provide the best educational experience for the students. Student satisfaction with the ultrasound laboratories and student eagerness to learn clinical concepts through ultrasound imaging has been very high since the first year of integration of ultrasound laboratories into the Gross Anatomy course.

Clinical Ultrasound Elective

Based on student feedback and a high level of student interest in the ultrasound program, a Clinical Ultrasound Elective course was developed. This course was first offered to second-year students in March 2012 to improve student learning in clinical disciplines and provide students with hands-on skills before departing for rotations. During the 2012-2013 academic year, the elective course consisted of seven ultrasound hands-on laboratories that were enriched with clinical correlations:

- Clinical Ultrasound Elective Laboratory 1. Musculoskeletal ultrasound of the upper limb
- Clinical Ultrasound Elective Laboratory 2. Musculoskeletal ultrasound of the lower limb
- Clinical Ultrasound Elective Laboratory 3. Ocular ultrasound
- Clinical Ultrasound Elective Laboratory 4. Advanced echocardiography
- Clinical Ultrasound Elective Laboratory 5. FAST exam (focused assessment with sonography for trauma)
- Clinical Ultrasound Elective Laboratory 6. Breast ultrasound exam with use of breast biopsy model
- Clinical Ultrasound Elective Laboratory 7. Needle-guided procedures with use of ultrasound models

The Clinical Ultrasound Elective course was very successful and received overwhelmingly positive student evaluations. On completion of the course, 100% of students replied "Yes" to the post-semester survey question, "Would you recommend this course to other students?" This positive response resulted in a 70% ultrasound elective course participation for the next year's class despite the fact that there was no elective requirement for second-year students. The elective course continued to be offered through 2014 until it was included as part of the new, required four-semester Clinical Ultrasound course. Formal survey of second-year students revealed that 94% of students agreed that the elective course helped them develop their diagnostic skills.

Clinical Ultrasound Course

The Clinical Ultrasound course for first- and second-year medical students was successfully included in ATSU-KCOM's curriculum during the 2014-2015 academic year as a replacement for the Clinical Ultrasound Elective course and the Gross Anatomy ultrasound laboratories. During semester 1, the Clinical Ultrasound course laboratories are aligned with the Gross Anatomy laboratories. During semesters 2-4, ultrasound laboratories correlate with the systems blocks, and students are exposed to the clinical applications of ultrasound and its use to diagnose pathological conditions (See Table 1).

When planning the Clinical Ultrasound course, the main goals were: (1) to provide students with bedside ultrasound skills at the point-of-care through hands-

Table 1. Ultrasound Laboratories in the Ultrasound Curriculum

Semester 1 Ultrasound Labs	Semester 2 Ultrasound Labs	Semester 3 Ultrasound Labs	Semester 4 Ultrasound Labs
Lab 1. Introduction to ultrasound and neck ultrasound	Lab 1. Abdomen	Lab 1. Lung	Lab 1. Nerve imaging
Labs 2 and 3. Upper limb MSK	Lab 2. Gastrointestinal	Lab 2. Endocrine	Lab 2. Ultrasound needle-guided procedures
Labs 4 and 5. Lower limb MSK	Lab 3. Echocardiography	Lab 3. Obstetrics	Lab 3. FAST exam
Lab 6. Neck	Lab 4. Advanced Echocardiography	Lab 4. Gynecology	
Lab 7. Ocular ultrasound	Lab 5. ECG/echocardiography workshop Lab 6. Upper limb vascular ultrasound Lab 7. Lower limb vascular ultrasound Lab 8. Pelvis and urinary system ultrasound	Lab 5. Breast	

Abbreviations: ECG, electrocardiography; FAST, focused assessment with sonography for trauma; MSK, musculoskeletal ultrasound.



Figure 1. Medical Students Learning Ultrasound Imaging during Ultrasound Laboratories.
A - Medical students learning knee anatomy during the lower limb musculoskeletal ultrasound laboratory.
B - Medical students learning breast normal anatomy and pathology using Breast Ultrasound Training Model (Kyoto Kagaku).

on practical experience; (2) to improve integration of clinical and basic science education through the use of clinical cases and ultrasound simulation; and (3) to incorporate ultrasound imaging into other courses, such as anatomy, osteopathic manipulative medicine (OMM), and physiology.[11, 21]

Because ultrasound education is a fairly new component of medical school curricula, there were limited supplemental materials and textbooks available at course implementation. Therefore, we developed detailed handouts and PowerPoint® (Microsoft Corp.) presentations for the students so that they could be successful in the ultrasound course. To increase the hands-on experiences of students with the ultrasound techniques, the class was split in half to have 3-4 students per ultrasound machine during each ultrasound laboratory. To promote self-learning, open hours for free-scan ultrasound practice were available for students every day after their curricular activities (~10 hours per week), which was much appreciated by students since it helped them improve their proficiency with the ultrasound technology.

Many ultrasound laboratories included clinical cases, which utilized a clinical topic that was demonstrated through ultrasound imaging. For example, when studying ultrasound imaging of the neck vessels, students were first presented a case on carotid artery disease with a related carotid endarterectomy surgery video, which illustrated related anatomical structures. Then students were presented with the ultrasound demonstration on

Table 2. Ultrasound Laboratories for the Clinical Ultrasound Course Using Ultrasound Phantoms

Ultrasound Laboratory	Ultrasound Training Model	Structures of Interest/Objectives

Obstetrics ultrasound	Fetus Ultrasound Examination Phantom SPACEFAN-ST (Kyoto Kagaku)	• Placenta
		• Fetus
		  ○ Fetal head with the face profile
		  ○ Heart
		  ○ Stomach
		  ○ Cerebellum and third ventricle
		  ○ Spine
		• Sex of the fetus
		• Fetal position, breech or vertex
		• Fetal age using
		  ○ Biparietal head diameter
		  ○ Head circumference
		  ○ Femur length

Gynecology ultrasound	Transvaginal SonoHysterography and Sonosalpingography Ultrasound Training Model (CAE Healthcare)	• Urinary bladder • Pouch of Douglas with free fluid • Uterus • Uterine tubes • Endometrial stripe • Left and right ovaries • Ovarian follicles • Uterine fibroma • Ovarian mass/abscess
Breast ultrasound	Breast Ultrasound Training Model (Kyoto Kagaku)	• Breast layers • Axillary lymphatic nodes • Lactiferous ducts • Benign tumor • Cysts • Intraductal papilloma • Ductal carcinoma
Lumbar puncture	Lumbar Puncture and Spinal Epidural Training Model (CAE Healthcare)	• Iliac crests • Spinous processes of L3-L5 • Interspace of L3/L4 and L4/L5 • Ligamentum flavum • Epidural space • Subarachnoid membrane • Subarachnoid space containing cerebral spinal fluid • Measure cerebral spinal fluid pressure
Central line	Gen II Ultrasound Central Line Training Model (CAE Healthcare)	• Internal jugular vein • Common carotid artery • Algorithm of the procedure
Thoracentesis	Midscapular Thoracentesis Ultrasound Training Model (CAE Healthcare)	• Ribs • Intercostal spaces • Lung ○ Left pleural space in costodiaphragmatic recess • Algorithm of the procedure

FAST exam and abdominal aorta	FAST Exam Real Time Ultrasound Training Model (CAE Healthcare) Abdominal Aortic Aneurysm Ultrasound Training Model (CAE Healthcare)	• Right upper quadrant, free fluid in hepatorenal recess
		• Left upper quadrant, free fluid in splenorenal recess
		• Lung
		  ○ Right and left pleural spaces in costodiaphragmatic angles
		  ○ Signs of pneumothorax
		• Pericardial effusion
		• Free fluid in pelvis
		• Abdominal aorta measurements
		• Inferior vena cava

Abbreviation: FAST, focused assessment with sonography for trauma.

how to perform the carotid artery ultrasound examination and identify possible atherosclerotic plaques. After the demonstration, students scanned each other and mastered scanning skills (See Figure 1). The introduction of clinical cases provided correlations between the ultrasound laboratories and clinical courses, such as Internal Medicine and The Complete Doctor. These correlations allowed students to visualize and learn the imaging material better and in a more clinically relevant context.

In planning the new Clinical Ultrasound course, significant assets were committed by the college to add ultrasound phantoms to the ultrasound laboratories,

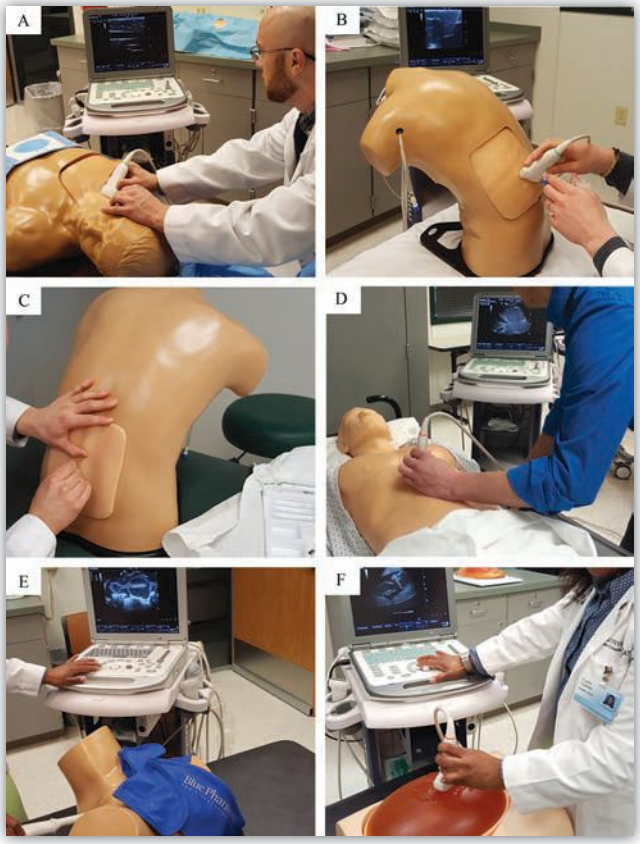


Figure 2. Ultrasound Training Models Used for the Clinical Ultrasound Course
A - Gen II Ultrasound Central Line Training Model (CAE Healthcare).
B - Midscapular Thoracentesis Ultrasound Training Model (CAE Healthcare).
C - Lumbar Puncture and Spinal Epidural Training Model (CAE Healthcare).
D - Focused Assessment with Sonography for Trauma (FAST) Exam Real Time Ultrasound Training Model (CAE Healthcare).
E - Transvaginal Sonohysterography and Sonosalpingography Ultrasound Training Model (CAE Healthcare).
F - Fetus Ultrasound Examination Phantom SPACEFAN-ST (Kyoto Kagaku).

including simulators with pathological conditions that allow a realistic approach to teaching ultrasound imaging during the clinical blocks (See Figure 2, Table 2). Some phantoms simulate pathological conditions, while others allow for needle-guidance training.

While integrating ultrasound into the first and second years of osteopathic medical education, we also identified the curricular areas of anatomy, osteopathic manipulative medicine (OMM), physiology, and internal medicine as ones that would benefit most from the inclusion of ultrasound. A workshop combining electrocardiography and echocardiography has been integrated into the cardiology block, and has been well received by students. Importantly, it significantly improved their understanding of the electrophysiology of the heart.[11] Students were able to better correlate electrical activity with cardiac mechanical events and understand cardiac physiology.[11]

While integrating ultrasound into the ATSU-KCOM curriculum, an ultrasound component was added to the OMM course.[21] It included six ultrasound assignments that required students to obtain ultrasound images of musculoskeletal structures, which were correlated with the body regions presented in the OMM course. Students scanned cranial and cervical structures and lumbar, sacral, and thoracic regions. Students were required to obtain images of the spinous processes of L4 and L5 and the base of the sacrum, laminae, and erector spinae muscles. Students also had to find the atlas (C1), its posterior arch, and the vertebral artery and vein.

Dental Ultrasound Laboratories

The integration of ultrasound has also opened new opportunities for dental medical education[22] because we introduced ultrasound technology to first-year dental students at A.T. Still University's Missouri School of Dentistry & Oral Health. The ultrasound laboratories focused on head, neck, and abdominal anatomy. Laboratories introduced dental students to a new, noninvasive imaging modality that does not use ionizing radiation. Survey results indicated that students enjoyed the ultrasound laboratory exercise and felt ultrasound was an effective learning tool because it provided a better understanding of maxillofacial anatomy.[22]

Student-Initiated Research Resulting from the Ultrasound Curriculum

Successful implementation of the ultrasound curriculum triggered significant research interest among medical students on a variety of topics, such as determining whether an ultrasound experience reinforced learning in Gross Anatomy [5] or the efficiency of assessing ultrasonography skills using a practical exam.[23] Students also researched 3-dimensional/4-dimensional ultrasound technology and its impact on medical education and rural health (unpublished study). Students also began to study how point-of-care ultrasonography has been used in urban versus rural areas.

Conclusions

Medical imaging presents significant challenges to medical students and, despite its importance, only 5% of total teaching time is dedicated to radiology in medical education.[24] The training that students receive through the KCOM ultrasound curriculum may help them better understand other diagnostic imaging modalities that are widely used in medical practice and become more versed in medical imaging in general. Ultrasound training has the

potential to enhance the learning experience for students and improve the quality of their future patient care.

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Disclosure

None reported. **MM**

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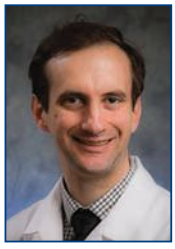
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Integration of 3-Dimensional/4-Dimensional Ultrasound Technology into Undergraduate Medical Education: Student Perception of Innovative Obstetrics Education

by Shannon McAllister, BA, Seth McIntire, MS & Tatyana Kondrashova, MD

Results of the current study suggested that undergraduate medical students are receptive, motivated, and capable of learning how to perform and interpret an obstetric examination on an ultrasound phantom.







Shannon McAllister, BA, (top), and Seth McIntire, MS, (bottom left), Osteopathic Medical Students, and Tatyana Kondrashova, MD, PhD, (bottom right), Department of Family Medicine, Preventive Medicine and Community Health are at A.T. Still University—Kirksville College of Osteopathic Medicine, Kirksville, Missouri.
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Abstract

The current study assessed level of comfort of medical students using 3-dimensional/4-dimensional (3D/4D) ultrasound technology after participating in an obstetrical ultrasound educational activity. The majority of students agreed that they were capable of performing and interpreting 2-dimensional and 3D/4D obstetrical ultrasounds and that the training benefited their clinical decision-making skills. Additionally, students agreed that access to 3D/4D ultrasound technology would encourage patients to seek physician care and act as a useful tool for patient education.

Introduction

Ultrasound technology converts high-frequency sound waves into visual images of a patient's tissues, blood flow, and organs.[1] In 2-dimensional (2D) ultrasound imaging, the sound waves are delivered and reflected back along the same path to create a 2D image.[2] In 3-dimensional (3D) ultrasound imaging, the sound waves are reflected back at several different angles, creating a 3D image.[2, 3] With 4-dimensional (4D) ultrasound imaging, the user can visualize movement of 3D structures in real time.[4] Ultrasound imaging is used in a wide variety of diagnostic settings with precise and safe results.[5] One of the most common uses of ultrasound imaging is in obstetrics and gynecology (OB/GYN).[6] Recent studies note that OB/GYN physicians urge practitioners to "consider adopting 3D imaging ultrasound as the first assessment tool for specific gynecological indications."[6] Unlike ultrasound technology, computed tomography imaging exposes the patient to ionizing radiation and increases the risk of cancer.[7] The 3D/4D ultrasound images offer enhanced diagnostic ability and greater identification of problems. For instance, the level of detail and depth offered by a 3D ultrasound can identify certain fetal abnormalities, such as a cleft lip, sooner and with more accuracy.[8] A 4D ultrasound, which shows movement of the scanned object, can aid in the diagnosis of internal issues with the musculoskeletal system and internal organs, such as the heart and blood vessels.

In the last two decades, ultrasound imaging has become an important point-of-care tool in acute care specialties, such as emergency medicine, intensive care medicine, and internal medicine, due to its versatility.[9] With so many positive aspects of ultrasound imaging and

its increasing prevalence in the clinical setting,[10-12] there is growing support for incorporating ultrasound imaging into undergraduate medical education.[13] Ultrasound training is most commonly used to aid in anatomical relationships.[14] Also, early ultrasound education in a patient-centered curriculum is feasible and may improve physical examination skills of students.[15] Compared with other modalities, ultrasound as a teaching tool has distinct advantages,[16] including use of ultrasound training models (or phantoms) for practical training.[17] Ultrasound models are life-like mannequins or phantom simulators that use new tissue technology compatible with diagnostic ultrasound systems and provide realistic training and assessment without the risk, inconvenience, and expense of standardized patients. Previous studies demonstrated ultrasound training models significantly improved learning outcomes[18, 19] and may be superior to traditional methods.[17, 20]

Integration of ultrasound technology into medical education will not only enhance the student's anatomical and clinical knowledge, but also increase preparedness for future practice with a technology that is quickly becoming an invaluable tool for point-of-care diagnostic imaging.[21, 22] Studies suggest that students who used physical examination assessment and ultrasound imaging had greater diagnostic accuracy and improved estimation of organ size compared with those who used physical examination skills alone.[23, 24] One limitation of ultrasound imaging is that it is operator dependent. Given the increased prevalence of ultrasound imaging in point-of-care medicine, it is important to educate undergraduate medical students so they are familiar and competent in ultrasound technique and interpretation.[9]

The primary objective of the current study was to assess level of comfort of medical students using 3D/4D ultrasound technology after participating in an obstetrical ultrasound laboratory. A survey was used to determine the student's level of comfort interpreting a 2D and 3D ultrasound image using an obstetrical phantom and to evaluate student perception of incorporation of 3D/4D ultrasound technology into medical education and whether this technology was beneficial for development of clinical decision-making skills.

Methods

Second-year osteopathic medical students participated in the current study. An obstetrics ultrasound laboratory was included in the curriculum at the institution of the current study as part of the Clinical Ultrasound course and during the Women's Health block in the third semester. The local

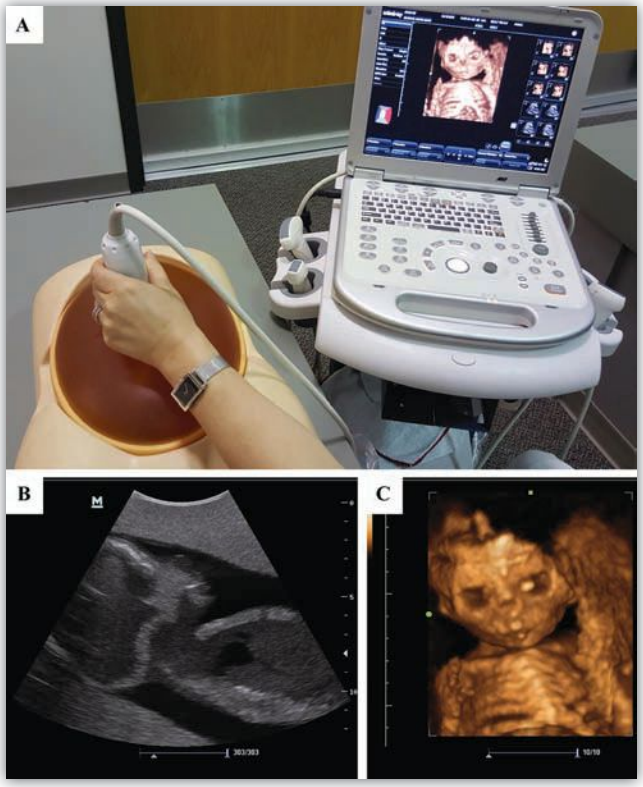


Figure 1. Ultrasound Setup for the Obstetrical Ultrasound Laboratory. A, Scanning a Fetus Ultrasound Examination Phantom SPACEFAN-ST (Kyoto Kagaku) using an ultrasound machine (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.); B, 2-Dimensional grayscale ultrasound image of the Fetus Ultrasound Examination Phantom; C, 3-Dimensional ultrasound image of the Fetus Ultrasound Examination Phantom.

institutional review board granted exempt status for all educational procedures used in the current study.

Student participants had a working knowledge of ultrasound techniques and applications from 2 semesters of clinical ultrasound coursework prior to the obstetrical laboratory. At our institution, the clinical ultrasound course is taught in 4 semesters during the first 2 years of medical school. During semester 1, students learn how to use the ultrasound machine and perform the upper and lower limb musculoskeletal ultrasound and the neck vascular and ocular ultrasound examinations. Semester 2 includes abdominal, echocardiography, upper and lower extremity vascular, and pelvic ultrasound examinations. Second-year ultrasound courses are more clinically oriented, so semester 3 focuses on lung, endocrine, obstetrics, gynecology, and breast ultrasound examinations. During semester 4, students master nerve imaging, needle-guided procedures, and focused assessment with sonography for trauma (FAST).

The obstetrics ultrasound laboratory was preceded by a PowerPoint® (Microsoft Corp.) presentation that explained the objectives and clinical relevance of the

Table 1. Student Responses to Likert Question Survey Items on Ultrasound Use (N=147)

Survey Item*	Likert Responses, No. (%)					Mean (SD)
	Strongly Disagree	Disagree	Neither Agree Nor Disagree	Agree	Strongly Agree	
I feel capable of operating an ultrasound machine with 3D/4D technology (n=145)	1 (0.7)	4 (2.8)	4 (2.8)	102 (70.3)	34 (23.4)	4.1 (0.6)
I feel capable of performing an obstetrics ultrasound exam in a clinical setting under supervision (n=147)	0 (0)	3 (2.0)	3 (2.0)	76 (51.7)	65 (44.2)	4.4 (0.6)
I find it challenging to interpret a 2D ultrasound image (n=147)	35 (23.8)	90 (61.2)	4 (2.7)	14 (9.5)	4 (2.7)	2.1 (0.9)
I find it challenging to interpret a 3D ultrasound image (n=141)	22 (15.6)	79 (56.0)	12 (8.5)	23 (16.3)	5 (3.5)	2.4 (1.0)
The use of the 3D/4D ultrasound probe during the obstetrics ultrasound lab was beneficial for the development of my clinical decision-making skills (n=146)	0 (0)	5 (3.4)	15 (10.3)	63 (43.2)	63 (43.2)	4.3 (0.8)
I believe that ultrasound technology is a useful tool to provide care for underserved populations (n=146)	0 (0)	2 (1.4)	0 (0)	23 (15.8)	121 (82.9)	4.8 (0.5)
I believe that 3D/4D ultrasound technology is a useful tool for patient education (n=146)	0 (0)	1 (0.7)	2 (1.4)	39 (26.7)	104 (71.2)	4.7 (0.5)

*Some students did not respond to all survey items.

ultrasound exercise followed by a live demonstration of the scanning technique using a fetus ultrasound phantom (Figure 1). Detailed handouts with instructions were also provided to students. The obstetrics ultrasound laboratory focused on identifying structures of interest and performing measurements to determine fetal age. To enhance student success, additional instruction was provided during the scanning time. Students used a Mindray-7 ultrasound machine with a 4CD4s volume 4D transducer (bandwidth 2-6 MHz; Shenzhen Mindray Bio-Medical Electronics Co., Ltd.). Students performed a supervised obstetrical ultrasound examination using 2D and 3D technology on the fetus ultrasound phantom. The fetus ultrasound phantom allowed for an ultrasound training examination of a routine second trimester screening and contained a 23-week-old fetus (26 cm) in utero. The fetus included skeletal structures; soft tissues of the brain, thorax, and abdomen; and external genitalia. The phantom also allowed visualization of the uterus with amniotic fluid, placenta, and umbilical cord. The oval-shaped phantom could be set in 4 positions for breech (face up or down) or vertex (face up or down) fetal positions.

After completing the obstetrics ultrasound laboratory, students participated in a voluntary anonymous paper survey created specifically for the current study. The 11-item survey contained 7 Likert questions, 2 "yes-or-no" questions, and 2 open-ended questions. Students had 5 minutes to complete the survey. The survey was designed to assess student perception of 2D and 3D/4D ultrasound technology in medical education and its value for future practice. The following Likert questions were used: (1) I feel capable of operating an ultrasound machine with 3D/4D technology; (2) I feel capable of performing an obstetrics ultrasound exam in a clinical setting under supervision; (3) I find it challenging to interpret a 2D ultrasound image; (4) I find it challenging to interpret a 3D ultrasound image; (5) The use of the 3D/4D ultrasound probe during the obstetrics ultrasound lab was beneficial for the development of my clinical decision-making skills; (6) I believe that ultrasound technology is a useful tool to provide care for underserved populations; and (7) I believe that 3D/4D ultrasound technology is a useful tool for patient education. A standard Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree) was used to evaluate agreement or disagreement. Survey questions 8 and 9 asked about the benefits of using 3D/4D ultrasound technology in rural and medically underserved communities: (8) Do you believe that access to 3D/4D technology is particularly useful in rural health care? and (9) Do you think providing access to 3D/4D ultrasound technology in a rural population would encourage patients to seek care from their physician? Answer choices were yes or no. The last 2 survey items were open-ended questions: (10) What is one thing you would like to see as part of the Obstetrics Ultrasound Lab that we did not include? and (11) Please leave comments with regards to the use of 3D/4D ultrasound technology in medical education.

All data analysis was completed using SAS software version 9.4 (SAS Institute, Inc., Cary, NC). Descriptive statistics reported frequencies and percent of responses to each survey item, frequencies and percent for each Likert question after combining agree and strongly agree responses, and means and standard deviations for each Likert question after assigning numeric values to responses (1=strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, and 5=strongly agree). Sets of Likert questions were averaged to form scales and compared with the yes-or-no responses of questions 8 and 9. The three scales included likelihood of using ultrasound technology in future practice (questions 1, 2, 5, 6, and 7), comfort level (questions 1, 2,

3, and 4), and capability of performing 3D/4D ultrasound imaging and obstetrical ultrasound examination with supervision (questions 1 and 2). Pearson correlations between Likert questions (1-7) and binary questions (8-9; 1=yes, 0=no) and qualitative analyses of the open-ended questions were performed. The latter included searching for common words and themes by copying student responses into a spreadsheet that was searched by keywords. Examples of keywords included: "real patient," "pathology," "future practice," and others. After completing a count of the keyword usage, each entry was checked for responses that did not mention the keyword but included a theme related to it. For example, students who requested to scan a "pregnant woman" were included in the category of students who used the keyword "real patient." A value of $P<.05$ was considered statistically significant.

Results

One hundred forty-seven second-year osteopathic medical students participated in the current study. Student responses to the Likert questions are presented in the Table 1. When combining agree and strongly agree responses, 136 of 145 (93.8%) students felt capable of operating an ultrasound machine with 3D/4D technology, 141 of 147 (95.9%) felt capable of performing an obstetrics ultrasound examination in a clinical setting under supervision, 18 of 147 (12.2%) found it challenging to interpret a 2D ultrasound image, 28 of 141 (19.9%) found it challenging to interpret a 3D ultrasound image, 126 of 146 (86.3%) felt the use of the 3D/4D ultrasound probe was beneficial for the development of clinical decision-making skills, 144 of 146 (98.6%) believed ultrasound was a useful tool to provide care for underserved populations, and 143 of 146 (97.9%) believed 3D/4D ultrasound was a useful tool for patient education. For the yes-or-no questions, 128 of 145 (88.3%) of students believed access to 3D/4D ultrasound would be particularly useful in rural health care, and 127 of 146 (87.0%) thought providing access to 3D/4D ultrasound in a rural population would encourage patients to seek care from their physician.

Significant correlations were found between student responses to different survey items. The choices of whether they believed that access to 3D/4D ultrasound technology was particularly useful in rural health care (question 8) were positively correlated with agreement levels that the use of the 3D/4D ultrasound probe during the obstetrics ultrasound laboratory was beneficial for the development of clinical decision-making skills ($r=0.38$, $P<.001$, question 5) and with agreement levels about whether they believed 3D/4D ultrasound technology was a useful tool for patient education ($r=0.39$, $P=.001$, question 7). All other Likert question correlations with question 8 were not significant (all $P>.20$). Student responses to whether they thought providing access to 3D/4D ultrasound technology in a rural population would encourage patients to seek care from their physician (question 9) were positively correlated with student agreement levels to the following statements: students felt capable of operating an ultrasound machine with 3D/4D technology ($r=0.20$, $P=.04$, question 1), the use of the 3D/4D ultrasound probe during the obstetrics ultrasound laboratory was beneficial for the development of clinical decision-making skills ($r=0.38$, $P<.001$, question 5), they believed ultrasound technology was a useful tool to provide care for underserved populations ($r=0.23$, $P<.001$, question 6), and they believed 3D/4D ultrasound technology was a useful tool for patient education ($r=0.19$, $P=.02$, question 7). Student responses were negatively correlated with student agreement levels to the following statements: they found it challenging to interpret a 2D ultrasound image ($r=-0.19$, $P=.02$, question 3) and a 3D ultrasound image ($r=-0.23$, $P<.001$, question 4). Correlation between these student responses and student agreement levels to question 2 was not significant ($P=.11$).

Qualitative analysis of the open-ended survey items indicated 27 (18.3%) students requested the opportunity to scan pregnant patients and 37 (25.2%) requested incorporating pathological fetal models and including more interpretation of fetal development and pathologies. Twelve (13.6 %) students expressed interest in using 3D/4D ultrasound technology in their future practice, 9 (6%) believed the use of 3D/4D ultrasound technology increased their anatomical knowledge, 9 (6%) mentioned the benefit of using 3D/4D ultrasound technology for patient education, and 2 (1.3%) felt they were more prepared for their OB/GYN rotations after participating in the ultrasound educational activity.

Discussion

Results of the current study suggested that the majority of second-year osteopathic medical students felt comfortable with the use of 3D/4D ultrasound technology during the obstetrics ultrasound laboratory; 93.8% of students agreed they felt capable of operating an ultrasound machine with 3D/4D technology. Further, 95.9% of students agreed they were capable of performing an obstetrics ultrasound examination in a clinical setting under supervision. The format of this training exercise allowed medical students to interpret ultrasound images and identify fetal structures on a phantom. All students were able to obtain images of the fetal spine, stomach, heart chambers, and femur and to provide

measurements for determining the fetal age and diagnosing the fetal position as breech or vertex. They also scanned and positively identified the assigned structures, visualized the phantom's facial structures using the 3D/4D probe, and performed correct fetal measurements, which suggested that students were indeed competent in ultrasound imaging and interpretation.

The majority of students in the current study felt comfortable interpreting 2D and 3D ultrasound images using an obstetrics model. Previous research demonstrated the importance of simulation-based learning in medical training, where students trained to use ultrasound and phantoms were better prepared to interpret images compared with classroom-based learners.[25] In the current study, 12.2% and 19.9% of students agreed it was challenging to interpret 2D and 3D ultrasound images, respectively; however, all students were still able to find and interpret the assigned fetal structures and measurements. The ability to accurately identify and interpret ultrasound images is an important aspect of medical training, and it can have an impact on physician competence and patient safety. In a review of the role of medical simulation, physicians trained with simulation-based techniques outperformed and were more competent than traditionally trained physicians for a specific procedure, and using simulation-based education increased patient safety.[26] Given these benefits and the greater prevalence of medical simulation in medical education and training in modern medical school curricula,[26] it is imperative to begin simulation training at the undergraduate medical student level.

Results of the current study suggested undergraduate medical students were receptive to incorporating 3D/4D ultrasound technology into their education and future practice. We found that 86.3% of students agreed that the use of the 3D/4D ultrasound probe during the exercise was beneficial for the development of their clinical decision-making skills. This finding was supported by the open-ended student responses, where students suggested they feel more prepared for OB/GYN rotations. Further, 6% of students indicated that seeing the image in 2D and then in 3D helped augment their knowledge of anatomy. This finding suggested that 3D/4D ultrasound technology may have the additional benefit of increasing the anatomical understanding of medical students, and this supposition is supported by a previous study that found the use of ultrasound technology in undergraduate medical education increased students' anatomical knowledge.[27] In the current study, the qualitative analysis of the open-ended survey items found that students were overwhelmingly positive about the incorporation of 3D/4D ultrasound education into the curriculum; 98.6% of students agreed that 3D/4D ultrasound technology was a useful tool for patient education and beneficial for their future practice. In addition, 13.6% of students indicated their intention to use 3D/4D ultrasound technology in their future practice, and 6% specifically mentioned that using 3D/4D ultrasound technology would help patients better understand their own health status. One student suggested that the use of 3D/4D ultrasound technology would increase the patient's understanding of pathology and normal anatomy without extensive training.

Several survey items involved student perception of the use of ultrasound technology in a rural population. A previous study suggested that, despite the increasing overall use of point-of-care ultrasound in medicine, access to bedside ultrasound in rural emergency departments is significantly diminished.[28] One solution to increase access to point-of-care ultrasound in rural medicine involves the expansion of ultrasound training during medical education.[29] In the current study, student belief that 3D/4D ultrasound technology was particularly useful in rural health care was positively correlated with the belief that ultrasound training was beneficial for clinical-decision making skills and patient education. Given these results and as more medical schools include ultrasound training in undergraduate medical education, the advocacy of these future physicians may result in ultrasound technology being incorporated to a greater extent in rural medicine, where it has the highest potential for benefit because access to advanced imaging is not readily available.[29] Additionally, the current study found student belief that providing access to 3D/4D ultrasound would encourage patients to seek care from their physician was positively correlated with belief that ultrasound technology was a useful tool to provide care for underserved populations and patient education. A pilot study investigating the use of ultrasound technology with rheumatoid arthritis patients found that patients' concerns about pharmacotherapy were reduced after viewing their inflamed joints using real-time ultrasound images; however, there was no significant change in medicine adherence.[30] Additional studies are needed to explore correlations between patient compliance with physician appointments and the use of 3D/4D point-of-care ultrasound in rural populations.

One limitation of the current study was that students did not have access to a pregnant standardized patient when performing the obstetrical examination and, therefore, could not detect movement with the 4D probe. A common comment by students was their desire to practice scanning a pregnant woman with the 3D/4D probe to see fetal

movement in real time and to hear the heartbeat. Moreover, the phantom model was congenitally normal. The most frequent comment made by students was their desire to scan models with congenital abnormalities, so they could attempt to diagnose them.

Conclusion

Results of the current study suggested that undergraduate medical students are receptive, motivated, and capable of learning how to perform and interpret an obstetric examination on an ultrasound phantom. The majority of students agreed that they were capable of performing and interpreting 2D and 3D/4D obstetrical ultrasounds and that the training increased their clinical decision-making skills. Additionally, students agreed that 3D/4D ultrasound technology would encourage patients to seek care from their physician and act as a valuable tool for patient education. Finally, results of the current study support the further implementation of ultrasound technology in the early years of undergraduate medical education

Acknowledgments

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Disclsoure

None reported. **MM**

Introduction of a Combined Gastrointestinal Histopathology Laboratory Exercise into an Undergraduate Medical School Curriculum

by Kathryn Dominick, BS, Dalton McDaniel, BS, Emily Tilton, BS, Kale Flory, BS & Peter Kondrashov, PhD

The current study suggests a combined histopathology laboratory is a valuable learning tool that can provide unique integration of clinical and basic science knowledge through the use of virtual microscopes.



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Abstract

To improve training in histology and pathology, an integrative, case-based histopathology laboratory exercise that used virtual microscopy was offered to first-year medical students during the KCOM gastrointestinal block. Students showed improvement in their understanding of histology and pathology after completing the exercise. Most students agreed that the combined histopathology laboratory helped them improve their understanding of histology and pathology in the gastrointestinal system and link normal histological and pathological changes to better understand disease processes.

Introduction

Education and training in histology and pathology have been critical in medical school curricula. Even though histology is a fundamental course taught early in training, students have difficulty carrying this knowledge into their pathology studies.[1] To solve this problem, medical schools have started to incorporate case-based, integrative laboratories that combine histology and pathology.[1] Research suggests that reorganization of a traditional, organ systems histology course so it includes a laboratory connecting histology, physiology, and pathology results in significantly improved histology examination scores.[2]

The institution of the current study implemented a systems-based, patient-centered curriculum in 2014. During each content block, students work through one organ system at a time, learning normal anatomical and physiological function first before learning pathological dysfunction, clinical diagnoses, and treatments. In course evaluations, students indicated that although they were exposed to normal histology and pathology during each systems block they struggled to incorporate histology knowledge with pathology studies.

An efficient way of integrating histology and pathology is through the use of virtual microscopy.[1] Virtual microscopes (VM) are computer-based programs that permit viewing and annotating of digital slides obtained from a camera-equipped microscope with slide-scanning capability. The transition from glass slides and microscopes to VM has been beneficial to student learning[3] because VM lacks the mechanical barriers of using a microscope, such as focus, staining, lighting, and poor sample. Further, VM is easier to use, provides high resolution and better control of the area of study, and promotes learning of histology and pathology rather than the mechanics of the microscope. Students are able to view

more digital slides than during a conventional microscope-based laboratory while having their instructors be more available for questions.[3] Also, VM uses web storage for images, increasing the availability of slides for students and residents to study outside the allotted laboratory time.[4] Because VM has created a student-centered, team-based learning environment, as opposed to a passive didactic approach, students can use their histopathology knowledge to solve clinical cases presented through the digital slides.[5] In one study, VM was included in pathology courses; students preferred virtual slides to glass slides for studying pathology, and their performance on examinations improved.[6]

In addition to teaching histology and pathology to medical students, VM is now integrated into the education and examination of physicians specializing in pathology. The European Association of Pathology Chairs and Residency Program Directors incorporates digital images with written questions in assessment of resident physicians.[4] Further, VM allows physicians to view hundreds of diseases from different organ systems to practice diagnostic skills. The virtual slide competency examination (VSCE) has been successfully used to evaluate the diagnostic skills of surgical pathology residents.[7] Results of the VSCE have been positively correlated with residents' VSCE scores and months of training ($r=0.83$), resident in-service examination score ($r=0.70$), and Accreditation Council for Graduate Medical Education global ratings for diagnostic and patient care activities ($r=0.28$).[7] These positive correlations support the use of VM to improve diagnostic reasoning in undergraduate medical education and postgraduate training.

At the institution of the current study, medical histology is taught through lecture and laboratory. In the histology laboratory, VM has been used since 2010 and was well received by students and faculty, as reflected in student course evaluations. However, the current pathology course is mostly taught through lecture, with no laboratory time for students to identify diseases on the histopathological level. To integrate histology and pathology so students are better prepared for board examinations and clinical rotations, we created a histopathology laboratory that included the use of VM. Students worked in groups to diagnose a case by studying a digital slide and using pertinent patient history and their knowledge of histology and pathology. The goal of the current study was to determine if the combined histopathology laboratory improved student understanding of histology and pathology.

Methods

The College institutional review board granted exempt status for the current study.

Participants

At the institution of current study, a histopathology laboratory was introduced during the gastrointestinal system block in the second semester of the first-year medical school curriculum. The laboratory was conducted one week prior to the block examination and after the gastrointestinal histology and pathology lecture portions had been completed. Attendance was required, and students received participation credit. The 172 student participants were divided into 2 laboratory sections. During the 1-hour laboratory sessions, students worked in assigned groups of 2-3 individuals to diagnose the case given to them and complete the laboratory assignment. The assignment was distributed using Google forms (Google, Inc.). Each form included the group's table number, member names, and case number. During the laboratory, students completed a laboratory assignment, prelaboratory and postlaboratory quizzes, and a survey.

Laboratory Assignment

Six possible cases were used for the laboratory assignment, and student groups were randomly assigned a single case. Each case included a brief patient history, a VM slide of the pathological tissue, and VM slides of normal histology of gastrointestinal viscera. The following cases were used in the current study:

- Case 1: 68-year-old male presents with recurrent attacks of alternating diarrhea and constipation with painful cramps and tenderness in the lower abdomen.
- Case 2: 24-year-old male presents with crampy abdominal pain and blood in stool. Systemic examination reveals pigmented spots in the oral cavity and finger clubbing.
- Case 3: 12-year-old male presents with pain in right lower quadrant of abdomen.
- Case 4: 74-year-old male on broad spectrum antibiotics for upper respiratory tract infection presents with watery diarrhea, abdominal cramps, and fever.
- Case 5: 32-year-old female presents with recurrent attacks of abdominal pain, gassiness, bloating, and changes in bowel habits.

Table 1. Student Improvement on the Histopathology Quiz

Quiz Questions	Total No. Students[a]	Students Showing Improvement, No. (%)	*P* Value[b]
1. When examining a biopsy for possible Crohn colitis, you expect to see inflammatory infiltrates in which of the following layer(s)?	66	38 (58%)	.22
2. In a patient with suspected Peutz-Jegher syndrome, which characteristic pathological structure can be found in the colon?	100	84 (84%)	<.001
3. Presence of which of these cell types in the muscularis externa of the appendix is the most diagnostic feature of acute appendicitis?	70	47 (67%)	.004
4. When compared to the normal colonic wall, colonic diverticulum typically contains which of the following layer(s)?	103	44 (43%)	.14
5. In a patient with *Clostridium difficile* infection, which colonic structure(s) is/are seen packed with neutrophils and other inflammatory debris?	114	61 (54%)	.45

[a] The total number of students excludes those students who answered the question correctly on both prelaboratory and postlaboratory quizzes.
[b] A binomial test for proportion was used to determine if the proportion of students who improved on a question was significant ($P \leq .05$).

Table 2. Student Responses to the prelaboratory and postlaboratory Likert scale quiz questions (n=172).

Quiz Question	Strongly agree and agree. No. (%)	Disagree and strongly disagree. No. (%)	Neutral. No. (%)
Prelaboratory Likert question 1. I currently have a strong understanding of gastrointestinal histology.	64 (37%)	37 (22%)	71 (41%)
Postlaboratory Likert question 1. I currently have a strong understanding of gastrointestinal histology.	89 (52%)	18 (10%)	64 (38 %)
Prelaboratory Likert question 2. I currently have a strong understanding of gastrointestinal pathology	22 (13%)	72 (42%)	77 (45%)
Postlaboratory Likert question 2. I currently have a strong understanding of gastrointestinal pathology	65 (38%)	40 (23%)	67 (39%)

- Case 6. 24-year-old male with complains of solid food dysphagia and food impaction.

To determine the appropriate diagnosis for the presented case, groups answered histology, pathology, and clinical questions on the Google form designed to guide them toward the diagnosis. The following questions were included on the form:

- Based solely on the case history, what labs/tests would you think about ordering?
- Look at your pathology slide and name the organ. Identify and describe the layers of the organ present on the slide.
- Compared to normal histology, what features appear to be abnormal on your pathology slide?
- What is your differential diagnosis? (list at least 3)
- Your patient wants to know why you think it is your #1 diagnosis. Please explain your reasoning behind this diagnosis.

During each laboratory, faculty and pre-doctoral anatomy fellows were available to assist with interpretation of the pathological tissue. Fellows were medical students who had completed two years of medical school and were taking an additional year to participate in teaching and research. After the students submitted their assignments, the pathology instructor reviewed each case, starting with the patient history and explaining the normal histological and pathological changes using the VM slide.

Outcome Measures

At the beginning of the laboratory, students completed a prelaboratory quiz. The quiz included five multiple-choice questions on gastrointestinal pathology and two Likert scale questions about whether students had a strong understanding of gastrointestinal histology and pathology (Tables 1, 2). For multiple-choice questions, students were given a point for each correct answer. At the end of the laboratory, students completed a postlaboratory quiz with the same questions. Asking the same questions both times allowed us to assess the change in student understanding of gastrointestinal system histology and pathology after completing the laboratory.

After the laboratory, students completed a survey about their experiences with the histopathology laboratory. The survey consisted of three open-ended and three Likert scale items.

Open answer questions:

- What did you like best about this laboratory?
- What did you like least about this laboratory?
- How could we improve this laboratory?
- Likert-type items/questions:
- This laboratory helped to improve my understanding of gastrointestinal system pathology.
- This laboratory helped to improve my understanding of gastrointestinal system histology.
- This laboratory helped me to link normal histology and pathological changes to better understand diseases/dysfunctions of the gastrointestinal system.

Statistical Analysis

Prelaboratory and postlaboratory quiz scores were analyzed for differences for each question by subtracting the prelaboratory score from the postlaboratory score.

A binomial test for proportions was used to determine whether the proportion of students who answered a question correctly was significantly different from 0.5. Data from students who answered the question correctly both times were removed since there was no room for improvement. For overall improvement in understanding of the gastrointestinal system, scores for all prelaboratory and postlaboratory questions were added separately to calculate total prelaboratory and total postlaboratory scores. The total score difference was calculated by subtracting the total prelaboratory score from the total postlaboratory score. Again, students who scored a five both times were excluded. The frequency distribution was calculated. Score differences for the two Likert scale questions were calculated from the prelaboratory and postlaboratory quiz for both questions. A binomial test for proportions was used to determine if the proportion of students who felt some improvement in their understanding of the gastrointestinal system was different from 0.5. For the survey, data from the three Likert scale items were analyzed using a binomial test for proportion to determine if the proportion of students who felt improvement in their understanding of the gastrointestinal system was significantly different from 0.5. Values of $P \leq .05$ were considered statistically significant. Analyses were conducted using SAS 9.4 (SAS Institute Inc.).

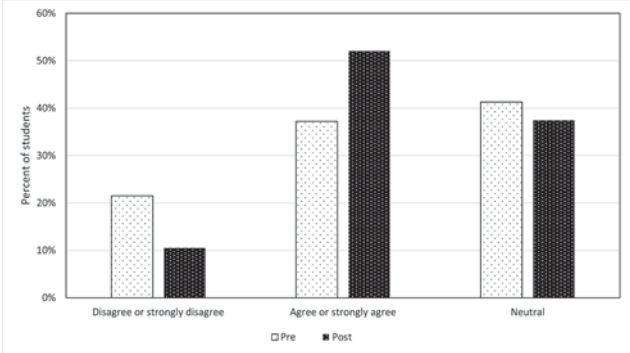


Figure 1. Student responses to the prelaboratory and postlaboratory quiz question about whether students had a strong understanding of gastrointestinal histology.

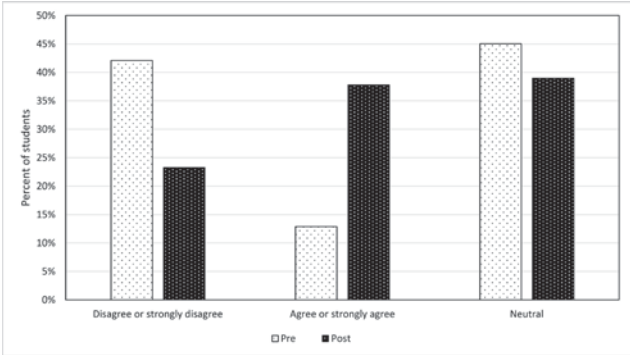


Figure 2. Student responses to the prelaboratory and postlaboratory quiz question about whether students had a strong understanding of gastrointestinal pathology.

Results

Students had significant score improvement on quiz questions 2 ($P < .001$) and 3 ($P = .004$; Table 1). Based on the total quiz scores for 172 students, 17 (11%) students had no improvement, meaning they either had the same total score on both the pre- and the postlaboratory quizzes or their scores went down, 54 (34%) students improved by 1 point, 54 (34%) students improved by 2 points, 28 (18%) students improved by 3 points, and 7 (4%) students improved by 4 points.

When answering the first Likert scale question on the prelaboratory quiz, 64 of 172 (37%) students strongly agreed or agreed and 37 of 172 (22%) students strongly disagreed and disagreed that they had a strong understanding of gastrointestinal histology, while 71 (41%) students were neutral (Figure 1, Table 2). On the postlaboratory quiz, 89 of 172 (52%) students strongly agreed or agreed, while only 18 of 172 (10%) students strongly disagreed or disagreed that they had a strong understanding of gastrointestinal histology, and 64 (38%) were neutral about it (Figure 1, Table 2). For the second Likert scale question on the prelaboratory quiz, only 22 of 172 (13%) students strongly agreed or agreed, while 72 of 172 (42%) students strongly disagreed and disagreed that they had a strong understanding of gastrointestinal pathology, and 77 (45%) students were neutral (Figure 2, Table 2). On the postlaboratory quiz though, 65 of 172 (38%) students strongly agreed or agreed, while 40 of 172 (23%) students strongly disagreed or disagreed that they had a strong understanding of gastrointestinal pathology, and 67 of 172 (39%) students were neutral about it (Figure 2, Table 2).

The postlaboratory survey indicated that 117 of 172 (68%) students strongly agreed or agreed that the combined histopathology laboratory helped them improve their understanding of gastrointestinal system histology and only 13 of 172 (8%) students strongly disagreed or disagreed and 41 of 172 (24%) students were neutral (Figure 3). Thus, more students felt the laboratory helped them in

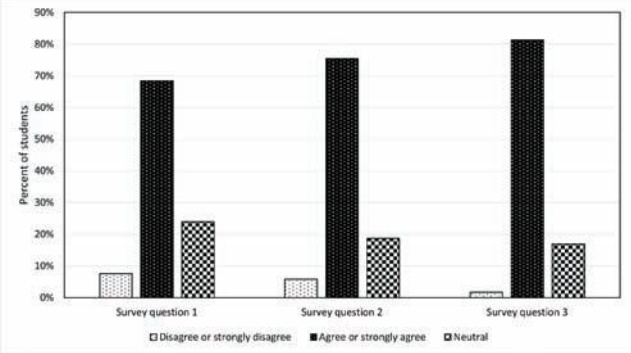


Figure 3. Student responses to postlaboratory survey Likert scale items. Survey item 1 was "This laboratory helped to improve my understanding of gastrointestinal system pathology." Survey item 2 was "This laboratory helped to improve my understanding of gastrointestinal system histology." Survey item 3 was "This laboratory helped me to link normal histology and pathological changes to better understand diseases/dysfunctions of the gastrointestinal system."

understanding gastrointestinal system histology ($P<.001$). The majority of students, 129 of 172 (75%) strongly agreed or agreed that the combined histopathology laboratory helped them improve their understanding of gastrointestinal system pathology (Figure 3). Only 10 of 172 (6%) students strongly disagreed or disagreed, and 32 of 172 (19%) were neutral, which provided evidence that students found the laboratory helpful in improving their understanding of gastrointestinal system pathology (Figure 3; $P<.001$). The majority of students, 139 of 172 (81%) strongly agreed or agreed that the combined histopathology laboratory helped them link normal histology and pathological changes to better understand diseases and dysfunctions of the gastrointestinal system, while only 3 of 172 (2%) students strongly disagreed or disagreed, and 29 (17%) were neutral about it (Figure 3). These results indicated that students felt the laboratory helped them link normal histology and pathological changes to better understand diseases/dysfunctions of the gastrointestinal system (Figure 3; $P<.001$).

Responses to the open-ended items of the survey allowed students to share what they liked most and least about the laboratory, and what they thought could be improved. Students indicated it was beneficial to have histology and pathology slides included with the patient history to better diagnose the patient case. One of the students stated, "I like having to figure out what the patient has based on the abnormal histology and symptoms/history given. I also very much appreciated having the normal slides right next to the abnormal ones for reference."

Students also commented on how they often forgot to apply histology to pathology and indicated the laboratory exercise made them realize the importance of histology in clinical medicine. As one student explained, "I liked that it was presented like a 'case' and that we weren't just focusing on the slide, but on how the slides relate to actual disease. I think we sometimes lose track of how histology relates to medicine, and it's nice being able to see normal and abnormal at the same time." Another student wrote, "Bringing pathology and histology together really helped me see a larger picture of the diseases we discussed in pathology and also helps me see the importance of histology." Students also commented on the usefulness of VM and whole slide imaging for pathology slides: "These images were much better quality [compared to static images from lecture/textbook] so I felt like I had a better understanding of the morphology for some of the pathology."

Discussion

The current study assessed the integration of histology and pathology using a combined histopathology laboratory exercise that included the use of VM to help students improve their understanding of histology and pathology. Our results suggested that the integrated laboratory helped students to better understand gastrointestinal histology and pathology. Students had significant improvement for two of the five quiz questions from prelaboratory to postlaboratory. Overall, 90% of the students showed some improvement in quiz scores from prelaboratory to postlaboratory quiz. For the Likert scale quiz questions, the number of students who agreed or strongly agreed with the questions increased from prelaboratory to postlaboratory quiz, and the number who disagreed or were neutral decreased.

In a similar study investigating the effects of collaborative learning, junior and senior medical students were enrolled in a pathology practical course that used VM.[8] The students studied two different histopathological slides using VM, one individually and one collaboratively in small groups.[8] After studying the slides, students were quizzed over the material.[8] The mean scores of the quizzes that covered the material studied using collaborative learning were significantly higher than the mean scores of the quizzes that covered the material studied individually.[8] These results support the data from the current study; our students were required to work in groups of three to discuss their findings and determine a diagnosis, which

resulted in improved scores on the postlaboratory quiz and better student perception of their histology and pathology knowledge.

In addition to our quantitative results, survey responses suggested the majority of students felt that the combined histology-pathology laboratory helped them improve their understanding of gastrointestinal histology and pathology. A previous study showed similar exercises resulted in a greater understanding of histopathological slides when collaboratively studied.[8] Overall, written student feedback from our survey was positive, and students wrote that having the histology and pathology slides made it easier to diagnose the patient case.

The current study had several limitations. First, because of scheduling limitations, the laboratory was only one hour. Insufficient time meant we could only discuss a few gastrointestinal pathologies and may explain why 61% of students disagreed or felt neutral about the postlaboratory Likert scale question related to whether they had a strong understanding of gastrointestinal pathology. Having more time would allow inclusion of multiple patient cases to increase student exposure to gastrointestinal histopathology. In the open-ended portion of the survey, one student suggested, "Working through more than one case may be beneficial. I learned more much more on the case that I worked on through the process than the other cases that were presented to us."

Overall, the current study suggests a combined histopathology laboratory is a valuable learning tool that can provide unique integration of clinical and basic science knowledge through the use of VM. The laboratory was very well received by students and resulted in a marked improvement in scores on the postlaboratory quiz.

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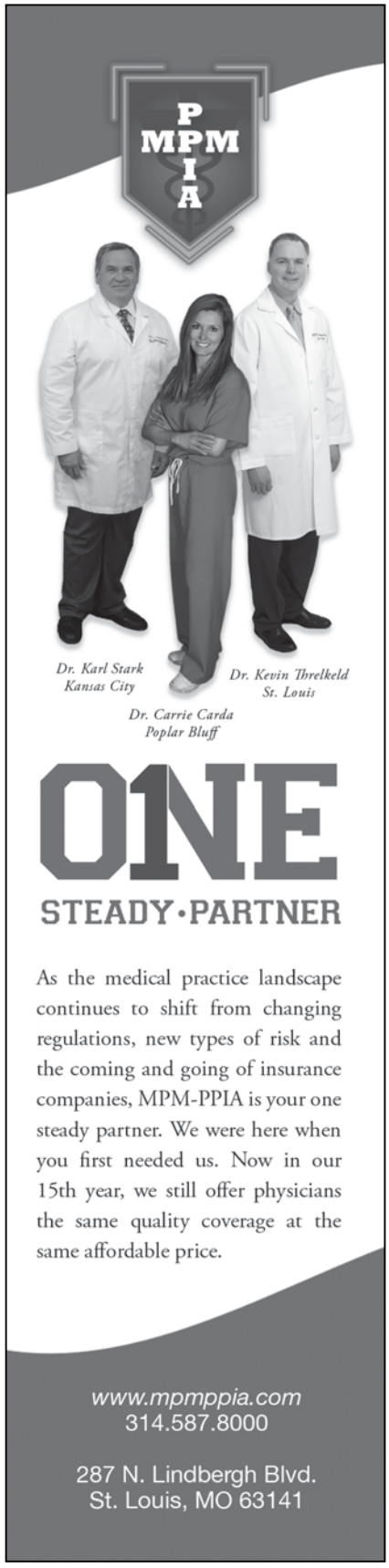
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Disclosure

None reported.

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A Comparison of Point-of-Care Ultrasonography Use in Rural Versus Urban Emergency Departments Throughout Missouri

by Michael Mengarelli, BS, Anthony Nepusz, BS & Tatyana Kondrashova, MD

Considering the known benefits of point-of-care ultrasonography in the emergency department, patients presenting to hospitals that lack this technology may be subjected to longer and more expensive care.







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Abstract

We surveyed emergency department directors at 56 Missouri hospitals about availability of ultrasound equipment, primary uses for ultrasonography, and factors that could increase ultrasonography use in the emergency departments. Results indicated large-sized hospitals, typically in urban areas, used ultrasonography more than medium-sized or small-sized hospitals. Lack of ultrasound equipment and appropriately trained physicians contributed to limited use of ultrasonography in small-sized hospitals, typically in rural areas.

Introduction

Introduced into clinical practice in 1956, ultrasonography has established itself as a reliable, quick, and safe imaging modality.[1] Advancements in this technology have transformed once static-filled images into crisp, living portrayals of internal spaces and organs. Physicians increasingly rely on ultrasonography to visualize pathology and it may assume the role of tomorrow's stethoscope.[2] Because of more compact, lightweight, and less expensive ultrasonography machines, bedside ultrasonography has become a core imaging evaluation in many emergency departments.[3, 4]

Bedside point-of-care ultrasonography[5] is performed in the emergency department by an emergency physician at the patient's bedside. When using bedside point-of-care ultrasonography, emergency physicians can develop a greater understanding of the patient's case and rapidly integrate the results of the ultrasonography examination into an immediate treatment plan. The traditional consultative imaging model requires the emergency physician to order an examination and rely on the radiologist for imaging analysis, resulting in delays in the performance of the examination and its interpretation.[4] Furthermore, this model potentiates the risk of the radiologist not being fully aware of the clinical facts of the case or patient presentation.

Bedside point-of-care ultrasonography has proven itself as a powerful diagnostic tool in emergency situations ranging from soft tissue examinations to cardiac assessments.[4, 6] One of the most common emergency room presentations is acute abdominal pain.[7] It represents an expensive and time-consuming workup and can be attributed to a wide-ranging differential diagnosis.[8] For most patients with abdominal pain, imaging

is a required procedure in the treatment protocol, and ultrasonography can reduce some of the costs associated with the workup. In a recent study, 139 pediatric emergency room patients were evaluated for appendicitis using point-of-care ultrasonography.[9] The generated images resulted in quicker next-step decisions, adjustments in treatment, and faster treatment plans. The hospital's estimated savings was $565 per patient and was attributed to the use of ultrasonography. Changes in care management as well as direct and indirect costs were also calculated and indicated a total savings of $78,504 over the period of six months.[9] Given this example, it is difficult to reject the efficiency of point-of-care ultrasonography when considering cost of care savings.

Access to advanced care, such as point-of-care ultrasonography, is readily available in large-sized hospitals found in larger, urban areas.[4] However, few studies have evaluated access to the same resources in small-sized hospitals that are often found in rural areas.[10] Therefore, the purpose of the current study was to evaluate and compare point-of-care ultrasonography use in emergency departments in various-sized hospitals throughout Missouri. We hypothesized that large-sized hospitals would have greater access to bedside point-of-care ultrasonography and would use it to a greater degree than medium-sized and small-sized hospitals.

Methods

In the current study, emergency department directors or supervisors from hospitals throughout Missouri were surveyed regarding the use of ultrasonography in their departments. The College institutional review board granted exempt status for the study.

A list of hospitals was obtained from the Missouri Department of Health & Senior Services.[11] Large-sized hospitals were defined as having at least 95 beds, medium-sized hospitals had 50-94 beds, and small-sized hospitals had up to 49 beds. Large-sized hospitals typically had a minimum of 6500 emergency room visits annually, medium-sized hospitals had 2500-6499 emergency room visits annually, and small-sized hospitals had up to 2499 emergency room visits annually.

The survey included three questions about the availability of ultrasound equipment, primary uses for ultrasonography, and factors that could increase ultrasonography use. Because the survey required knowledge of the ultrasonography methods used in the emergency department, only emergency department directors or supervisors were asked to complete the survey. Surveys were administered electronically through Google Forms (Google, Inc., Mountain View, CA) and were emailed to the emergency department directors or supervisors identified from the list of hospitals. In cases where respondents had technical difficulties accessing the form, the surveys were administered over the telephone. Standard scripts were used for telephone respondents and included information about the purpose of the study and the level of involvement necessary to complete the survey. It took about 10 minutes for respondents to complete the survey. The survey was available to respondents for three weeks.

Survey questions used in the current study were as follows: (1) Is there bedside ultrasound equipment/an ultrasound machine available in the emergency department at your facility? (2) What are the primary uses of the ultrasound machine in your emergency department? and (3) What factors would increase the use of ultrasound in your emergency department? Available responses to question 1 were yes or no. Available responses for question 2 were trauma (focused assessment with sonography in trauma [FAST] exam), lung (pneumothorax), cardiac (echocardiography), abdominal aortic aneurism, abdomen: hepatobiliary ultrasound, abdomen: renal ultrasound, pregnancy (first, second, or third trimester), deep vein thrombosis, carotid arteries ultrasound, soft tissue, vascular access, ultrasound-guided procedures, or other. Available responses for question 3 were equipment availability, training availability, or other. Other responses were formatted with free-form text entry in the Google Form so respondents could write in their response.

The survey was closed after the three-week participation period, and the responding hospitals were grouped into the large-sized, medium-sized, or small-sized hospital categories.[11] Survey responses were summarized using frequency and percentage. The Mantel-Haenszel χ^2 test and Fisher exact test were used to test for associations between the hospital size and survey responses. Values of $P \leq .05$ were considered statistically significant.

Results

Of the 136 Missouri hospitals with emergency departments, 56 (41%) hospitals completed surveys. Of the 59 large-sized hospitals in Missouri, 20 (34%) completed the survey. Of the 29 medium-sized hospitals, 12 (41%) completed the survey, and of the 48 small-sized hospitals, 24 (50%) completed the survey. Sixteen of the 20 (80%) large-sized hospitals were located in urban or suburban areas, and 23 of the 24 (96%) small-sized hospitals were located in rural areas.

Table 1. Primary Uses of Ultrasonography in Missouri Emergency Departments Based on Hospital Size

Primary Use	Hospital Size, No. (%)			Total, No. (%)
	Large-Sized Hospitals	Medium-Sized Hospitals	Small-Sized Hospitals	
Trauma	16 (80%)	5 (71%)	4 (40%)	25 (68%)
Lung	3 (15%)	0	1 (10%)	4 (11%)
Cardiac	8 (40%)	1 (14%)	3 (30%)	12 (32%)
Abdominal aortic aneurysm	8 (40%)	1 (14%)	5 (50%)	14 (38%)
Abdomen: hepatobiliary	3 (15%)	0	3 (30%)	6 (16%)
Abdomen: renal	5 (25%)	0	4 (40%)	9 (24%)
Pregnancy	15 (75%)	2 (29%)	5 (50%)	22 (60%)
Deep vein thrombosis	5 (25%)	0	5 (50%)	10 (27%)
Carotid arteries	0	0	1 (10%)	1 (3%)
Soft tissue	11 (55%)	0	2 (20%)	13 (35%)
Vascular access	17 (85%)	5 (71%)	6 (60%)	28 (76%)
Ultrasound-guided procedures	7 (35%)	2 (29%)	1 (10%)	10 (27%)
Other	1 (5%)	0	0	1 (2.7%)

Large-sized hospitals had at least 95 beds, medium-sized hospitals had 50-94 beds, and small-sized hospitals had up to 49 beds. These hospitals typically had at least 6500, 2500-6499, or up to 2499 emergency room visits annually, respectively.

Based on responses to question 1, bedside ultrasound within the emergency departments was available at 37 of the 56 (66%) hospitals. The availability of ultrasound was significantly and directly associated with the size of the hospital ($P<.001$). All 20 (100%) large-sized hospitals reported having available bedside ultrasound. Only 7 of 12 (58%) medium-sized and 10 of 24 (42%) small-sized hospitals reported having available bedside ultrasound.

Based on responses to question 2, bedside ultrasound was primarily used for vascular access (76%), trauma (68%), and pregnancy (60%) (Table 1). Of the ultrasonography imaging applications used in the emergency departments, only soft tissue scans were associated with hospital size ($P=.02$): 55% for large-sized, 0% for medium-sized, and 20% for small-sized hospitals. Use of ultrasonography for trauma-related scans appeared to have a linear relationship with hospital size, but the data were too sparse to test. After combining medium-sized and large-sized hospitals into a single category, small-sized hospitals used ultrasonography less frequently for trauma ($P=.049$). All other associations were not significant (all $P>.07$).

Based on responses to question 3, 30% of large-sized, 50% of medium-sized, and 63% of small-sized hospitals indicated that making equipment more available would increase ultrasonography use in their emergency departments. Making equipment more available showed a linear relationship with hospital size ($P=.03$). Of respondents, 65% of large-sized, 83% of medium-sized, and 63% of small-sized hospitals indicated that making training more available would increase ultrasonography use in their emergency departments. Making training more available was not associated with the size of the hospital ($P=.43$). For other responses to question 3, 40% of large-sized, 50% of medium-sized, and 42% small-sized hospitals indicated that other, unspecified factors that might increase ultrasonography use in their emergency departments. These other factors were not associated with the size of the hospital ($P=.85$).

Discussion

Recent technological advancements and widespread use of ultrasonography have increased accessibility for more affordable machines.[10] However, new point-of-care ultrasonography machines still represent a major purchase for small hospitals, and administrators are increasingly sensitive to such expenditures because of the fiscal challenges associated with operating a small hospital.[12] In the current study, 100% of emergency departments at large-sized hospitals throughout Missouri were equipped for point-of-care ultrasonography, but only 42% of small-sized hospitals were similarly equipped. Most of the large-sized hospitals were located in urban or suburban areas, and almost all of the small-sized hospitals were located in less populated, rural areas. Thus, our findings suggested a decreased use of bedside ultrasonography in rural areas compared with urban or suburban areas. For small-sized hospitals, the cost of ultrasonography machines may be a determining factor in the availability of this technology. Although the initial expense of purchasing a point-of-care ultrasonography machine may be prohibitive, the long-

term benefits and savings accompanying point-of-care ultrasonography use should be considered.

Multiple studies have identified the benefits of ultrasonography in numerous patient scenarios, such as shock, acute dyspnea, and various other emergency department presentations.[6, 13, 14] In the current study, the three most common uses for bedside ultrasonography in the emergency department were vascular access, trauma, and pregnancy. Because ultrasonography can efficiently contribute to an accurate diagnosis and assist in providing the appropriate interventional care, ultrasound equipment investment should be considered vital for better patient care.

Trauma is a common emergency department presentation, and numerous benefits in its diagnosis and treatment are associated with point-of-care ultrasonography. Trauma is the leading cause of death in the United States in patients aged 45 years and younger, and over 26.9 million cases present to the emergency department annually.[15] Point-of-care ultrasonography is broadly used for assessment of trauma patients in larger hospitals most often found in urban areas.[16] The American College of Surgeons recommends point-of-care ultrasonography as the imaging test of choice when implementing their Advanced Trauma Life Support protocol for the assessment of trauma patients.[17] Further, this protocol indicates the FAST exam, as a system of point-of-care sonographic imagery, should be performed simultaneously with resuscitative efforts and systems assessment.

However, as shown in the current study, small-sized and medium-sized hospitals are less likely to use point-of-care ultrasonography for the evaluation of trauma patients compared with larger-sized hospitals. While it is unlikely for small-sized hospitals, typically found in rural areas, to have the capacity to manage severe trauma patients, these hospitals are often the first stop for trauma patients requiring a higher level of care. Thus, these hospitals are in even greater need of this equipment considering the fact that other types of imaging such as MRI might be unavailable or less suitable for certain trauma patients. Multiple studies have shown the efficacy of point-of-care ultrasonography for the initial assessment of trauma patients.[4, 5, 18] In one study,[19] 136 trauma patients were evaluated using point-of-care ultrasonography and were compared with 127 control patients who were assessed by other means. The patients assessed with ultrasonography received the next level of care 64% of the time sooner than those in the control group.[19] As a result, those trauma patients evaluated with point-of-care ultrasonography had fewer days in the hospital, fewer complications, and reduced cost of care.[19]

The use of point-of-care ultrasonography requires the emergency physician to have the necessary skills for image acquisition and interpretation. Many of the surveyed hospitals in the current study indicated lack of training as an impediment to greater use of point-of-care ultrasonography in their emergency departments. Multiple studies have proposed a consensus concerning core medical student clinical point-of-care ultrasound learning objectives across all allopathic and osteopathic medical schools in the United States.[20-22] Ninety core clinical ultrasonography milestones have been established that medical students should obtain before graduation.[22] In May 2012, the Accreditation Council for Graduate Medical Education designated ultrasonography as the twelfth patient care skill of 24 required subcompetencies for all emergency medicine residencies under the next accreditation system.[23] As a result, the American College of Emergency Physicians now lists ultrasonography as a core competency in the training of new and practicing emergency physicians.[23] Therefore, medical schools across the country have included ultrasonography training in their medical school curriculums and residency programs,[7] which should increase the number of emergency physicians trained for bedside ultrasonography use[24-27] and mitigate the shortage of ultrasonography-trained physicians in the near future. Thus, hospital budgets need to prioritize obtaining ultrasound equipment for the emergency departments to offer this refined, efficient, and cost-saving health service.

The current study had several potential limitations. Although we had a 41% response rate from emergency departments throughout Missouri, response bias may have impacted our results. Specifically, nonresponding emergency departments may have had more or less access to bedside ultrasonography in their departments. To increase our response rate, we adapted our survey approach by including telephone surveys in addition to electronic surveys. If telephone survey responses had been aggressively pursued at the beginning of the three-week participation period, telephone surveys may have provided more responses from those who agreed to participate but did not submit a survey or from the hospitals that encountered technical difficulty accessing the electronic survey. This additional approach may also have resulted in more detailed answers to the survey questions.

Conclusion

Results from the current study suggest that large-sized hospitals used point-of-care ultrasonography significantly more than medium-sized or small-sized hospitals. Considering the known benefits of point-of-care ultrasonography in the emergency department, patients presenting to hospitals that lack this technology may be subjected to longer and more expensive care. Since small-sized hospitals are mostly found in rural areas, our data suggest a shortage of this technology in rural environments. Additional efforts are needed to increase the use of point-of-care ultrasonography in small-sized rural hospitals by providing initial financial support to purchase equipment and increasing opportunities for personnel training.

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Disclosure

None reported. **MM**

Gross Anatomy Education Today: The Integration of Traditional and Innovative Methodologies

by Jeremy J. Houser, PhD & Peter Kondrashov, PhD

Student preparation for board examinations was improved after implementation of the new anatomy curriculum, which successfully combined cadaveric dissection laboratory with modern teaching modalities, including multimedia resources and ultrasound imaging.





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Abstract

The current study surveyed first-year osteopathic medical students about dissection, multimedia dissector, split laboratories, VH (virtual human) dissector, ultrasonography, and prior experience of anatomical concepts. Students perceived cadaveric dissection, multimedia dissector, and ultrasonography laboratories as important contributors for learning anatomy. Students felt cadaveric dissection was an important factor in their medical school selection. Study results suggested students perceived integrated anatomy courses that utilized dissection and multimodal approaches to deliver anatomical information as highly effective.

Introduction

In 1896, A.T. Still stated, "You cannot have too much dissection. It will help you to verify your mental conception of the body's structure."[1] Today, this belief holds true in the Department of Anatomy at A.T. Still University's Kirksville College of Osteopathic Medicine (ATSU-KCOM). Medical education has drastically changed since Dr. Still's time, but cadaveric dissection is still perceived as an important component of medical education at this institution.

For many medical students, gross anatomy is the cornerstone of their medical knowledge. Exponential growth in knowledge and innovations in medical education have changed the landscape of the first two years of medical school, particularly in relation to the distribution of curricular hours.[2] Similarly, digital resources have allowed for the development of animations, videos, and 3-dimensional reconstruction, which has changed how medical schools deliver anatomical information.[3] It has yet to be seen whether alternative methodologies will be as effective as hands-on cadaver dissection or whether they will fill a supplementary role. However, evidence suggests that combining traditional cadaveric laboratory and innovative methodologies elicits better educational outcomes in anatomy.[4-7]

From the founding of the American School of Osteopathy in 1892 to modern-day ATSU-KCOM, cadaveric dissection has been included in the freshman curriculum. As with most medical schools, prior completion of an anatomy course is not required to matriculate. A recent study conducted at ATSU-KCOM found that premedical anatomy experience had no impact on medical anatomy grades, unless three or more anatomy courses, including at least one with human cadaveric laboratory, were taken.[8] This finding suggests that multiple

repetitions of anatomy exposure with human cadaveric dissection may help students master medical gross anatomy material. Few undergraduate institutions offer cadaver-based anatomy courses, though, so having a human cadaver dissection anatomy course as a prerequisite does not seem feasible. Further, such repetition may be best delivered through numerous modalities within the medical school curriculum.

During the first two years, ATSU-KCOM utilizes a partially integrated, systems-based curriculum. The first semester is foundational, and although the content is partially aligned, the courses run independently to deliver their fundamental material. The remaining three semesters are systems-based with integrated courses. The medical gross anatomy course is taught during the first two semesters and is designed to provide students with a detailed understanding of human anatomy along with essential embryology, radiology, and clinical correlations. The course is divided into the following sections: back, upper extremity, lower extremity, head and neck, thorax, abdomen, and pelvis. The thorax, abdomen, and pelvis sections are taught in the second semester and integrated into the cardiovascular, gastrointestinal, and renal blocks. Approximately 90 hours are spent in traditional lectures, 100 hours in cadaver dissection laboratory, 18 hours in ultrasonography laboratory (as part of a separate course), and 20 hours in case-based learning and small group discussions. In roughly half of the dissection laboratories and when all students are present for dissection, the student-to-cadaver ratio is 6:1. In the remaining 20 of 39 laboratories, the majority of the dissection is performed by a team of three students, while the other team initially attends a case discussion or an ultrasonography laboratory. After returning from the non-dissecting activities, these students join the dissecting team to finish the dissection and participate in the assessment. During these split laboratories, the faculty-to-student ratio is 1:10; this ratio is 1:20 during the whole-class laboratories. A study involving two class years of ATSU-KCOM students found no significant difference (P=.34) in student performance on lab practical identification examinations between the dissecting and non-dissecting groups.[9] However, students who did not dissect pelvic and abdominal neurovasculature did not perform as well on those identification questions. Despite this result, evidence suggests the split laboratory model is beneficial because it provides curricular time for the delivery of much of the ultrasonography content and some clinical correlations.

In 2011, ATSU-KCOM introduced ultrasonography imaging into the gross anatomy course during the first year of medical school. A clinical ultrasonography elective course was offered to second-year students to provide them with a review of anatomy and to prepare them for clinical rotations. A recent study found that second-year students who participated in the elective course had better retention of important anatomical concepts.[10]

Along with the introduction of the ultrasound component, the gross anatomy course at ATSU-KCOM underwent substantial changes in 2011-2012. These changes included split laboratories, inclusion of clinical cases, and integration of electronic resources, including a multimedia dissector developed in-house, a cross-sectional VH (virtual human) Dissector for Medical Education atlas (Touch of Life Technologies, Inc.), 3-dimensional Anatomy.TV (Primal Pictures, Informa UK Ltd.), Netter's 3D Interactive Anatomy (Elsevier), and Acland's Video Atlas of Human Anatomy (Wolters Kluwer Health). Of these electronic resources, the multimedia dissector and the VH Dissector images are assessed using pre-laboratory quizzes that are meant to ensure adequate preparation for the cadaveric dissection laboratory. Student knowledge of the anatomical material is evaluated using block and cumulative final written examinations that emphasize the clinical application of basic science content in a board-like case presentation format and using tagged laboratory examinations, which include radiological and cross-sectional images.

The purpose of the current study was to survey first-year osteopathic medical students to determine student perception of the benefit of dissection, multimedia dissector, split laboratories, VH Dissector, ultrasonography, and prior anatomy experience on their mastery of anatomical and radiological concepts.

Methods

The local institutional review board granted exempt status for the current study.

Participants and Data Collection

First-year osteopathic medical students from the graduating class of 2020 participated in the study at the end of their second semester. The mean age of the entire class of 172 students was 24 years (range, 21-36years), and the male-to-female ratio was 95:77. The mean (SD) Medical College Admission Test score was 27/504 (2.98/6.8), cumulative grade point average (GPA) was

3.61 (0.22), and science GPA was 3.54 (0.26).

Students were surveyed about the importance of cadaveric dissection for medical school selection and the benefits of various components of the medical anatomy course for mastery of anatomy and radiology concepts. The seven-item survey (Figure 1) was designed specifically for the current study and was based, in part, on content from a previous study.[8] The survey used a Likert-like scale with responses ranging from very important/beneficial to not important/beneficial. The survey items were validated in the previous study.[8] The current survey was delivered electronically to students using the Blackboard Learning Management System (Blackboard, Inc., Washington, DC). It was available for three days and took approximately five minutes to complete. Students were sent an email requesting their participation in the survey. To facilitate optimal participation, time was allotted prior to the last two gross anatomy and ultrasonography laboratories to complete the survey at the end of second semester. Participation was voluntary, without compensation, and had no impact on course grades. The results were anonymized before being sent out for statistical analysis. Students who did not participate in the survey were excluded from the study. Survey responses from each student were matched with the student's final grade for the medical gross anatomy course from the first semester.

Figure 1. Survey of osteopathic medical students on the importance of cadaveric dissection for medical school selection and the benefits of various components of the medical anatomy course to their mastery of anatomy and radiology concepts.

1) When making your decision about which medical school to attend, how important was the inclusion of human cadaver dissection in making your decision?
Very Important Important Moderately Important Slightly Important Not Important

2) How beneficial have cadaver dissections been to your mastery of anatomical concepts?
Very Beneficial Beneficial Moderately Beneficial Slightly Beneficial Not Beneficial

3) How beneficial has the multimedia dissector been to your mastery of anatomical concepts?
Very Beneficial Beneficial Moderately Beneficial Slightly Beneficial Not Beneficial

4) How beneficial have split laboratories been to your mastery of anatomical concepts?
Very Beneficial Beneficial Moderately Beneficial Slightly Beneficial Not Beneficial

5) How beneficial has VH Dissector been to your mastery of anatomical and radiological concepts?
Very Beneficial Beneficial Moderately Beneficial Slightly Beneficial Not Beneficial

6) How beneficial has ultrasonography been to your mastery of anatomical and radiological concepts?
Very Beneficial Beneficial Moderately Beneficial Slightly Beneficial Not Beneficial

7) How beneficial do you think your undergraduate anatomy course(s) were to your mastery of anatomical concepts in medical gross anatomy?
Very Beneficial Beneficial Moderately Beneficial Slightly Beneficial Not Beneficial

The anatomy course grades used in the current study came from the laboratory (45% weighted) and lecture (55% weighted) scores to produce a cumulative course grade for the first semester. The laboratory score was determined from points earned from pre-laboratory quizzes, in-laboratory identification quizzes, dissection quality points, and laboratory practical examinations. The lecture score was determined from total points earned on six multiple-choice, written examinations and one cumulative final examination.

The average anatomy subscores from COMLEX I of ATSU-KCOM students before the new anatomy curriculum was implemented (years 2008-2011) and after it was implemented (years 2012-2015) were collected to evaluate the efficacy of the current anatomy curriculum after the 2011-2012 change.

Statistical Analyses

Survey question responses were numerically coded for statistical analysis. The Likert-like choices of not important/beneficial were scored as zero points, slightly important/beneficial as one point, moderately important/beneficial as two points, important/beneficial as three points, and very important/beneficial as four points. Summary statistics reports were generated to provide frequency of responses for each question. Wilcoxon signed rank tests were used to determine whether the median response for each question was significantly different from the moderate choice (i.e., moderately important/beneficial). SAS version 9.4 (SAS Institute, Cary, NC) was used for statistical analyses, and $P \leq .05$ was considered statistically significant.

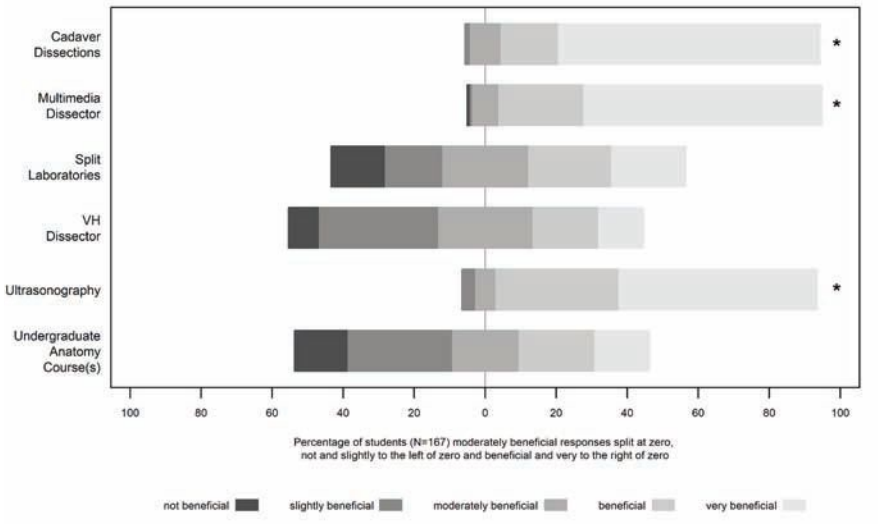
Results

The survey participation rate was 97.1% (167 of 172 first-year osteopathic medical students). For the medical gross anatomy course, the final grade distribution was 20.4% (n=34) of students earned an A (90%-100%), 51.5% (n=86) earned a B (80%-89%), and 28.1% (n=47) earned a C (70%-79%). The average grade was 83.8% with a low of 70.4% and a high of 96.3%.

Of the 167 students who completed the survey, 141 (84.4%) indicated that the inclusion of human cadaver dissection was important or very important when making their decision about which medical school to attend. Thirteen students (7.8%) indicated inclusion of human cadaver dissection was not important or slightly important. The median response for this question was significantly higher than the moderately important response ($P < .001$).

Of the six survey questions asking about the benefits of various components of the medical gross anatomy course in

Figure 2. Percentage of student responses to the survey questions asking about the benefit of various components of the gross anatomy course and previous anatomy experience to their mastery of anatomical and/or radiological concepts. The 'Moderately Beneficial' response straddles the zero. * P<.001



relation to mastering anatomical or radiological concepts, the following three areas had the largest percentage of responses in the beneficial to very beneficial categories: cadaver dissection (n=150, 89.8%), multimedia dissector (n=152, 91.0%), and ultrasonography (n=151, 90.4%) (Figure 2). The median responses for these three questions were significantly higher than the moderately beneficial response (all P<.001), represented by zero in Figure 2. Cadaver dissection and ultrasonography had no responses for the not beneficial category, and the multimedia dissector had one response for not beneficial.

The following three areas had the largest percentage of responses in the not beneficial to moderately beneficial categories: split laboratories (n=93, 55.7%), VH Dissector (n=115, 68.9%), and undergraduate anatomy course(s) (n=86, 51.5%) (Figure 2). The median responses for these three questions were not significantly different from the moderately beneficial response (all P≥.09).

Discussion

Since the turn of this century, numerous curricular changes have occurred at medical schools, which are comparable only to those that occurred a century ago when Abraham Flexner published his report.[2, 5, 11] These changes had a major effect on the design and delivery of basic science courses. For example, courses were modified to include more clinical content and non-discipline–related competencies, such as professionalism, teamwork, and leadership.[2, 12-14] As a result, medical institutions across the United States and Europe have reduced curricular hours dedicated to basic sciences, especially anatomy because dissection was replaced with prosection, plastic models, or digital resources.[3, 15-17] ATSU-KCOM's curriculum went through similar curricular modifications. Redesign of the gross anatomy course was considered since previous studies reported a lack of evidence on the efficacy of dissection versus other methods[18] and suggested that cadaveric laboratory was inefficient and unnecessary in teaching anatomy.[16, 17] However, given the wealth of evidence about the efficacy of the cadaveric laboratory, instead of getting rid of cadaveric dissection, the gross anatomy course at ATSU-KCOM was modified to include other components as well, such as ultrasonography, clinical cases, and digital resources. This change was a positive experience for faculty and students and was supported by studies showing integrated, functionally related, and clinically relevant anatomy curricula are highly efficient[4] and allow for long-term retention of anatomical knowledge.[6]

Even though curricular hours dedicated to anatomy education have decreased at medical schools over the last 15 years, a study by Drake and McBride[2] found that surveyed medical schools retained a cadaveric laboratory in some form. Recent studies showed that an anatomy cadaver dissection course is the most important tool for teaching macroscopic anatomy[7, 19] and offers a significant advantage over multimedia simulation.[20] Results from the current study also suggested availability of a cadaver dissection laboratory as part of undergraduate medical curriculum significantly influenced medical school selection of students, which seems to indicate the value of cadaveric dissection laboratory is recognized by prospective students. Similarly, first-year osteopathic medical students of the current study considered cadaveric dissection an important experience that helped them master anatomical concepts. This result supports data from other studies that looked at the role of cadaveric dissection in a medical surrciulum.[21] The other two areas that students of the current study considered highly

important for their anatomy education were the multimedia dissector and ultrasonography laboratory. These results support the existing literature about the efficacy of integrated anatomy courses that utilize multimodal approaches in delivering anatomical information.[4, 6]

The introduction of split laboratories at ATSU-KCOM allowed for the inclusion of ultrasound laboratories and clinical cases in the anatomy curriculum. Although students enjoyed using ultrasonography to strengthen their knowledge of anatomy, their responses to having split laboratories were less positive, which suggested that they value their time at the dissection table but are a little short-sighted when it comes to the evaluation of the whole curriculum. Other studies showed similar results when evaluating student perception of reciprocal peer teaching; students felt that they had less hands-on experience because they only dissected half the time in a split laboratory.[22] Another area assessed in the current study that did not get positive responses was the VH Dissector. The VH Dissector provides an important link between the cadaveric laboratory and imaging, but it was not regarded by students as being important. We believe this result can be attributed to first-year medical students not yet having found a relevant use for this instrument. Future research should evaluate the student perception of this component of anatomical education in students who have been exposed to clinical medicine and view anatomy mainly through the prism of radiology. Although anecdotal, former students have noted that using the VH Dissector helped them interpret radiological images during their clinical rotations in the third and fourth years.

Although positive and informational, student survey data can only provide subjective satisfaction information about the efficacy of the current anatomy curriculum, which prompted us to compare the COMLEX I anatomy subscores of ATSU-KCOM students before the new anatomy curriculum was implemented (years 2008-2011) and after it was implemented (years 2012-2015). The scores showed marked improvement, where scores from 2012-2015 were higher than those from 2008-2011 and increased by an average of 36 points. These objective data suggested that student preparation for board examinations was improved after implementation of the new anatomy curriculum, which successfully combined cadaveric dissection laboratory with modern teaching modalities, including multimedia resources and ultrasound imaging.

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Disclosure

None reported.

MM

Implementation of Oral Case Presentations in an Immunology Course

by Melissa K. Stuart, PhD

Introduction of the oral case presentations exercise into the Immunology course has enhanced the clinical relevance of material presented during traditional lectures, improved retention of basic science and medical knowledge, and increased student satisfaction with their educational experience.



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Abstract

Implementation of oral case presentations (OCP) in the Immunology course at A.T. Still University—Kirksville College of Osteopathic Medicine has significantly improved written examination scores and student satisfaction with the course by enhancing its clinical relevance. With six faculty facilitators, an average class size of 172 students can complete the exercise in a single day. The exercise requires small group meeting rooms, each equipped with a computer and wall-mounted monitor, but no other physical resources.

Introduction

The oral case presentation (OCP) is an effective tool for teaching and evaluating medical students as they develop competence in communication skills, medical knowledge, and clinical reasoning.[1–3] Although approaches to the OCP may vary, most incorporate elements represented by the mnemonic "SNAPPS," which refers to summarizing the patient's history and physical findings, narrowing the differential, analyzing the differential by comparing and contrasting the possible diagnoses, probing for additional information about uncertainties, planning management of the patient's medical issues, and selecting a case-related issue for self-directed learning.[4] The OCP can be adapted to all stages of medical training, from the pre-clinical years[5] through residency programs.[4,6] In this paper, I describe implementation of an OCP exercise in an Immunology course taken by first- or second-year osteopathic medical students at A.T. Still University—Kirksville College of Osteopathic Medicine (ATSU—KCOM).

The OCP exercise was introduced into the Immunology course in 2011. At that time, Immunology consisted of 21 contact hours, and was by far the shortest course in an academic term that totaled 283 contact hours. Perhaps due in part to its small footprint, Immunology compared unfavorably in student evaluations to larger courses taught during the same term, the largest of which comprised 90 contact hours. To emphasize the importance of Immunology in medical education despite the brevity of the course, the Immunology OCP was implemented with three major goals in mind: 1) to enhance the clinical relevance of material presented during traditional lectures, 2) to improve written examination scores, and 3) to increase student satisfaction with the course. The Immunology OCP exercise was modeled after similar exercises performed in our Medical Microbiology and Infectious Diseases courses, which have been highly successful in achieving the same goals.[5] Now in its seventh year, the Immunology OCP has a proven record of producing high-yield results while using few faculty and physical resources.

Methods

Study Participants

This study received exempt status from the ATSU–KCOM Institutional Review Board. ATSU–KCOM osteopathic medical students participating in the study fell into three experimental groups. Group I students (n=352) took Immunology as a single, comprehensive 21-hour course in Quarter 2 of the curriculum; they did not participate in the Immunology OCP exercise. Group II students (n=335) also took Immunology as a single 21-hour course, but these students participated in the OCP exercise. For Group III students (n=513), curricular changes led to the division of Immunology into an 11-hour foundational course in Semester 1, followed by a 10-hour clinical course in Semester 3. Group III students participated in the OCP exercise during the Semester 3 clinical course. Groups I and II each comprised two classes of students, whereas Group III included students from three classes.

Clinical Cases

All clinical immunology cases were adapted by the author from printed texts, e-books, or reputable on-line resources that describe case studies.[7–10] The cases were developed around the chief complaints of abdominal pain, bowel upset, breathing difficulty, cough, diarrhea, joint pain, numbness, and skin lesions. Differential diagnoses included immunodeficiencies, autoimmune diseases, and hypersensitivities. Case packets were created using the template developed by Chamberlain et al.[5] Each packet consisted of 1-3 printed pages containing one or more photographs of the patient; the patient's chief complaint and associated symptoms; the patient's history, vital signs and physical examination results; and laboratory and medical procedure data that required interpretation by the student.

Case Presentations

Groups of 5 students and one facilitator were assigned to small group meeting rooms equipped with a computer and wall-mounted monitor. Each student in the group randomly received a unique paper case and had 10 minutes to read and take notes over the data. Students were not allowed to consult reference materials or their peers during the reading period. After returning the case packets to the facilitator, each student gave a 3-minute oral presentation that summarized the main issues of the case, explained the lab and medical procedure data, and explained why each diagnosis in a list of five choices should be ruled in or ruled out. The student was aided during the oral presentation by a PowerPoint slide containing case exhibits, and by the hand-written notes taken during review of the case packet. After the presenting the case and defending the diagnosis, the student spent the next three minutes fielding questions from his or her peers and the facilitator. For each group of five students, the entire exercise required 50 min to complete. Typically, six groups were run simultaneously, allowing 30 students to complete the exercise each hour, and an average class size of 172 students to complete the exercise in a single day.

Student performance was evaluated using a rubric that assessed six microskills: 1) behaving and speaking in a professional manner; 2) adding value to the discussion by asking probing questions of the presenter; 3) covering important aspects of the patient's signs, symptoms, history and physical; 4) thoroughly explaining laboratory and medical procedure data; 5) justifying why each answer choice in the differential diagnosis list should be ruled in or ruled out; and 6) correctly answering a basic science question associated with the case. The basic science question varied, but often involved asking the presenter to identify the molecular defect causing an immunodeficiency, the molecular target of an autoimmune disease, or the mode of action of an immunotherapeutic treatment. New cases were introduced at planned intervals to minimize the advantage gained by students in later sessions who might unfairly discuss the cases with classmates who completed the exercise earlier in the day.

The OCP exercise was scheduled to take place three to seven days before the last unit examination in the Immunology course. Because the course ends long before the academic term is over, students completed the OCP exercise an average of 4 weeks before they took the Immunology comprehensive final examination at the end of the academic term.

Statistical Analysis of Final Exam Scores and Likert Scale Data

To determine whether the Immunology OCP exercise impacted student learning, scores earned by students on the Immunology comprehensive final examination before (Group I) and after (Groups II and III) implementation of the OCP were compared by one-way ANOVA ($P<0.05$). Post hoc comparisons were done using the Bonferroni correction to the p-value ($P<0.05$). The questions on

the comprehensive final examinations taken by students in Groups I and II were consistent except for minor changes made for clarity. The comprehensive final exams taken by Group III students largely omitted the basic science questions found on Group I and II final exams, but contained the same clinical questions as before, plus additional clinical questions.

Student satisfaction with the Immunology course before and after implementation of the OCP was evaluated using the 4-point Likert item, "Achievement in this course advances me toward being a physician," where 1=strongly agree, 2=agree, 3=disagree, and 4=strongly disagree. Likert scores were compared between groups by one-way ANOVA ($P<0.05$), followed by post hoc comparisons done with the Bonferroni correction to the p-value ($P<0.05$).

Anonymous Student Comments Regarding the Immunology OCP

Students had the opportunity to express their opinions about the Immunology OCP through anonymous written comments submitted via the on-line Immunology course evaluation. Course evaluations were completed after students had taken the Immunology comprehensive final examination at the end of the academic term.

Results

Students who participated in the Immunology OCP (Groups II and III) scored significantly higher on the Immunology comprehensive final examination than Group I students, who did not participate in the exercise (one-way ANOVA, $P<0.001$; Bonferroni post hoc test, $P<0.001$) (Table 1). Among students who took Immunology as a single 21-hour course, the mean final exam score improved from 76.5% (Group I) to 81.8% (Group II) upon implementation of the Immunology OCP. Between the two groups of students who participated in the OCP, those who took the 10-hour clinical Immunology course in Semester 3 (Group III) scored significantly higher on the comprehensive final exam than those who took Immunology as a single, 21-hour course in Quarter 2 or 3 (Group II) (one-way ANOVA, $P<0.001$; Bonferroni post hoc test, $P<0.001$) (Table 1). Final exam scores earned by Group II and Group III were 81.8% and 87.0%, respectively.

Student satisfaction with the Immunology course, as assessed using the Likert item, "Achievement in this course advances me toward being a physician," also significantly improved upon implementation of the OCP (Table 2). Students who participated in the OCP (Groups II and III) strongly agreed with the statement, reflected by Likert scores of 1.21 and 1.18, respectively. Both scores were significantly better than the 1.78 rating conferred by Group I students, who did not participate in the OCP (one-way ANOVA, $P<0.001$; Bonferroni post hoc test, $P<0.001$). There was no significant difference in Likert scores between Groups II and III (one-way ANOVA, $P<0.001$; Bonferroni post hoc test, $P=0.94$).

In general, anonymous student comments submitted as part of the Immunology course evaluation were positive toward the OCP exercise (Table 3). Negative comments focused on the perception that some facilitators tended to give lower scores than others, and that cases or case-associated basic science questions were not uniform in difficulty.

Discussion

Since introducing the oral case presentations exercise into the Immunology course at ATSU–KCOM, comprehensive final examination scores and student satisfaction with the course have improved significantly. Final exam scores have risen from the mid-70 percent range earned by students who did not participate in the Immunology OCP, to the low- or mid-80 percent range earned by students who did participate in the exercise. With implementation of the OCP, concurrence with the statement, "Achievement in this course advances me toward being a physician," has improved from "agree" to "strongly agree" in student ratings. Students report that the OCP allows them to integrate basic science knowledge into a clinical setting and helps them think like physicians. Such statements are taken as evidence that the OCP enhances the clinical relevance of the lecture-based material that comprises the bulk of the Immunology course.

As expected, students reported that the OCP made them feel better prepared for the unit exam that came three to seven days after the OCP exercise. Somewhat surprising was the persistence of the exercise's beneficial effect through the end of the academic term, resulting in higher scores on the Immunology comprehensive final exam taken one month after completion of the OCP exercise than in years prior to OCP implementation. The lasting impact of the OCP on student learning was also reflected in student perceptions of preparedness for the COMLEX Level 1 board examination, which is taken at the

Table 1. Comparison of mean comprehensive final examination scores in Immunology before (Group I) and after (Groups II and III) implementation of Immunology Case Presentations.

Group[a]	N	Mean (%)	SEM[b]	Comparisons	P value
I	351	76.5	0.51	Group I vs. Group III	<0.001*
II	335	81.8	0.61	Group I vs. Group II	<0.001*
III	513	87.0	0.45	Group II vs. Group III	<0.001*

[a]For students in Groups I and II, Immunology was taught during Quarter 2 or Quarter 3 as a single, comprehensive 21-hour course covering basic and clinical aspects of Immunology. For Group III, Immunology comprised an 11-hour foundational course in Semester 1, followed by a 10-hour clinical course in Semester 3. The mean final exam score for Group III derives from Semester 3, the term during which Case Presentations were performed.

[b]SEM, standard error of the mean.

*Significant difference was found in the mean scores of students in the three groups using one-way ANOVA (P <0.001). Post hoc comparisons were done using Bonferroni correction to the p-value. Significant differences were found between all of the subgroups (P <0.001).

Table 2. Comparison of mean Likert scores for the statement, "*Achievement in this course advances me toward being a physician*," before (Group I) and after (Groups II and III) implementation of Immunology Case Presentations.[a]

Group[b]	N	Mean	SEM[c]	Comparisons	P value
I	64	1.78	0.08	Group I vs. Group III	<0.001*
II	207	1.21	0.03	Group I vs. Group II	<0.001*
III	338	1.18	0.02	Group II vs. Group III	0.94

[a]Likert scale, 1=strongly agree, 2=agree, 3=disagree, 4=strongly disagree.

[b]Group designations are as described in the footnote to Table 1.

[c]SEM, standard error of the mean.

*Significant difference was found in the mean scores of students in the three groups (P <0.001) using one-way ANOVA. Post-hoc comparisons were done using Bonferroni correction to p-value. Significance difference was found between Group I and Group III (P<0.001) and between Group I and Group II (P<0.001). No significant difference was found between Group II and Group III (P=0.94).

Table 3. A sampling of anonymous student comments written about the Immunology OCP, reprinted from Immunology course evaluations.

Positive Comments
• Excellent, excellent, excellent. Case presenations are a pain and they are stressful for me. However, I would not know the material half as well as I do without them.
• The case presentations helped me to prepare very well for the block exams and gave us a chance to discuss and apply the information we learned.
• The case presentations were a great method for integrating the material into what will be future use/long term knowledge.
• The case presentations were one of the most stressful things I have had to do during my time at KCOM. That being said, it was great in that it made you compare and contrast different diseases. Ruling diseases "in" or "out" really tested a comprehensive knowledge of the subject. Overall a great/stressful exercise!
• I loved the clinical/differential diagnosis workshop. It was a ton of fun and really made me feel excited about becoing a doctor and finally putting all this science to use!
• I loved every minute of the class and felt that everything I was learning was going to help someone later on in my career.
• The case presentations really made you think like a physician and helped in preparing for the block exams.
• Case presentations were a great idea even though it was pretty stressful preparing for them. The threat of being embarrassed in front of your peers is strong motivation!
Negative Comments
• There is too much variation in the grading of a case presentation based on the instructor you received.
• Case presentations are hard to study for. I would say more help is needed on laying out how to study for them. Also, lots of discrepancies in grading depending on which grader you had!
• I think some of the basic science questions were not fair. Some cases received "easier" more predictable questions than others. Otherwise it was great.

end of the second year of osteopathic medical education. Since implementing the Immunology OCP, 94% to 99% of students have reported feeling adequately to extremely well-prepared in Immunology for the COMLEX Level 1 exam, up from a low of 68% before the OCP exercise was introduced. Graffam[11] notes that intentional engagement and active learning change the nature of learning in such a way that knowledge gain and recall abilities are improved, an assertion supported by our experience with the Immunology OCP exercise.

It should be noted that the Immunology final exams given to students in Groups I and II varied little from year to year, enabling direct comparison of exam scores between these two groups. However, the curricular changes that divided Immunology into separate foundational and clinical courses necessitated changes to the final exam taken by students in Group III. For all three groups, the same core clinical questions were asked on the final exam, but the Group III exam contained additional clinical questions and omitted questions covering basic immunological concepts. Fewer lectures were covered on the Group III exam, resulting in less material to study. A more important advantage enjoyed by Group III students was the timing of the Immunology final exam, which came later in

their medical education. Exposure to additional coursework allowed Group III students to make connections between knowledge gained in Immunology with knowledge gained from the Pathology and Medicine courses. In short, the improvement seen in Group III Immunology comprehensive final examination scores most likely derived from a combination of factors, including the Immunology OCP.

Onishi[12] distinguishes between OCP exercises that have short (1-2 minutes) and long (5-10 minutes) formats. To improve clinical reasoning, the short presentation offers the advantages of requiring abstraction of information, time efficiency, and fostering informal interactions with the audience.[12] Long presentations allow educators to be more involved in the diagnostic reasoning process as they listen to detailed descriptions of the patient's signs and symptoms.[12] A frequently used short-format case presentation is the One-Minute Preceptor (OMP), which employs six microskills.[4] These include requiring the student to commit to a diagnosis, probing for supporting evidence, teaching general rules, reinforcing what is right, correcting mistakes, and identifying the next learning steps.[4] The Immunology OCP used a mixed approach, falling between the short and long case presentation formats while blending elements of SNAPPS and the OMP, with good results.

Although students expressed concern that some facilitators graded more harshly than others during the OCP, steps were taken to minimize inter-rater variability. In all three courses where we use OCP exercises, we have found that a useful method for reducing inconsistencies is to enter the data for each case into a spread sheet, so that the scores assigned to each item in the grading rubric can be compared across facilitators by a single evaluator. Adjustments are made if discrepancies are found in the number of points deducted by different facilitators for the same infraction. Using this method, the mean scores across all facilitators typically differ by less than 5%. Although the perfect evaluation instrument for the OCP has yet to be developed,[13–15] our simplified rubric, in conjunction with written comments made by the facilitators, provides valuable feedback to the students as they develop oral case presentation skills.

Conclusions

Introduction of the oral case presentations exercise into the Immunology course at ATSU—KCOM has enhanced the clinical relevance of material presented during traditional lectures, improved retention of basic science and medical knowledge, and increased student satisfaction with their educational experience. The Immunology OCP complements similar exercises we conduct in our Medical Microbiology and Infectious Diseases courses. Together, these three courses have fostered development of oral communication and clinical reasoning skills that will serve our students well during their third and fourth years of medical training.

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Disclosure

None reported. **MM**

Human Patient Simulation as a Teaching Tool

by Benjamin L. Schrant, DO, Lisa L. Archer, RN & Robert Long, AAS

ATSU would like to see medical students designing and building their own simulation scenarios, so that students will have the ability to challenge themselves as well as their colleagues and demonstrate mastery of content.







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Abstract

The KCOM campus hosts a modern, state of the art human patient simulation (HPS) laboratory, which allows simulation of neonatal, pediatric, obstetric, and adult patients. Students are able to utilize the HPS lab to become comfortable with physical exam skills, procedural skills and communication skills before attempting them in a true clinical environment. Involvement of students from other disciplines has facilitated interprofessional education. Involvement of community health providers has expanded the richness of the student experience.

Facility Overview

The Kirksville College of Osteopathic Medicine of A. T. Still University (ATSU) is located in Kirksville, Missouri. The 125-year-old College matriculates 172 students annually through its medical program. Students spend two years in Kirksville before moving to large population centers for two years of hospital-based clinical training. In 2014, ATSU opened the Missouri School of Oral and Dental Health (MOSDOH) on the Kirksville campus, which, along with the nursing program at Truman State University in Kirksville, is yielding increased opportunities for interprofessional education.

The Human Patient Simulation (HPS) laboratory is one of the most recent additions to the KCOM campus. The facility, in use since 2014, houses 14 simulation rooms, which are used by students for a wide variety of educational activities. The mainstay of our simulation curriculum rests upon eight Laerdal SimMan 3G simulators. Students also train on a Gaumard Birthing Simulator and Neonatal simulator, and Laerdal SimJunior pediatric simulators. A dedicated endoscopy suite affords students early experiences with colonoscopy, esophogastroduodenoscopy, and bronchoscopy. The students' experience is completed with pre- and post-briefing sessions in one of our two lecture halls in the new complex.

Simulation Curriculum

Simulation in medical education is rapidly expanding to provide training in many different aspects of medical care. Simulation has been recommended as a means to increase patient safety.[1] We utilize our simulation laboratory to train students in skills beyond diagnosis and treatment. The HPS laboratory is used to reinforce professional communication skills and to provide a forum for interprofessional education. Improper communication is responsible for a large number of medical errors that directly impact patients every year.[2] Interprofessional education allows our students to attack interprofessional challenges early in their education; making professional collaboration and best patient outcomes a goal as soon as it can be introduced.[3]

We strive to match the simulation curriculum to the same subject



Figure 1. KCOM First-year medical students collaborating with TSU nursing students on a plan of care for a critical patient.



Figure 2. Interprofessional encounter with first-year KCOM medical students and fourth-year Truman University nursing students. This nursing student did an initial assessment of the patient then called for the medical student to report critical assessment findings.

matter that the students are receiving in the classroom. For instance, when students are in their cardiology block, potential simulation cases include cardiogenic pulmonary edema or acute onset atrial fibrillation. We see these simulation exercises as excellent opportunities to help the students retain what they are learning in the classroom and to allow them to apply their knowledge in a physician role. Students participate in simulation exercises throughout their cardiac, pulmonary, gastrointestinal, musculoskeletal, renal, and endocrine curriculum blocks. Students are encouraged to develop skills in the simulation lab that are not currently part of their classroom education, such as effective telephone communication, patient hand-off, and consultation with physicians and other health professionals. Some sessions in the laboratory include triaging and managing multiple patients simultaneously, simulating an evening as a house intern.

The students' time in the HPS laboratory complements their clinical work in several other courses. We work to improve skills learned in the Complete DOctor course (a physical exam skills course) by simulating physical exam findings that are difficult to present via standardized patient exercises; (wherein students examine actors portraying disease symptoms). For example, we routinely set the simulators to abnormal heart (arrhythmias, murmurs) and lung sounds (pulmonary edema) that the students would otherwise have minimal tangible exposure to prior to their third and fourth clinical educational years. The HPS laboratory also provides a unique opportunity for the students to observe physiological responses to drugs. Many scenarios (e.g., hypertensive crisis) provide opportunity to observe how a selected treatment regimen affects the physiology of their patient in real-time. Furthermore, they gain practice with other skills such as selection, titration, and dosing of drugs.

Individuals present at every HPS lab session include full time HPS staff members (laboratory director, laboratory technician, and medical director) as well as physicians, residents and advanced medical students (Figure 1). Notably, we utilize the expertise of the Northeast Regional Medical Center (NRMC) resident physicians. The residents assist us by using their knowledge to help the simulated scenarios run smoothly and accurately. Following the laboratory exercise, the resident physicians often assist with the debriefing sessions to ensure that students are receiving diagnostic and treatment information from physicians, who actively manage the types of conditions that are being discussed. Clinical faculty members are also present at every session.

The NRMC resident physicians play a vital role in the realistic simulation curriculum that we are able to offer. Because many of the College-associated residency programs utilize the HPS lab as a central component of their training, we are able to offer first and second year medical students resident level training and exposure in the fields of anesthesiology, family medicine, internal medicine, and surgery. The resident physicians also work very closely with medical students during very difficult and/or complex simulations, such as Advanced Trauma Life Support (ATLS) scenarios. This symbiotic relationship yields an enriched teaching experience for the resident physicians, and valuable learning experiences for less-advanced medical students.



Figure 3. A medical student making a call on the simulation phone to the control room to speak with the "attending physician" for consultation.

Emphasis on High Fidelity

We take great care to achieve the highest possible reality in our HPS laboratory. We have noted that it's often the "little things" that increase the fidelity of the scenario and decrease the awkwardness that some students feel when interacting with the simulators. Some of these small touches include patient identification armbands, a variety of oxygen therapy devices, real hospital beds,real defibrillation, active communication directly with the simulator, and available physician consultation. We encourage students to speak directly via telephone with any individuals that they feel may assist them with treating the simulated patient. Being able to speak with attending physicians, laboratory personnel, and other ancillary staff has helped to make the student experience in the HPS laboratory more comfortable, while at the same time reducing the amount of guessing that takes place. This communication exercise also educates students about ancillary services and their roles in the healthcare setting, thus aiding the students' knowledge regarding whom to contact for needed services or diagnostics.

The HPS lab at KCOM offers courses in Advanced Cardiac Life Support, Pediatric Advanced Life Support, Basic Life Support, and Neonatal Resuscitation Protocol (NRP). Our facility is a fully accredited American Heart Association training center. The above courses are conducted with the highest possible fidelity. Students are able to physically practice skills that could not previously be learned with simulated patients, such as defibrillation, cardiac pacing, cardioversion, intraosseous infusions, central line insertions, and esophageal intubations. The NRP course is taught in our simulated labor and delivery suite, allowing simulation of a very realistic transition from neonatal delivery to resuscitation.

The HPS laboratory team builds simulations to suit the needs of our students, and simulations are often created at the request of the students. We have assisted students in creating custom experiences that are the best fit for their special-interest clubs, learning level, or target exercise. We have even gone so far as to lay artificial turf in the HPS laboratory to best recreate the environment of a football field for the Sports Medicine Club!

Interprofessional education is of great importance to the training of our medical students. We work with other educational programs in the community such as MOSDOH, the Truman State University Nursing Program, and the Adair County Ambulance District (Figure 2). The interprofessional exercises that students take part in serve as primers to improve understanding and professionalism when interacting with non-physician healthcare providers. These interprofessional simulations are always a "crowd favorite" and are some of our most requested simulations.

New Technology

Technology plays a large role in the overall experience of the students in the HPS lab. One of our recent innovations in the HPS Lab is the integration of a "no-dial" phone system. Picking up a phone in an HPS room immediately connects the student to the simulation control area, obviating the need for memorized phone numbers and incorrectly-placed calls. When a student picks up the phone, they are greeted by an individual acting as the switchboard operator and asked how their call can be directed(Figure 3).Depending on the nature of their request, they may be connected directly to a simulated hospital department or they can page specific individuals (e.g., an attending physician). With this innovation, we have seen a vast improvement in communication skills of our students. When they pick up a phone, the students speak directly to a consulting physician compared to previously when they were forced to "speak to the air" which resulted in a low fidelity of simulation. Student thoughts have tended to be formed more completely than before, and their hand-off communication ability has become more accurate and concise. This type of training is not duplicated in any other area of our medical curriculum and therefore stands out as a much needed emphasis for every scenario. We believe this communication experience will translate into safer patient environments, where clear communication comes naturally.

The KCOM HPS lab simulators can be operated completely wirelessly. Wireless technology has opened many opportunities for the use of our simulators. For instance, students are able to practice moving patients in beds and between beds. We are also able to take our simulators outside of the HPS facility, which has fostered simulation demonstrations at local schools and national conferences (e.g., the American Osteopathic College of Anesthesiologists).

The KCOM HPS Lab employs a dedicated Laerdal certified simulation technician, the only one within an osteopathic medical school, one of nine in the state of Missouri, and one of 123 in the United States and Canada. The presence of our technician allows us to conduct annual and emergent maintenance on the University's eight Laerdal 3G simulators and two Laerdal junior simulators, and ensures that all simulators are operating at peak performance for medical education learning experiences.

Simulation Experience Examples

Our facility is able to simultaneously operate all eight SimMan3G simulators. With a typical group of five medical students per simulator, we can serve approximately 40 students in the HPS lab in one session. The medical students are responsible for all aspects of care that occur within the simulation, including medication management, order entry, ancillary services coordination, and physician consultation.

Near the end of their second year, the medical students participate in level 1 trauma scenarios with support from NRMC ATLS providers. This particular exercise begins as the students receive a patient report from local emergency medical service providers. Next, the students treat their patient via the ATLS standards of care, which includes coordinating transfer of the simulator to the emergency department bed, primary and secondary surveys, performance of emergency procedures (e.g., needle decompression and endotracheal intubation), analysis of laboratory and radiological results, and coordination of post resuscitative care.

Our students' favorite simulation modality may be the simulated night as a house officer. The lights in the simulation laboratory are dimmed and clocks are adjusted to a late hour. As the medical students begin their simulation experience, they first receive an I-PASS report about their patients (typically 3) from the resident physician that is going off shift. Nursing personnel (such as TSU nursing students) then place calls to request that the students address some of the typical patient care issues faced by a house officer, e.g., insomnia, hypertensive urgency, and a postoperative hypotensive patient. As the students are not bound to a particular educational unit, these simulated house officer nights test the student's retention of knowledge from the sum of their medical education. Additionally, these particular simulation exercises assist with development of skills that may prove difficult to teach in a classroom, such as severity of illness evaluation, triage, and interprofessional communication.

Future Directions

As our staff looks to the future, we anticipate more direct student involvement. We would like to see medical students designing and building their own simulation scenarios. In this way, students will have the ability to challenge themselves as well as their colleagues and demonstrate mastery of content. Increased interprofessional education (IPE) is one of our future goals, and we would prefer to integrate it within the majority of our simulation curriculum. Finally, we anticipate data collection for some small pilot studies that have been conducted in the fall of 2017.

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Disclosure

None reported. **MM**

Medical Applications for 3D Printing: Recent Developments

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With the development of printing techniques and materials suitable for particular medical applications, research interest is increasing.



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Abstract

This is a review of some of the recent developments in the application of 3D printing to medicine. The topic is introduced with a brief explanation as to how and why 3D is changing practice, teaching, and research in medicine. Then, taking recent examples of progress in the field, we illustrate the current state of the art. This article concludes by evaluating the current limitations of 3D printing for medical applications and suggesting where further progress is likely to be made.

Introduction

The American Society for Testing and Materials (ASTM) International Committee F42 has adopted the term additive manufacturing (AM) for techniques that produce physical objects from three-dimensional (3D) digital data via the "process of joining materials to make objects from 3D model data, usually layer upon layer, as opposed to subtractive manufacturing methodologies".[1] This refers to a series of industrial AM processes commonly referred to as 3D printing, which employ computer-automated manufacturing (CAM) processes to fabricate physical 3D objects layer by layer from computer-aided design (CAD) models. Thus additive manufacturing, commonly known as 3D printing, is a manufacturing method in which objects can be created by fusing or depositing materials onto, or into, a substrate. The materials deposited can be powders, plastics, ceramics, metals, liquids or living cells, making the process hugely versatile. The process is also repeatable, accurate, and cost-effective for small production runs, allowing the reliable production of customized parts. It also allows fast production and collaboration between physicians and researchers, who can now share a physical object over the internet and recreate it quickly with high precision.[2]

The technology, history and operation of 3D printers has been described elsewhere.[3,4] This paper focusses on the medical applications of 3D printing, presents recent research, and its implications for medical applications. We have defined categories of medical applications to classify existing research into 3D printing in medicine. Each is described in brief below:

Surgical Planning

One of the possible applications of 3D printing that have emerged is surgical planning. This involves studying the anatomy and physiology of defects in complex organs such as the brain or the heart, or anatomical specimens such as the pelvis or the spinal cord, and

using the information for surgical planning. 3D models can assist surgeons to study the impaired organs before the operation, explore various approaches and acquire hands-on experience before entering the operating room. This process shortens operation time significantly, and ultimately improves the outcome of the operation for the patients, the surgeons, and the patients' care providers.

Prostheses

Recent advancement in 3D printed patient-specific prostheses allows a wide range of disabled people affected either by an accident or a genetic deformity to carry on their normal life.[5] With the aid of high quality imaging technology, 3D printing has the capability to create a precise anatomic prosthesis used in various medical applications.[6,7] This has also made significant impact on the field of dentistry.[8,9]

Medical Education and Training

Using cadaveric materials to train novice medical physicians has been the subject of controversy. This is both due to ethical issues as well as the cost of the processes. 3D printing techniques may offer a novel and effective substitute by reproducing accurate complex anatomical organs from high resolution CT imaging for many cases, including those in which using a cadaver is not an option. In addition, the ability of 3D printing to reproduce a number of copies of any anatomical subject in different sizes gives a great advantage in training facilities.[10]

Medical Research

The advent of printers gentle enough to print cells directly has resulted in the automated production of cell structures for toxicity testing, and the development of new treatments for various diseases and tumors. Up to 50% of drugs that pass preclinical testing are later found to be toxic to humans, while others may be non-toxic to humans despite being toxic in animal testing.[11] Consequently, the ability to reproducibly print tissues that match the actual cellular arrangement in natural tissues and organs allows researchers to accelerate the research process. Here we describe some of the recent advances in medical research for these applications.

Organ Printing

3D printing is already used in the production of human organ and tissue structures for research, as described in the medical research section. These can be integrated with biocompatible microfluidics to create highly complex structures to mimic the function of native human organs.[12] The next step is printing organs that can be transplanted into human donors, or even printing organs in the body in-situ in the operating room. While this technology is less mature than others described in this article, it has the potential to revolutionize medicine, making organ transplants and current synthetic artificial organs obsolete.[13]

Drug Delivery

Drug delivery will undoubtedly change as 3D printing becomes integral to pharmaceuticals. Drugs can be printed not only in specified doses for each individual, but with multiple sustained release and immediate release layers, which allow the dosage profile to be modified. This enables personalized treatments, and also helps patients under heavy medication, who may be able to reduce the number of pills they need to take. 3D printed drug delivery devices which fit exactly to the anatomy of a patient are also under development.

The breadth of fields described in this introduction shows how much 3D printing technologies are changing medicine. In fact, the applications of 3D printing in medicine are now so numerous that an exhaustive and comprehensive study of them all is practically impossible. Several recent reviews have examined one particular field, such as Mehndiratta et al.'s review of 3D printing based on medical imaging,[14] Martelli et al.'s review of 3D printing in surgery[15] and Pati et al.'s review of bioprinting for tissues and organs.[16] This review will look at developments from within the last three years (from 2014 to date) in each of the applications we have defined above to demonstrate the current state of the art.

Latest Developments by Application

Surgical Planning

Operational surgery on a complex congenital heart condition requires a highly skilled and experienced surgeon who can also make quick decisions during the operation. Making instantaneous decisions during the operation inevitably may lead to longer operating times, which may cause adverse impacts on the surgical outcome. Vodiskat et al. used a 3D printing model of the congenital heart defect used for preoperative planning.[17] They have employed two different commercially available 3D printing technologies (Polyjet Objet Eden 350, MakerBot Replicator) for reconstruction of the congenital heart defect in three

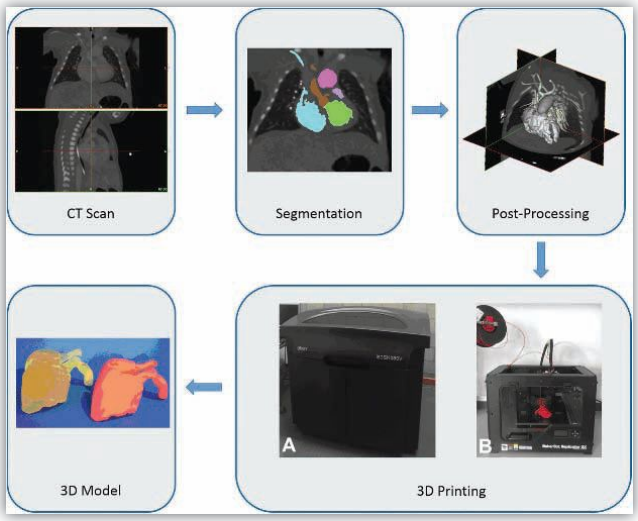


Figure 1. Flowchart of creating a 3D printed model of congenital heart defects from CT scan data.[16]

different patients. Their methodology is shown in Figure 1. They concluded that, provided that an excellent CT scan data is available, a cost-effective 3D printed model can be created to be used for preoperative planning.

Old pelvis fracture is one of the most challenging fractures to fix. This is mainly due to the complex anatomy of the pelvis and the difficult access to the operational sites. Wu et al. evaluated the use of 3D printed pelvic models for preoperative planning.[18] Over the course of four years, they studied nine different clinical cases, and evaluated their surgical reconstruction based on the 3D printed models of the fractured pelvises. They demonstrated that there was a good correlation between the preoperative planning and postoperative results extracted from X-ray examination in all cases. They recommended higher numbers of patients are required to further consider the use of 3D preoperative models for the pelvis fracture surgery.

Truscott et al. presented three case studies of 3D printing models that can assist surgeons with preoperative planning. They created 3D models of pelvis and femur, eye socket and scapula from the corresponding CT scan data.[19] They used 3D printing laser-sintering technology to make an eye socket out of Titanium. They concluded that, in comparison to a CNC process, using this technique minimizes the amount of material wasted.

Prostheses

In a study conducted by Suaste-Gómez et al., an ear prosthesis was 3D printed using polyvinylidene fluoride (PVDF).[20] The prosthesis response to pressure and

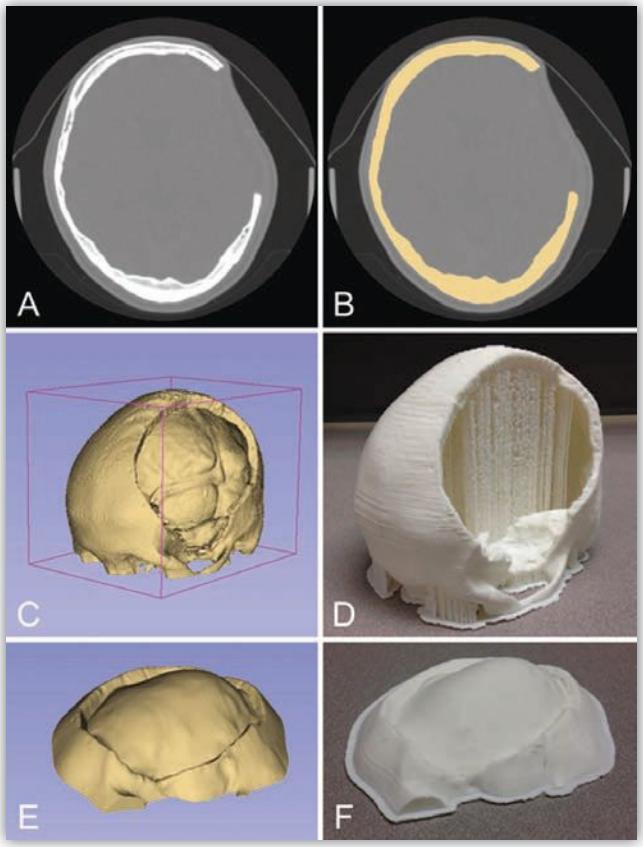


Figure 2. 3D printed skull and mold (D,F) from high resolution CT scan data (C,E) using the fused deposition modelling method.[20]

temperature was studied using an integrated astable multi-vibrator circuit. Their novel 3D-printed PVDF-made ear prosthesis showed high sensitivity to pressure changes. This is a promising result for extensions of this technique to other fields of biomedical engineering.

Commercial patient-specific cranioplasty prostheses are very expensive. Alternatively, acrylic bone cement is widely used in the field as a cost-efficient approach. However, the manual fabricating of the bone cement is cumbersome and may not lead to a satisfactory implant in many cases. Tan et al. created a 3D printed skull from high resolution CT scan data using FDM.[21] The mold was used as a template to shape the acrylic implant. They showed that their approach to make patient-specific acrylic cranioplasty implants with a low-cost 3D printer is successful; however further studies are required to assess the application in the clinical setting. The printed prosthesis and CT scan data are shown in Figure 2.

Ahlhelm et al. combined the 3D printing lithography-based ceramic manufacturing technique with so-called



Figure 3. Anatomically accurate 3-D printed brain model.[24]

freeze-foaming technique in order to achieve inherent open-porous-interconnected foam structures of the bone.[22] They demonstrated that these novel potential bone replacement structures might serve as possible next-generation material which can be used for personalized implantation.

In a study conducted by Parthasarathy et al., a novel design approach for creating periodic cellular structures was proposed.[23] The material was fabricated using a metal 3D printed technique. They concluded that 3D printed implants, made out of the proposed material, would fulfil the need for lighter implants and meet the esthetic and functional requirements for patients with skull defects.

3D printing techniques have been used recently to reproduce patient-specific tissue-mimicking materials. In a study by Wang et al., two types of dual-material 3D printed meta-materials were designed to replicate the properties of soft tissues.[24] They showed that the proposed 3D printed materials have great potential in fabricating patient-specific tissues. Advantages included accurate mechanical properties, which can vary depending on gender, age, ethnicity, and other physiological/pathological characteristics.

Medical Education and Training

In general, 3D-printed models are anatomically accurate, provided that high quality CT scan data are available. However, in many cases 3D-printed models are typically inflexible, which makes application difficult in cases involving soft tissue, such as the brain. Ploch et al. proposed a very fast and cost effective method using combined 3D printing, molding, and casting, to create realistic models of human brains which are physiologically accurate as well as deformable.[25] They used a surrogate gelatin-type material that closely mimics the mechanical properties of the human brain. Their models are shown in Figure 3. They concluded that this technique can be used to make personalized deformable brain models, which can be used for surgical planning or for medical training.

A study by McMenamin et al. presented crucial elements which directly or indirectly affect the accuracy of the 3D printed replica of human anatomical objects for training purposes.[26] They discussed the required image data quality, which can potentially produce high quality replicas. They also presented a cost analysis of making a 3D printed replica in comparison with other alternatives. They concluded that the 3D printing is the most rapid and economic technique to reproduce human specimens for medical education. They demonstrated that realistic 3D printed replicas require many scans.

Medical Research

The development of 3D printing for modelling the behavior of cancers has a huge impact on assessing the viability of the responses of the various forms of the disease to different treatments. Using HeLa cells, researchers at TsingHua and Drexel Universities have defined a process to deposit HeLa cells into a 10 x 10 x 2 mm hydrogel structure to create synthetic cervical tumors to investigate the growth of the disease.[27] Alongside this, they created similar tumors using existing 2D methods. They report that their model showed different behavior from previous 2D models, proliferating more quickly and forming cellular spheroids. They note that this method can be especially effective if combined with techniques to deposit multiple types of cell, and investigate the microcellular tumor environment.

The development of microfluidics in bioprinting allows better control over experiments on 3D cell cultures, and the move towards more complex tissue structures like those in native tissues. Researchers at Drexel University have created cell-laden 3D microfluidic structures embedded in PDMS with improved leak protection compared with existing structures.[28] This innovation allows them to guide cells through the microfluidic network to create complex tissue structure. They report a material deposition repeatability of 10 μm with their custom-made deposition apparatus, and the capacity for heterogeneous cell co-cultures using a dual nozzle process. This is part of a large body of work improving the integration of microfluidics with cell cultivation to facilitate all kinds of medical research.

3D printed cells in hydrogel scaffolds have been used by researchers in the University of Dresden to grow cultures of microalgae and microalgae/human cell combinations.[29] The microalgae, exposed to light, were able to grow quickly and the chlorophyll content increased 16-fold over the first few days. The

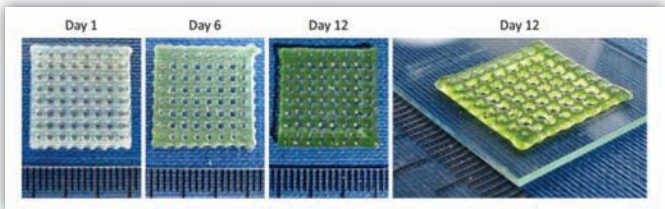


Figure 4. Growth of algae within the impregnated hydrogel at 1, 6 and 12 days.[28]

progress of the algae over 12 days is shown in Figure 4. The microalgae were capable of delivering oxygen to the human cells closely patterned in their midst. The researchers claimed that the principle of such a technology delivering oxygen or secondary metabolites as therapeutic agents was proven, but noted that much effort was still required to bring about any feasible therapies with their technology.

Organ Printing

Researchers at Cornell University demonstrated the 3D bioprinting of full-size tri-leaflet heart valves using hydrogels as a scaffold for the cells.[30] They print two different cell types: aortic smooth muscle cells and aortic valve leaflet interstitial cells onto the prefabricated hydrogels. The cell-impregnated sections retained their tensile strength and were viable over seven days in culture. The printed cells had good spreading, resulting in a robust structure, and high phenotype retention, indicating they functioned as intended. They note, however, that the tensile strength of the resulting prototypes was too low to function properly as a heart valve, and made several recommendations for future work. These include the inclusion of microfluidics to promote more robust cell growth. The CAD design, fabrication process and resulting valve are shown in Figure 5.

Researchers in Edinburgh describe the fabrication of functioning "mini-livers" using 3D printing.[31] Their innovation is the printing of fragile hiPS cells into a 3D alginate hydrogel matrix without damaging their viability or pluripotency. The cell structure was viable for 24 days after the printing. The pluripotency was measured by secretions of albumin, which peaked 21 days after the printing. The work is aimed at animal-free drug trials and personalized medicine, but shows that capability of the 3D printing technique using cultivated, patient-specific cells to produce 3D structures that are viable for weeks after printing and function as a native liver.

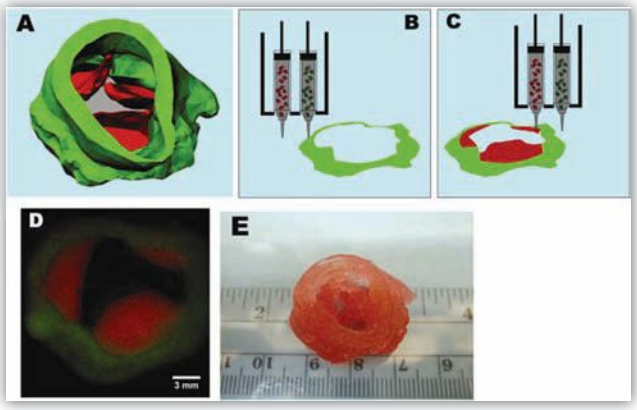


Figure 5. The bioprinting of an aortic valve conduit. (A) Computer model, (B) Printing a layer of SMC, (C) Printing a layer of VIC, (D) Flourescent image of first two layers, (E) The resulting aortic valve conduit as printed.[29]

Finally, the capacity to create organs matching the complexity of native organs brings about the distant possibility of improving these organs, or fabricating entirely new organs for specific functions. An international group of researchers in evolutionary biology have looked beyond the current state of the art and created a 3D morpho-space to describe not only biological structures in human organs but also cells and animal structures, including invertebrates.[32] The design space has on the three axes cognitive complexity, solid/liquid and developmental complexity. They note that a large section of the design space is a void, and bioprinting techniques allow this space to be explored to explore entirely new biological configurations and investigate fundamental questions about evolution.

Drug Delivery

Researchers at University College London have fabricated topical drug delivery systems using 3D bioprinting.[33] They investigated fused deposition modelling (FDM) and stereolithography (SLA) for the fabrication of devices to be worn on the nose and deliver salicylic acid for the treatment of acne. The salicylic acid is loaded into commercial polymer filaments using hot melt extrusion. 3D printing lends itself to this process, as scanned images of the patient's anatomy can be used to create devices that fit exactly, maximizing contact and delivering an even dose of the drug. They found that while both methods created suitable devices, the SLA method was more convenient as a fabrication process. The dosage can also be varied when the filaments used for printing are prepared.

To demonstrate the capacity of 3D printing to produce drug tablets of sufficient quality for prescriptions,



Figure 6. Cube, pyramid, cylinder, sphere and torus paracetamol tablets fabricated by Goyanes et al.[34]

Khaled et al. at the University of Nottingham attempted to print Guaifenesin Bilayer tablets (Mucinex) using a desktop 3D printer bought for under $1,000.[34] They compared the drug release profiles for their designs, and found that one of them showed a cumulative drug release profile that remained within 10% of the release profile of the commercial drug over a 14 hour dosage cycle. They also evaluated the weight variation, hardness, thickness and friability of the tablets they had produced.

Given the new design freedom that 3D printing in pharmaceuticals provides, Goyanes et al. investigated the effect of different shapes of tablet on drug release profiles.[35] They investigated torus, pyramid, cube, sphere and cylinder shapes using an FDM process to print paracetamol-loaded filaments of PVA. Their printed tablets are shown in Figure 6. They first demonstrated that the stability of the drug was unaffected by the printing process. They then investigated the amount of the drug that was released in each tablet and showed, as expected, a clear dependence on surface area to volume ratio. They state that these complex geometries would be impossible to fabricate using traditional powder compaction methods, and will allow better control over drug release profiles.

Discussion

This paper has described a large range of applications for 3D printing and bioprinting in medicine. Here, we will look at lessons learned from some of these recent developments, and try to make some realistic predictions for the future.

For many surgical operations, comprehensive evaluation and surgical planning are essential to achieve good results. In addition to conventional imaging examination, the 3D printing models of the affected organs or anatomies greatly assist surgeons to explore various options before entering the operating room.[15] 3D printed models created from a high quality CT scans assist surgeons to understand the feasibility of the operation plan, shorten the operation time, and consequently improve the outcomes.

3D printing techniques have shown a significant capacity to produce patient-specific prostheses that fully satisfy the esthetic and functional requirements of patients. The process of creating a 3D printed prosthetic is much quicker and less expensive in comparison to other alternative solutions. The 3D printing anatomical model can also be a great substitute to the conventional cadaveric material in training. They can improve surgical training with the ultimate goal to provide accurate, customized, high precision treatment.

3D bioprinting in research is continuing to mature, and its capacity to provide more accurate models in research of diseases such as cancer is demonstrated by the work of Zhao et al.[15] The integration of microfluidics with 3D bioprinting to build complex cocultures and tissue structures, as shown in the work of Snyder et al.,[16] is the subject of increasing research interest. This integration of the two disciplines may be the key to allowing the creation of working organs, as discussed in more detail below. 3D bioprinting has also facilitated research on early conceptual work for new therapies, exemplified by the work of Lode et al.[17]

The printing of full scale biological organs is still a long way from being a reality. The cases described here show that even at the current state of the art, fabricating a robust heart valve using cell printing is a long way from being a reality; while the resulting cell culture is robust in biological terms, current techniques do not allow the creation of a structure with the required structural integrity.[29] Printing a full organ currently remains an aspiration not because functional cells cannot be printed, but because the structure remains too complex for existing methods. Developments in the hydrogel matrices, printing techniques, and better integration with microfluidics are all important steps to move towards obtaining functioning, robust artificial organs by bioprinting. The latest bioprinters have the capacity for extrusion of angiogenic microfluidic networks alongside the tissue printing.[30]

The concept of 3D printers appearing in pharmacies is now close to being a reality. The possible benefits to this work are clear from the papers cited here. The 3D printing process for acne treatment shows how personalized drug delivery can truly become, with both the anatomy of the patient and their required dosage being considered in

the fabrication of a personalized device[3,2] The fabrication of pharmacy-quality tablets using an inexpensive printer by Khaled et al.[33] indicates the increased prevalence that printers may have in pharmaceuticals in the near future. The ability to print complex geometries in tablets will allow drug release to be controlled with more precision.[34] This is clearly one of the areas of 3D printing in medicine where the technology is mature and the practicalities of its deployment are now worth consideration.

3D printing is a method for conveniently creating customized one-off objects, and is transformative in a great number of medical applications. With the development of printing techniques and materials suitable for particular medical applications, research interest is increasing. The recent developments described here show that, while exciting and important advances have already been made in areas of research, teaching, surgical planning, and prosthetics, applications like personalized drugs, and organ printing are at an early stage of development.

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Disclosure

None reported. **MM**

Small Incision Lenticule Extraction SMILE – The Future of Refractive Surgery is Here

by John F. Doane, MD, Jae E. Cauble, BS, Jace J. Rickstrew, BS & J. Quinten Tuckfield, BS

At present, we expect SMILE candidacy to mirror LASIK candidacy.







Clockwise, John F. Doane, MD, FACS, is a board-certified ophthalmologist and LASIK surgeon in Kansas City with Discover Vision Centers. Jae E. Cauble, BS, and J. Quinten Tuckfield, BS, are medical students at Kansas City University of Medicine and Biosciences. Jace J. Rickstrew, BS, is a medical student at Kansas University School of Medicine.
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Abstract

Small Incision Lenticule Extraction (SMILE) is a relatively new one-step refractive procedure that has recently been approved by the FDA for the treatment of myopia. It is anticipated myopic astigmatism will be FDA-approved in 2019. The SMILE procedure is shown to have similar efficacy, safety, predictability, and stability as current surgical options, such as LASIK, but has been gaining popularity due to fewer potential complications, such as dry eye incidence and greater biomechanical stability, and faster recovery time. This article discusses the SMILE procedure, its benefits, risks, uncertainties, and potential future in the world of refractive surgery.

Introduction

More than 35 million eyes have undergone excimer laser vision correction (PRK & LASIK) worldwide, with over 14 million being performed in the US since its inception. LASIK has been the bulk of these procedures. So, is there room for improvement? The answer is a resounding "yes" if we consider the never-ending drive of man's ingenuity to improve the human condition. Engineers at Zeiss in Jena, Germany about nine years ago felt that they might be able to make corneal refractive surgery even better. (Figures 1-3).

What is SMILE?

SMILE is an intrastromal keratomileusis technique that requires a single laser, femtosecond, to create a 3 dimensional lenticule that is extracted through a small corneal incision ranging from 2- 5 mm. (Figure 4) There is no corneal flap and there is preservation of the anterior-most stromal lamella and Bowman's layer, excluding the region of the incision. As an analogy SMILE could be compared to other forms of corneal refractive surgery as modern small incision operative techniques (abdominal, orthopedic, etc.) would be to older larger incision operative techniques. SMILE provides several benefits for patients as it does not require moving from one laser platform to another, has no risk for traumatic flap displacement, offers better biomechanical corneal stability, and reduces postoperative dry eye symptoms as fewer corneal nerves are interrupted.[1-4]

Although SMILE may be a new refractive surgical option in the US it has had extensive study. Over 300 peer-reviewed articles have been published on SMILE to date.5-13 Discover Vision Centers was one of five clinical investigation sites involved



Figure 1. *Carl Zeiss Meditec VisuMax Femtosecond Laser*



Figure 2. *Disposable Curved Patient Interface*

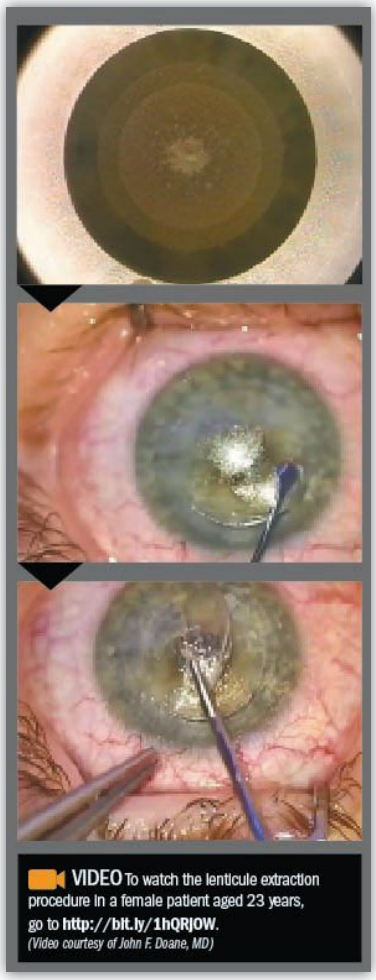


Figure 3. *Pictures from a SMILE procedure performed. (JFD). The top frame shows the femtosecond laser creating a lenticule of tissue and an access incision. The middle image demonstrates dissection between tissue planes anterior and posteriorly of the lenticule. The bottom image shows the lenticule being placed on the front of the corneal epithelium for inspection.*

in the Spherical and the Compound Myopic Astigmatism US FDA clinical trial study arms. Both studies are complete at this point. Commercial spherical myopia SMILE procedures began in the US in early March 2017. The FDA is reviewing the astigmatic results at present and expect myopic astigmatic SMILE to be approved in the first half of 2019. We expect the 1,000,000 SMILE procedure to be performed world-wide before the end of 2017. More than 1,000 SMILE procedures are being performed world-wide. The last time a refractive procedure had such a rapid uptake was in the middle 1990s when excimer laser vision correction overtook incisional keratotomy. As before, patients and surgeons alike migrate to what they perceive to be the best procedure in a given situation. I do not think excimer laser vision correction will disappear completely. It is still the majority of the cases we do (65% Excimer and 35% SMILE). But as more indications are approved for SMILE we anticipate it will likely be 90% of

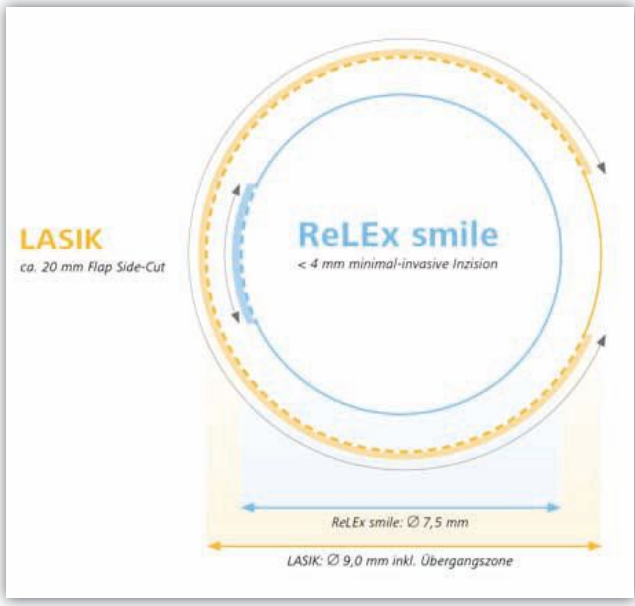


Figure 4. *Image demonstrating the difference in corneal incision in LASIK vs. SMILE.*
Source: http://www.premiumeyes.de/de/augenlasern/relex-versus-lasik/

the corneal refractive procedures we perform. The lack of a flap is attractive to those in the military and those involved in contact physical activities. Also, the lower likelihood of dry eye issues and greater residual tensile strength seems to resonate with patients.

There are still considerations that remain unknown. At this point, we have limited data that extends beyond five years. But, like LASIK the SMILE patients we treated five years ago in the FDA study are tracking just like LASIK patients so we do not expect any surprises. At present, we expect SMILE candidacy to mirror LASIK candidacy.

SMILE, The Future of Refractive Surgery?

As with most things, time will tell if SMILE can compete on the open playing field in a post-approval commercial refractive practice. More than 1,000 surgeons, at 600-plus laser centers in over 60 countries regularly perform the procedure and the number of trained US surgeons is continuing to expand since the FDA approval of SMILE.

Practice in a health model of the future.

Mercy in Arkansas, Kansas, Missouri and Oklahoma, is seeking BC/BE physicians to join thriving practices. Positions offer an excellent benefits package including health, dental, and vision benefits, life insurance, vacation and CME, retirement plan and more. Available opportunities may include:

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Mercy

From a clinician's standpoint, it is quite clear that if designed properly, a femtosecond laser is a breakthrough device for corneal microsurgery. As more data becomes available, we will know what level of impact a femtosecond laser can achieve as a stand-alone refractive surgical device.

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Disclosure

None Reported.

MM

Hypersomnia

by Pradeep C. Bollu, MD, Sivaraman Manjamalai, MD, Mahesh Thakkar, PhD & Pradeep Sahota, MD

Hypersomnolence is a state of reduced vigilance that affects the daytime function and adversely impacts the quality of life.





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Abstract

Adequate alertness is necessary for proper daytime functioning. Impairment of alertness or increase in sleepiness results in suboptimal performance and adversely affects the quality of life. While some causes of somnolence are intrinsic to the brain circuitry and neurochemical architecture, others are due to maladaptive behaviors and disorders affecting the normal sleep homeostasis. Identification of the problem and understanding the underlying etiology is the key to timely treatment and better outcomes.

Introduction

Hypersomnia is a state of excessive sleepiness which can result in decreased functioning and affect performance adversely. Hypersomnolence is defined as an inability to stay awake and alert during major waking episodes, resulting in periods of irrepressible need for sleep or unintended lapses into drowsiness or sleep. Lapses into sleep without prodromal symptoms of increasing sleepiness are called sleep attacks. Excessive daytime sleepiness (EDS) is one of the big public health problems of our time and is estimated to cause almost one-fifth of the motor vehicle accidents in this country. Patients with EDS have decreased workplace productivity, lower quality of life and increased risk of work-related injury.[1] Population-based surveys by National Sleep Foundation found that about 30% of the respondents suffer from enough EDS to interfere with their quality of life.[2]

In this article, we will discuss various disorders associated with Hypersomnolence and their division conforms to the current version of the International Classification of Sleep Disorders (ICSD-3). Some of them are due to fundamental causes within the brain while some others are due to mild adaptive behaviors, systemic disorders, and medications.

History of Hypersomnia

Gélineau (1880) is credited for giving narcolepsy its name though he did not make a clear distinction between episodes of muscle weakness and sleep attacks.[3] Loëwenfeld (1902) was the first to name the muscle weakness episodes triggered by emotions as 'Cataplexy'.[4] There were earlier case reports of narcolepsy by German physicians Westphal and Fisher[5] while the earliest account of narcolepsy may have been from Thomas Willis (1621-75) who described patients with a 'sleepy disposition who suddenly fall fast asleep'.[6] The epidemic of encephalitis lethargica in the early 20th century sparked significant interest in narcolepsy and sleep research. Von Economo (1930) proposed that the region of the posterior hypothalamus was lesioned in human narcolepsy. The classic tetrad of excessive daytime sleepiness, cataplexy, sleep paralysis, and hypnogogic hallucinations were described by Yoss and Daly at the Mayo clinic.[7] (Figure 1)

Neurobiology of Hypersomnia

The state of wakefulness and sleep are controlled by various neuronal systems localized in several brain

regions. Hypoactivity of wake-promoting systems, results in activation of sleep-promoting systems and promotion of sleep. In contrast, hyperactivity of wake-promoting systems results in inhibition of sleep promoting systems and promotion of wakefulness. The overarching control on the regulation of sleep-wakefulness is provided by the circadian process (Process C) that provides the alerting signal, and the homeostatic process (Process S) which maintains constancy of sleep. Several neurotransmitter and neuromodulators are involved in the regulation of sleep-wakefulness. However, amongst these the two main neurotransmitters/ neuromodulators implicated in hypersomnia are hypocretins (also known as orexins) and prostaglandin D2.

Hypocretins are two neuropeptides (hypocretin-1 and hypocretin-2) discovered in 1998[8,9] are important neurochemicals implicated in the pathogenesis of type I narcolepsy. They have a very important role in the regulation of wakefulness and muscle tone. Mice with constitutive knockdown of Hcrt gene display narcoleptic attacks with cataplexy-like behavior[1.0] Intracerebroventricular infusion of Hcrt in wild-type mice increases arousal to the level of complete insomnia, and this effect is abolished in histamine H1 receptor knock out mice. Autopsy studies in humans with narcolepsy also showed loss of hypothalamic Hcrt-producing neurons further implicating Hcrt in type-1 Narcolepsy.

Prostaglandin D2 (PGD2) is an endogenous somnogen that deserves a special mention. Its involvement in hypersomnia has been reported in mastocytosis[11] and African sleeping sickness.[12] Induction of prostaglandin synthase is seen in the brains of patients with various neurodegenerative diseases suggesting that PGD2 may be the common somnogen responsible for the sleepiness seen in these disorders. The somnogenic effects of PGD2 are believed to be mediated by adenosine[13]. Several other cytokines including interleukin - 1β, interleukin 6, Tumor necrosis factor α can also induce sleep.

In addition to the somnogens mentioned above, sleepiness due to medication use or withdrawal and in other medical disorders is associated with augmentation of sleep-inducing neurotransmitters or antagonism of alertness-inducing neurotransmitters. (Figure 2)

Central Disorders of Hypersomnolence

Narcolepsy Type 1

Narcolepsy type 1(NT 1) is characterized by a deficiency of hypothalamic hypocretin signaling. Along with excessive daytime sleepiness, REM sleep dissociation is its other important feature.

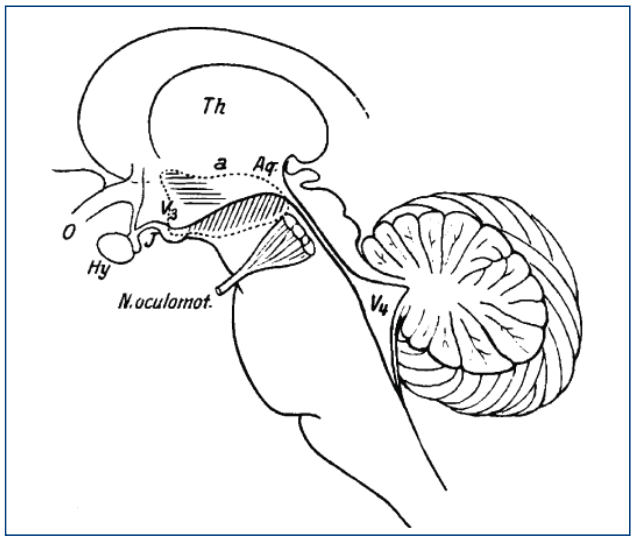


Figure 1: Drawing of human brainstem taken from Von Economo's original drawing. Lesions in the region of the horizontal lines caused prolonged insomnia while lesion in the region of diagonal lines caused prolonged sleepiness. Von Economo suggested that narcolepsy was caused by lesions in the region of posterior hypothalamus (site of the arrow). Picture obtained from Wikimedia Commons.

About 90% of these patients have low or undetectable concentrations of Hypocretin -1 in the cerebrospinal fluid (CSF). Cataplexy is a brief state of reduced muscle tone precipitated by emotional triggers and is the most specific of the REM sleep dissociations seen in Narcolepsy. Cataplexy may not be manifest in all the patients with narcolepsy type I and is very closely associated with low CSF hypocretin levels. Many patients with Narcolepsy type I have disrupted nocturnal sleep. Though not specific, hypnogogic and hypnopompic hallucinations along with sleep paralysis can also be seen. An increased frequency of obesity, other sleep disorders, and psychiatric comorbidities is also observed. Narcolepsy with cataplexy is closely associated with HLA

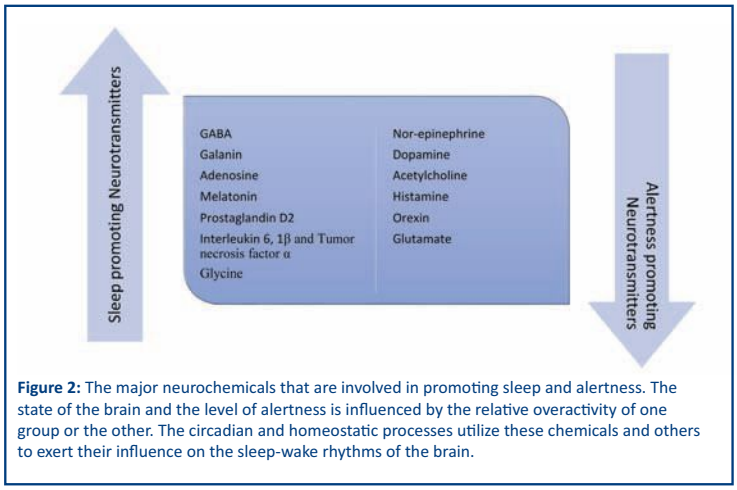


Figure 2: The major neurochemicals that are involved in promoting sleep and alertness. The state of the brain and the level of alertness is influenced by the relative overactivity of one group or the other. The circadian and homeostatic processes utilize these chemicals and others to exert their influence on the sleep-wake rhythms of the brain.

subtypes-DR 2/DR B1*1501 and HLA DQB1*0602. This strong association has led to the hypothesis that autoimmunity is a likely etiological mechanism, potentially explaining the selective neural destruction in the hypothalamus. If the HLA testing is negative, the CSF hypocretin levels are most likely normal.

Most typically, the age of onset is between 10 and 25 years. Sleepiness is typically the first symptom to manifest with cataplexy manifesting usually within one year of onset. Secondary Narcolepsy can also be seen in the setting of inflammatory disorders like encephalitis and tumors or lesions of the hypothalamus.

Narcolepsy Type 2

Patients with Narcolepsy type 2(NT 2) do not have cataplexy and constitute about one-fourth of the narcoleptic population. This disorder shares multiple features seen in NT 1. The exact cause of this disorder is uncertain. Similarly, the underlying genetic and environmental factors associated with NT 2 patients are unknown. The onset of this disorder typically occurs during adolescence. Cataplexy will develop later in the course the disease in about 10% of these patients at which time the disease needs to be reclassified as NT 1. Similarly, a low CSF hypocretin concentration (< 110 pg/mL or $<1/3^{rd}$ of mean concentrations in the population) should warrant a reclassification of the disease as NT 1. Both types of Narcolepsy have early onset of REM sleep after the patients fall asleep. Sleep Onset REM (SOREM) is defined by the onset of REM sleep within 15 minutes of falling asleep, and patients with Narcolepsy should have at least two SOREMs in the MSLT/ Overnight PSG combined.

Idiopathic Hypersomnia

Idiopathic hypersomnia(IH) is characterized by excessive daytime sleepiness without REM sleep intrusion not explained by another disorder. There should be no more than one sleep onset REM on the multiple sleep latency test and the preceding polysomnogram combined. This distinct entity described by Bedrich Roth in the late 1950s was initially called 'Sleep Drunkenness' and 'Hypersomnia with Sleep drunkenness.'[14] These patients typically have high sleep efficiency on the preceding polysomnogram and clinically report severe and prolonged sleep inertia (also known as sleep drunkenness) and non-refreshing naps. In the past, IH was divided into two types-one with long sleep time and one without long sleep time. Such a division is no longer used as there is no significant difference between the two groups The CSF hypocretin 1 concentrations in these patients are normal. A recent experiment showed that patients with IH have a bioactive CSF component with a mass of 500-3000 Da that could potentiate $GABA_A$ receptor function in vitro.

Kleine-Levin Syndrome

This syndrome is characterized by episodes of severe sleepiness in association with cognitive, behavioral and psychiatric disturbances. Each episode typically lasts for about ten days with prolonged episodes lasting several weeks to months. The first episode is often triggered by infection or alcohol with future episodes occurring every three months or so (range of 1-12 months). During the episodes, patients sleep for up to 20 hours a day only waking up to eat and void. Less commonly, hyperphagia and hypersexuality are also seen during the episodes. In between the episodes, the patients display remarkably normal sleep, feeding behavior, mood, and cognition. The disease starts during the second decade in most of the patients and is more common in males. This syndrome typically resolves after many years. Sometimes, a similar syndrome is also observed in the setting of menstrual cycle and is considered a variant of Kleine-Levin syndrome.

Hypersomnia due to Medication or Substance Abuse

Multiple different classes of medications have sleepiness as their side effect. Table 1 lists the different drug classes and the neurochemical basis of the sleepiness associated with them. Given the concise nature of this review, every medication that has sleepiness as a side effect could not be mentioned.

Hypersomnia Due to a Medical Disorder Sleepiness Despite Adequate Treatment of Obstructive Sleep Apnea

Sleepiness in the setting of obstructive sleep apnea (OSA) is usually attributed to the chronic sleep deprivation due to sleep fragmentation. On the same vein, sleepiness is expected to get better when OSA is treated adequately. However, a certain portion of people remains sleepy despite adequate treatment. Individual studies in the past have reported the prevalence rates from 6% to 55%[15] while a recent study by Gasa et al. found that about 13% of adequately treated OSA patients still had residual sleepiness with CPAP.[16] The affected patients are usually younger, report more fatigue, have higher ESS score at baseline and more PAP-related side effects.[16] Other predictors of sleepiness include diabetes, heart disease, mood disorders, hypothyroidism and other sleep disorders, especially insufficient sleep.[15,17] The exact mechanism for this

Table 1. Classes of Medications with Sleepiness as Their Side Effect

Class of medications	Drugs	Mechanism of Action
1. Hypnotic Medications	• Triazolam • Zaleplon • Zolpidem • Eszopiclone • Ramelteon • Suvorexant	The Z drugs (Zaleplon, Zolpidem, and Eszopiclone) act as $GABA_A$ agonists. Ramelteon is a melatonin receptor agonist. Suvorexant is an orexin antagonist.
2. Sedatives	• Antihistaminics • Anticholinergic • GABA agonists • Opiates	Act at the histaminergic and cholinergic receptors. $GABA_A$ agonists like barbiturates and benzodiazepines act to modulate the Cl^- channel.
3. Drugs of Abuse	• Ethanol • Cannabis • Opiates	Ethanol acts on $GABA_A$ receptor. Cannabis acts on Cannabinoid receptors. Opiates act on Opioidergic receptors.
4. Anti-hypertensives	• Alpha 1 adrenergic blockers • Alpha 2 adrenergic agonists • Beta-adrenergic blockers	Alpha 1 antagonists like prazosin and terazosin act on the postsynaptic alpha 1 adrenergic receptor while alpha 2 agonists act at presynaptic alpha 2 auto-receptor.
5. Anti-epileptics	Carbamazepine, Valproic acid,	Neurochemical basis of somnolence produced by many drugs in this class is still unknown. Some act as GABA-agonists.
6. Anti-parkinsonian agents	Drugs like Levodopa, dopamine agonists like ropinirole.	Act at dopamine receptors.
7. Skeletal muscle relaxants	Baclofen	GABA receptors; Some have anticholinergic effects
8. Gamma Hydroxy Butyrate	GHB / Sodium Oxybate. Used in the treatment of Narcolepsy	$GABA_B$ receptor
9. Antipsychotics	Quetiapine, Olanzapine, Haloperidol, etc.	Dopamine blockade; other effects at histaminic, cholinergic and alpha-adrenergic receptors.

condition is unclear thought animal studies showed that intermittent nocturnal hypoxia could result in irreversible damage to neuronal regions involved in sleep-wake regulation.

Post-traumatic Hypersomnia

Hypersomnia can be seen as a complication of head injury in up to 27% people.[18] In the acute phase of moderate to severe traumatic brain injury, the CSF hypocretin levels can also be low.[19] Imaging studies usually don't show any significant lesions but may sometime reveal injuries in the hypothalamic region and brainstem.

Hypersomnolence in Neurodegenerative Disorders

Hypersomnolence affects 16-50% of patients with Parkinson's disease[20] and can be seen in up to a quarter of patients with Multiple systems atrophy. Similarly, other parkinsonian disorders, spinocerebellar degeneration, Huntington disease are all associated with hypersomnolence.

Hypersomnolence in Genetic Disorders

Myotonic dystrophy, the most common adult onset form of muscular dystrophy can have hypersomnolence in up to one-third of the patients[21]. Other genetic disorders associated with primary CNS somnolence include Niemann Pick Type C disease, Norrie disease, Prader-Willi syndrome, Smith-Magenis syndrome, Moebius syndrome and Fragile X syndrome.

Hypersomnolence in Inflammatory, Vascular and Neoplastic Processes

Cerebrovascular disorders, infections, tumors and other inflammatory disorders can also cause somnolence especially when hypothalamus or rostral midbrain is involved

Hypersomnolence in Endocrine and Metabolic Disorders

Hepatic encephalopathy, adrenal and pancreatic insufficiency, chronic renal insufficiency and be associated

with somnolence. Conditions like hypothyroidism, iron deficiency, vitamin D deficiency have been suggested as possible causes of fatigue and sleepiness but lack a comprehensive characterization of the objective measurements of sleepiness and vigilance.

Hypersomnia in Psychiatric Disorders

Depression and Central hypersomnias share multiple common symptoms. The prevalence of depressive symptoms in NT1 ranges from 15%-37%[22,23] while in IH ranges from 15% to 25%.[24] On the same note, the prevalence of hypersomnia in Major Depressive Disorder(MDD) can be seen in more than two-thirds of the adult patients. Symptoms of hypersomnia can range from 23% to 78% in patients with bipolar depression(BD).[25,26] Hypersomnolence is one of the major features of Seasonal Affective Disorder and can be seen in up to two-thirds of the patients. Patients with MDD have shortened REM sleep latency, increased REM density and duration which may relate to an increased central cholinergic activity. Patients with BD may show disruption of circadian rhythm, especially delay in the sleep phase.[27]

Stimulant medications should be used with caution as there is an increased risk of psychotic symptoms with higher doses of the stimulants. Preclinical data suggest that H3 receptor antagonists might alleviate depressive symptoms. Sodium Oxybate can induce or worsen depressive symptoms.

Insufficient Sleep Syndrome

Everyone has biologically determined sleep needs for normal level of alertness and wakefulness. When the individual persistently fails to obtain this minimum sleep required, insufficient sleep syndrome ensues with increased somnolence. This state of chronic sleep deprivation has become one of the big public health concerns of the twenty-first century.[28] These patients do not have any issue with sleep initiation or maintenance, and physical examination reveals no medical explanation for the sleepiness. Associated features include irritability, difficulty with concentration, attention deficits, distractibility, reduced motivation, and malaise. A trial of sleep extension reverses the symptoms.

Evaluation of Sleepiness

Subjective Assessment

The clinical assessment of patients starts with the subjective assessment of their sleepiness. There are multiple sleep questionnaires that are used to assess subjective somnolence. Most commonly used is the Epworth Sleepiness Scale which has a maximum score of 24 and estimates the likelihood of someone falling asleep in eight different scenarios. Other assessment tools include Barcelona sleepiness index, Stanford sleepiness scale, Karolinska sleepiness scale, time of day sleepiness scale and Leeds sleep evaluation questionnaire.

Clinical Evaluation

Subjective assessment of sleepiness should be followed by a comprehensive sleep history and appropriate investigations. Sleep and wake routines of the patient should be evaluated using sleep log/dairy. An objective assessment of the circadian rhythms can be done using actigraphy. Actigraphy involves monitoring the active and inactive times during a two to four week period to get an overview of the sleep and wakeup times and to determine if the patient has delayed or advanced sleep phase rhythm.

Objective Assessment of Somnolence

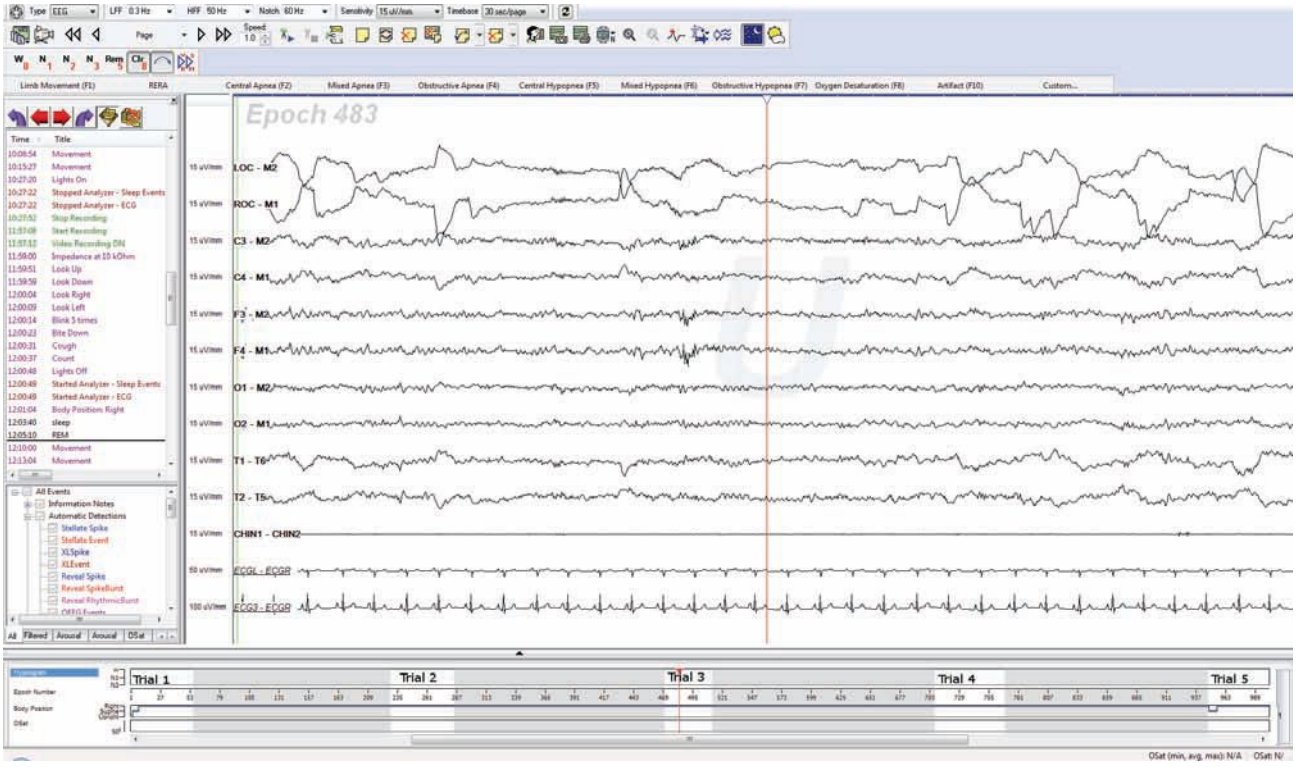
Multiple Sleep Latency test (MSLT) is a type of polysomnogram that can help with identification of patients with Narcolepsy. In this test, the patient is allowed to go to sleep during the five scheduled naps. Sleep onset REM is recorded if REM sleep appears within 15 minutes after sleep onset. The presence of two or more SOREMs along with a mean sleep onset latency of eight minutes or less is diagnostic of Narcolepsy. The MSLT is preceded by a baseline sleep study during which the patient is allowed to sleep to make sure that sleep restriction or other sleep disorders are not influencing the results in the five naps. It is also important to assess the sleep-wake routines of the patients in the preceding one to two weeks preferably using actigraphy. If there is a SOREM in the preceding night, it can be counted towards the total of two required SOREMs for making the diagnosis. (Figure 3)

Maintenance of Wakefulness Test (MWT) is another test during which the ability of the patient to stay awake is measured. The protocol for this test is not as standardized as MSLT but typically consists of four naps and the patients are asked to stay awake during all the four trials. This is the test of choice when safety is a concern. Other objective tests include Oxford Sleep resistance test, sustained attention to response task, measurement of eye and eyelid movements, pupillometry and driving simulators but are not commonly used in clinical practice.

Treatment of Hypersomnia

The treatment of hypersomnia should be primarily directed at the cause if there is one. Any factor that is adversely affecting the quantity and quality of sleep should be addressed before initiating therapy. Accordingly, the treatment of hypersomnia is both pharmacologic and non-pharmacologic.

Figure 3: A typical MSLT showing the patient having SOREM during trial 3.



Non-pharmacologic approaches include – Good sleep hygiene, scheduled daytime naps, and regular physical activity.

Sleep Hygiene

This includes practices to enhance good sleep. This includes avoiding stimulants like caffeine and nicotine before sleep, avoiding heavy meals and alcohol before bedtime, keeping the sleeping environment quiet and comfortable and maintaining a regular sleep schedule.

Scheduled Naps

These have been shown to reduce daytime sleepiness without adversely impacting the nighttime sleep quality. Care needs to be taken to keep the nap time to close to 15 to 20 minutes as naps longer than 30 minutes usually result in sleep inertia. The scheduled naps are very effective in Narcolepsy but are not that well studied in other hypersomnias.

Pharmacological Therapies

Gélineau administered various treatments for narcolepsy including bromides, strychnine, and amyl nitrate. Gowers endorsed caffeine usage and suggested the use of stimulant drugs. Other treatments proposed initially for the treatment of Narcolepsy include intrathecal injection of air, removal of cerebrospinal fluid, X-ray irradiation of the hypothalamic region.[3] Amphetamines were first used in the treatment of Narcolepsy in 1935.[29]

The most commonly used medications to address EDS have a common feature of enhancing dopaminergic tone. Modafinil and Armodafinil are milder and are often the medications of choice at the beginning of the treatment. They act at the dopamine transporter (DAT) and prevent the reuptake of dopamine. Headache and nausea are the most common side effects. Amphetamines salts (methylphenidate, dextro-amphetamine etc.) are generally stronger and more effective in treating EDS but have more abuse potential and side effects. They cause the release of nor-epinephrine and dopamine in the synaptic cleft and act on the DAT to prevent their reuptake.

Sodium Oxybate (Sodium salt of Gamma Hydroxy butyrate(GHB)) is a $GABA_B$ agonist and is approved for the treatment of both daytime sleepiness and cataplexy. It promotes slow wave sleep. Its mechanism of action is not fully understood. Several researchers have proposed its activity at its own receptor (GHB receptor).

Pitolisant is an H3 receptor inverse agonist. The histaminergic H3 receptors are regarded as inhibitory auto-receptors and are abundant in the central nervous system.

Pitolisant increases histamine release in hypothalamus and cortex. A recent double-blinded study showed its efficacy on both EDS and cataplexy and was better tolerated than modafinil. Pitolisant is not available in the United States at the time of this review.

Flumazenil is an antagonist of the benzodiazepine -binding domain in $GABA_A$ receptors. It has been studied in patients with idiopathic hypersomnia and shown to improve psychomotor vigilance and subjective alertness. Clarithromycin is another negative allosteric modulator of the $GABA_A$ receptor and shows subjective improvement of sleepiness. Levothyroxine also has been successful in patients with IH in improving ESS.

Caffeine is the most commonly used stimulant in the world and can be used in the treatment of EDS in hypersomnias. Higher doses of caffeine have comparable efficacy on EDS as Modafinil but is limited by the side effects.

Other treatments that are currently studied include intranasal orexin for Narcolepsy type I, immune-based treatments for Narcolepsy, Prostaglandin D2 receptor antagonists and Thyrotropin-releasing hormone.

Conclusion

In summary, hypersomnolence is a state of reduced vigilance that affects the daytime function and adversely impacts the quality of life. The level of alertness is mediated by the tone of circadian and homeostatic processes which in turn act through alerting and sleep promoting systems. Any imbalance in these two opposing neuronal systems results either in a state of reduced vigilance and increased sleepiness or difficulty with sleep and insomnia. In the case of hypersomnia caused by sleep disruption, chronic sleep deprivation, metabolic or endocrine disturbance, addressing the underlying etiology will usually be sufficient to improve sleepiness. On the other hand, disorders like Narcolepsy which are due to deficiency of Orexins, treatment options are limited to symptomatic improvement of sleepiness. A thorough history along with a good understanding of disorders of hypersomnolence is necessary for identifying these patients and helping them appropriately.

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Disclosure

None reported.

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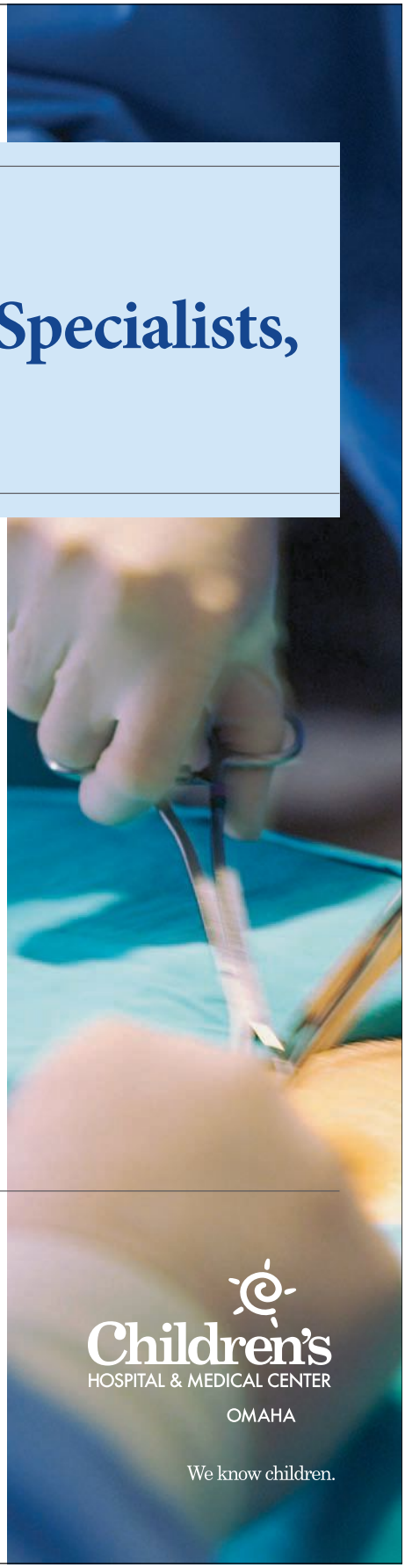
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