Missouri Medicine

The Journal of the Missouri State Medical Association www.msma.org May/June 2013

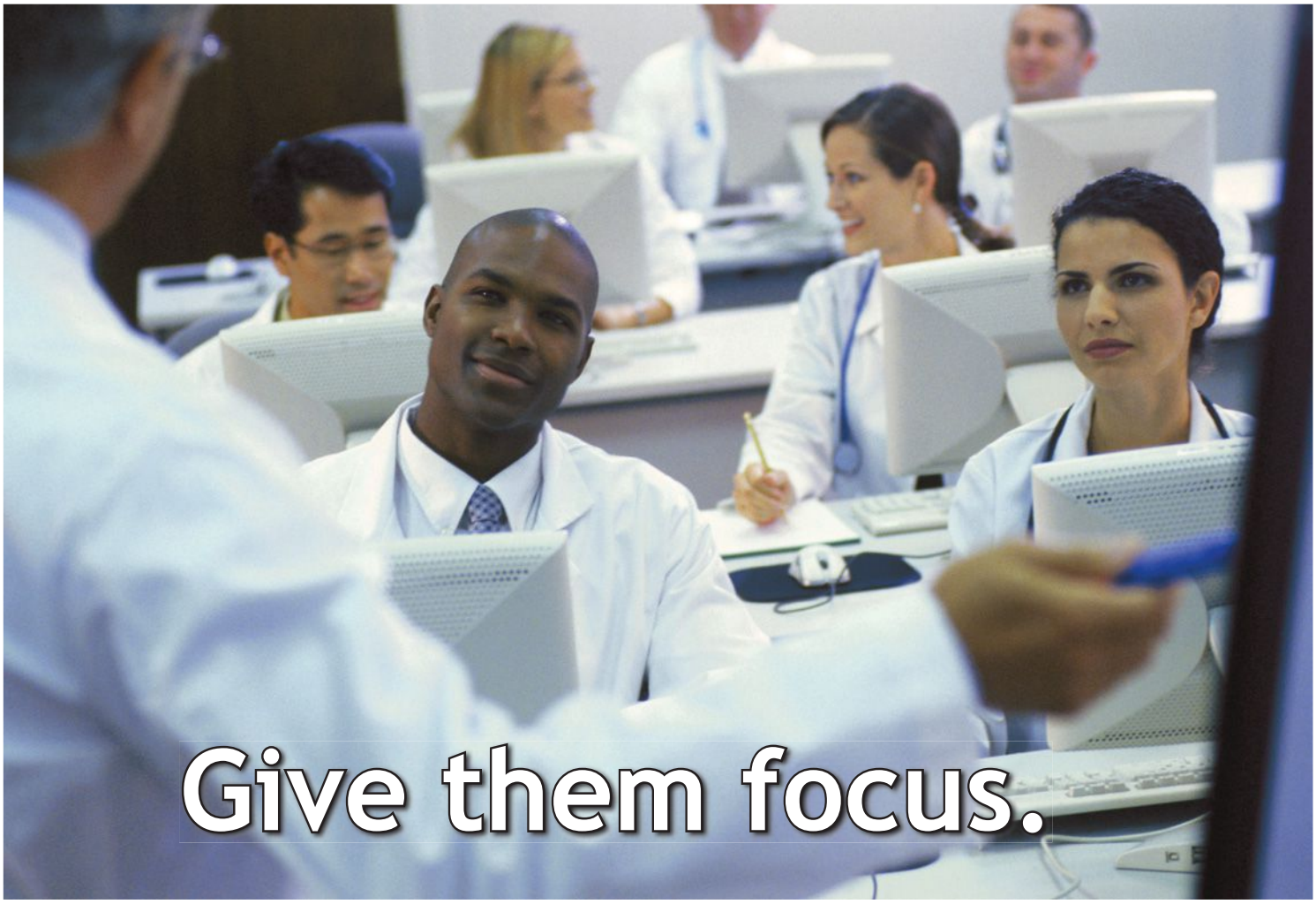


ONE MEDICINE

Collaborative Research on Human & Animal Disease

in cooperation with
Missouri University's
College of Veterinary Medicine
& School of Medicine

- 155th Annual Convention Wrap
- Retainer-Based Medicine
- Doctors in Unions?
- Into the Future with KCUMB
  KANSAS CITY UNIVERSITY OF MEDICINE AND BIOSCIENCES
- Residency Crisis
- A Physician's Duty to Warn
- Opioid Drug Therapy
- Adult Day Care



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Missouri Medicine

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Missouri State Medical Association
113 Madison Street ◆ P.O. Box 1028 ◆ Jefferson City, MO 65102
800-869-6762 ◆ Fax: 573-636-8552 ◆ www.msma.org/MissouriMedicine
Editor: John C. Hagan, III, MD ◆ jhagan@bizkc.rr.com
Managing Editor: Lizabeth R. S. Fleenor ◆ lfleenor@msma.org

About Missouri Medicine

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Missouri Medicine Editorial Board

Owner & Publisher

Missouri State Medical Association

Missouri Medicine Editor*

John C. Hagan, III, MD
9401 North Oak Trafficway, Ste. 200
Kansas City, MO 64155
Tel: 816-478-1230 / Fax: 816-454-8478
jhagan@bizkc.rr.com

Managing Editor

Lizabeth R. S. Fleenor
Missouri State Medical Association
113 Madison Street / P.O. Box 1028
Jefferson City, MO 65102
800-869-6762 / Fax: 573-636-8552
lfleenor@msma.org / www.msma.org

Contributing Editors*

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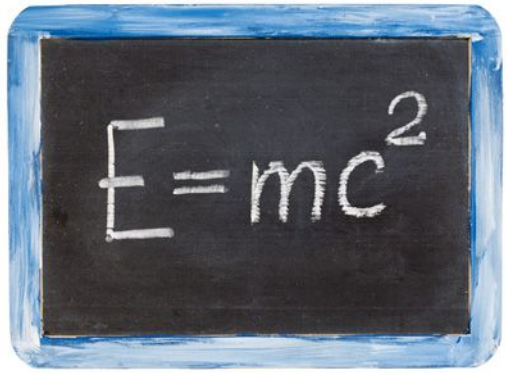
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MSMA Office & Staff Contact Information

113 Madison Street / P.O. Box 1028
Jefferson City, MO 65102
573-636-5151 / 800-869-6762 / Fax 573-636-**8552**
www.msma.org

Executive Vice President: Tom Holloway	Tel Ext - 123	tholloway@msma.org
Field Services: Fred Brown	Tel Ext - 130	fbrown@msma.org
Communications: Lizabeth Fleenor	Tel Ext - 134	lfleenor@msma.org
Govt Relations/Legal: Jeff Howell	Tel Ext - 128	jhowell@msma.org
Legislative Affairs: Kenny Jackson	Tel Ext - 122	kjackson@msma.org
Health Care Finance: Patrick Mills	Tel Ext - 126	pmills@msma.org
Scientific Affairs: Benita Stennis	Tel Ext - 138	bstennis@msma.org
Membership: Haley Wansing	Tel Ext - 135	hwansing@msma.org
Office: Linda Bremer	Tel Ext - 121	lbremer@msma.org
Membership Database: Lois Chronister	Tel Ext - 127	lois@msma.org
Reception: Fran Draper	Tel Ext - 120	fran@msma.org
Finance: Brenda Kinney	Tel Ext - 133	bkinney@msma.org
Administrative: Carol Meyer	Tel Ext - 132	cmeyer@msma.org

Dues, Dollars, Days, Diligence: Why They Matter As Much as



If you do not belong to the MSMA, you are neglecting
your responsibility to advocate for your medical profession,
your patients, your staff, your family,
likely your financial health,
surely your retirement, and how you look back on your career in Medicine.

by John C. Hagan III, MD

With apologies to Einstein, let's use his famous $E=MC^2$ and run a few calculations to determine the 'relative effectiveness' of Missouri physicians in promoting their core profession-saving causes: high quality care for patients, fair-prompt remuneration for professional services, protection from junk malpractice lawsuits, restoration of reasonable non-economic caps on malpractice awards, an end to economic credentialing, freedom for physicians to own hospitals and surgicenters,[1] public financial assistance both to institutions, and students for medical education. Lastly keeping "physician" designation and full scope of medical and surgical practice limited to properly trained Doctors of Medicine or Osteopathy. See my calculations on page 165.

Message to MSMA Members

To you, "the clued in," who have so diligently worked for the betterment of your patients and your profession: Keep up the good work! Without you medicine in Missouri would be moribund.

A) Make sure your MSMA dues are paid.

B) Make sure every physician in your group belongs to MSMA. Try and recruit at least one non-member from among the physicians you interact with daily.

C) Make a donation to Missouri Medical Political Action Committee (MMPAC).

D) Read and take action on weekly MSMA *Legislative Report*.

E) Tort Reform reinstatement did not pass this 2013 session but will be a major goal of the 2014 legislative year. Begin advocating now by having coffee, lunch or phone calls with your state Senator or Representative to educate them. During the next legislative session, use a day off to travel to Jefferson City and lobby on behalf of your patients and our profession.



John C. Hagan, III, MD, FACS, is a Kansas City ophthalmologist and *Missouri Medicine* Editor since 2000. *Contact: jhagan@bizkc.rr.com*

E) Educate your patients and staff on key medical issues and urge them to call, write, e-mail or visit their Governor and Legislators.

Message to MSMA Leadership

Thank you for your time and leadership. But you must do more. We need to retain present members; we need to recruit new members; we must warmly welcome young physicians-in-training and teach them to advocate for medicine. We need more money from leadership. Set the example, lead from the front.

I want to connect a few dots between opportunities for MSMA Leadership and the Missouri Society of Eye Physicians & Surgeons (MOSEPS) also known as "The Phoenix Society." MOSEPS has gone from the edge of financial and membership insolvency within five years to become one of the top two most politically effective state specialty organizations in the U.S. and Missouri (Hats off to the Missouri Anesthesiologists, also) while creating and sustaining a positive cash flow thus building reserves for the future. In 2013, the American Academy of Ophthalmology declared MOSEPS the "Model State Society" and gave us a financial grant to try and duplicate our model in other states.

These are the important lessons for MSMA leadership on how MOSEPS got to be a growing, energetic, well-led organization:

A) High priority effort to find the most qualified and interested physicians that are willing to devote time/talent to MSMA. Bring them into leadership early in their careers.

B) Maintaining members and recruiting new MSMA

members must be engaged by every level of leadership. Every MOSEPS board member receives a regular copy of our dues collection and is assigned a small number to personally contact to pay their dues. Letters, calls, e-mails, personal visits, and pleasantly packaged nagging come from several MOSEPS leaders. Any organization membership staff person will tell you that physician-to-physician membership and dues solicitation is 10 times more effective than a paper invoice in the mail. MSMA leadership (a larger group than MOSEPS) should personally assist in membership efforts year-round and look for new and more effective strategies.

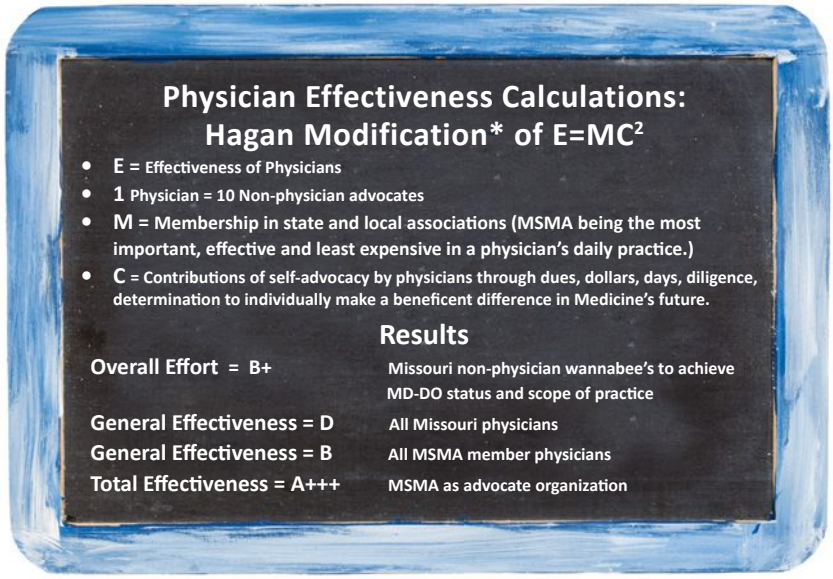
Our MOSEPS board has dramatically increased major gifts and average donation from our board and committee leadership. In the last 2012 general elections every MOSEPS leader donated at least $1,000, several over $50,000 and one over $100,000. Thoughtful placement of these PAC monies in leaders of both parties has given MOSEPS "player" status in the Missouri Senate and House.

MSMA leadership should open their wallets. Our highest MSMA officers should donate at least $1,000 per year and mid-level $500 and every leader $250, every member $150. *Missouri Medicine* would gladly donate much more page space for MMPAC "Diamond Level Donors" ($1,000). Since that designated level of giving was created in 2008, only your Editor has been a member each year. My personal opinion is every sitting board member of the MMPAC should contribute $1,000 each and every year. As we found in MOSEPS, nothing will so help a general increase from the broader body of membership than MSMA leadership 'acting like gems" in their own donations.

Message to Non-MSMA Physicians & Physicians-in-Training

Intelligent and principled women and men do not rise to the level of physician status by rejecting responsibility or ceding control of their patients' health care problems to lesser trained others. Nor do you neglect to advocate to your patients for healthy lifestyle changes (stop smoking, lose weight, take your medication). The "health message" is many times more effective when it comes directly from the patient's physician, as opposed to a lesser trained health care worker. So are the "legislative, insurance, malpractice reform, fair reimbursement, reasonable regulation messages" when presented by you to patients, legislators, and the public.

If you do not belong to the MSMA you are neglecting your responsibility to advocate for your medical profession, your patients, your staff, your family, likely your financial health, surely your retirement, and how you look back on your career in Medicine. Do not fob this off on physician members of the MSMA who have done, are doing, and will do the most of any organization in the Show-Me State to enhance the everyday practice of Medicine. MSMA dues are the third lowest in the nation ($395/year). If you cannot give MSMA your time, give us yearly dues. If you are an employed physician, by an institution or hospital system, your need for advocacy is even higher than the self-employed physician.



The physician collective, working together through MSMA, can protect the interests of our patients and profession against the grave threats Medicine in 2013-2014 Missouri faces.

Contact MSMA Membership Director Haley Wansing hwansing@msma.org If I can help you in anyway please contact me at jhagan@bizkc.rr.com One of the greatest ways I have served my patients is advocating for them through MSMA. Come on board right now!

1. http://www.amednews.com/article/20130429/government/130429948/4/

* This is the small print that normally a lawyer charges you $750/hour to read. Hagan Calculations are based on 43 years in physician advocacy on local, state, national level for Medicine; average political contributions of $15,000-25,000/year, leadership in many physician organizations, past and present, including four as President. Traditional mathematical models do not exist and would likely not be as accurate anyway.

How Outrageous Pricing & Egregious Profits Are Destroying Our Health Care



BITTER PILL

Analysis of Steven Brill's *Time* Magazine Article

by Arthur H. Gale, MD

The most important takeaway message from this landmark article is the detailed account of the outrageous pricing practices of hospitals and the important role played by their secretive chargemaster.

In the March 4, 2013, issue of *Time* magazine a 24,000 word article (the longest ever published in *Time's* existence) author-journalist Steven Brill identifies a major source, likely the most important, of high health care costs.

By "following the money" Brill concludes that hospitals and their arbitrary internal price list for their products and services - known as the chargemaster - are the main culprits. Surprisingly, the hero of the article turns out to be the much maligned Medicare, the only organization that has the power to stand up to the hospitals' outrageous pricing system.

Brill cites many examples of sky-high hospital charges and compares them to what Medicare pays. For example, one hospital charged a non-Medicare patient $199.50 for a troponin blood test. For a Medicare patient the charge was $13.94. Another hospital charged a patient $157.61 for a CBC. For a Medicare patient the charge was $11.02.

"Hospital finance people argue vehemently …they lose as much as 10% on the average Medicare patient. But even if the Medicare price should be, say, 10% higher, it's a long way from $11.02 plus10% to $157.61." The author quotes Jonathan Blum, deputy administrator of the Centers for Medicare and Medicaid Services: "I was driving through central Florida, and it seemed like every billboard I saw advertised some hospital with these big shiny buildings. So when you tell me that they are losing money on Medicare patients and shifting money costs from Medicare to other patients, my reaction is that central Florida is overflowing with Medicare patients and those hospitals are expanding and advertising for Medicare patients. So you can't tell me they are losing money when they serve Medicare patients."

Chargemaster prices are completely arbitrary. They have no connection to the real cost of providing a service or product. They differ from hospital to hospital. Hospital administrators don't want



Arthur H. Gale, MD, MSMA member since 1976, is a *Missouri Medicine* Contributing Editor. He practices Internal Medicine in St. Louis.
Contact: agalemd@aol.com

to talk about them. They say they are meaningless because insurance companies routinely get discounts. But they are not meaningless.

"Insurers will try to negotiate prices that are 30 to 50% above Medicare rates rather than discounts off the sky-high chargemaster rates. But insurers are increasingly losing leverage because hospitals are consolidating by buying doctors' practices and even rival hospitals. Getting a 50% or even a 60% discount off the chargemaster price of an item that costs $13 and lists for $199.50 is still no bargain." The fact is the insurer needs the hospital more than the hospital needs the insurer.

Brill says: "That so few consumers seem to be aware of the chargemaster demonstrates how well the health care industry has steered the debate from why bills are so high to who should pay them."

The ultimate defense of the hospitals, especially the non-profits, when challenged about their exorbitant charges, is their charity care. An ad by the American Hospital Association in a popular Congressional tip sheet urged Congress not to cut hospital payments because it would jeopardize the $39.3 billion in care for the poor that hospitals now provide. But that $39.3 billion figure is calculated on the basis of the chargemaster price. Based on what Medicare actually pays for this care, charity care costs the hospitals less than $3 billion. That's less than one-half of one percent of U.S. hospitals' annual revenue. Worse yet hospitals egregiously even include bad debt in their charity care!

Brill asks rhetorically what the wealthy 'non-profit' hospitals do with all their profits. His answer is that they add more buildings and add more beds despite the fact that the U.S. has more hospital beds than it can fill. They also use their profits to buy more equipment, hire more people, buy more physicians practices, buy rival hospitals, and of course raise their executive salaries.

The author cites data that show that inpatient care at hospitals is only marginally profitable. DRGs or fixed payments for various diseases have been successful in controlling hospital profits. On the other hand outpatient care is "wildly profitable," a veritable gold mine. Outpatient services include such items as clinical laboratories, radiology imaging, especially CT scans, same-day surgery, and cancer chemotherapy.

To illustrate his point, Brill cites the case of a patient who received an $87,000 bill for an outpatient procedure for the insertion of a spinal stimulator at facility owned by Mercy Health. By following the money closely he found that Medtronic sells the stimulator to the hospital for about $19,000. Because Mercy Health, where the procedure was performed, is part of a chain of hospitals it probably paid 5% to 15% less than that. The hospital sold the stimulator to the patient making a $30,000 profit, "a margin of more than 150%." The patient was never told the price of his stimulator or the cost of the procedure beforehand. He assumed that the $45,000 that his union insurance provided would cover just about any outpatient procedure. He never expected that his bill would be almost twice the covered amount. Eventually, by hiring a private medical billing specialist, the patient was able to get a reduction of his bill and ended up paying $10,000 out of pocket. That' a hefty sum for an average working man.

The author then launches into a withering critique of Mercy Health, a chain of 31 hospitals, with headquarters in St. Louis. The most recent IRS filing shows that the chain had $4.28 billion in revenue. Its executive vice president, Myra Aubuchon made $3.7 million, its president and CEO Lynn Britton made $1,900,000. In all, seven executives were paid more than $1,000,000 annually. Mercy is owned by a religious organization called Sisters of Mercy. Its stated mission is to carry out a healing ministry. Its charity care, according to its auditors, Ernst and Young, was worth 3.2% of its revenue. However the auditors caution that this figure is based on charges not actual costs. In other words, the charitable figure is based on the chargemaster. Since the actual costs are about one tenth of the chargemaster, charity care at Mercy amounts to about three-tenths of one percent of its revenue. For this insignificant amount of charity care Mercy and other non-profit hospitals get generous tax breaks.

Brill contrasts the fore-mentioned scenario with Medicare. He describes the case of an 88-year old man who collapsed from a heart attack. He survived two weeks in the intensive care unit of the Virtua Marlton hospital in Philadelphia. The patient then spent three weeks in a convalescent center. Virtua Marlton is part of a four-hospital chain. 2010 Federal filings showed that the CEO of this chain made over $3 million and two other executives received annual salaries of $1.4 million and $1.7 million respectively. The hospital had an operating profit of $91 million.

The patient received a bill totaling $268,227 from the two health care facilities. According to Brill, "Medicare made quick work of this bill paying just $43,320. The patient paid nothing." In similar cases throughout the country Brill states that Medicare has saved the taxpayer billions of dollars. He notes that "the convalescence home does not have to accept Medicare patients and their discounted rates. But it does accept them and encourages doctors to refer them."

Because of his research on how hospitals calculate charges Brill believes that 'Obama Care' won't work because

it won't lower costs. The players are all the same. Hospitals will continue to ratchet up prices as will private insurers, big drug companies, and device manufacturers .

Brill concludes "that the real issue isn't whether we have a single payer or multiple payers. It's whether whoever pays has a fair chance in a fair market. We don't have to scrap our system and aren't likely to. Put simply, the bills tell us that this is not about interfering in a free market. It's about facing the reality that our largest consumer product by far - one-fifth of our economy - does not operate in a free market." Brill implies that if private insurers could somehow acquire the bargaining power of Medicare we would have a truly free market in health care.

Brill has a number of suggestions for changing the system like taxing hospitals and outlawing the chargemaster. But because of the hospitals' enormous political clout both locally and nationally he realizes that most of his proposals are unrealistic at the present time.

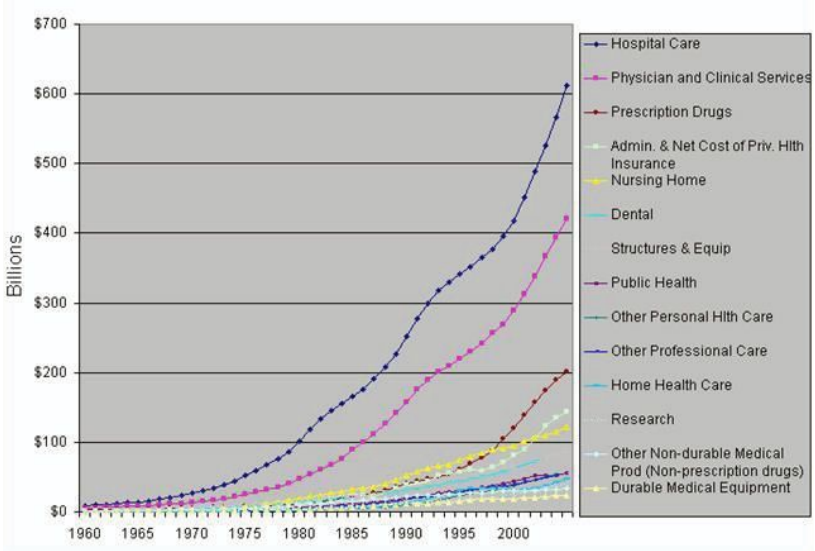
One of Brill's proposals that will resonate with doctors is reforming the tort liability system: "Finally, we should embarrass Democrats into stopping their fight against medical malpractice reform…Trial lawyers who make their bread and butter from civil suits have been the Democrat's biggest financial backers for decades. Republicans are right when they say tort reform is overdue." He also recognizes that Medicare underpays physicians. He proposes that Medicare patients who are financially able should be assessed an extra fee to increase physician reimbursement. For a lay person, Brill is uncommonly sensitive to the current plight of physicians.

In conclusion Brill states: "Over the past few decades, we've enriched the labs, drug companies, medical device makers, hospital administrators and purveyors of CT scans, MRIs, canes and wheelchairs. Meanwhile, we've squeezed the doctors who don't own their own clinics, don't work as drug or device consultants, or don't otherwise game a system that is so gameable. And of course, we've squeezed everyone outside the system who gets stuck with the bills." The one flaw in Brill's article, in my opinion, is that he leaves off this list insurance companies whose astronomical profits rival those of the hospitals.

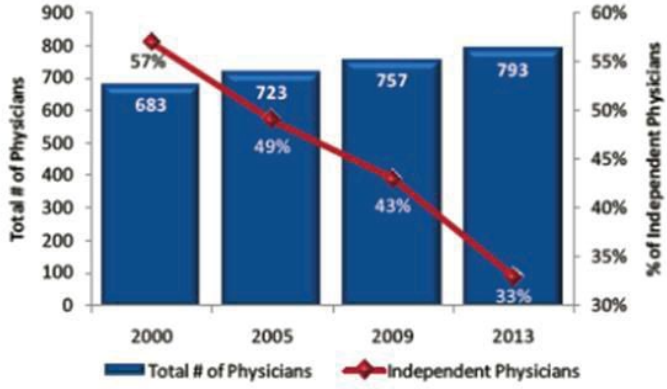
In my view, the most important takeaway message from this landmark article is the detailed account of the outrageous pricing practices of hospitals and the important role played by their secretive chargemaster. Because of the political power wielded by hospitals, this expose' of hospital charges will perhaps produce little or no substantive change. Its most enduring effect may be that the image of the hospital as a benign efficient community institution has been permanently tarnished. MM

1 Picture = 1,000 Words

Hospitals: Main Driver of Soaring Health Care Costs & Employed Physician Status



Total Physicians vs. Independent Physicians Projected Change, 2000 - 2012 (000s)



Source: Medical Group Management Association (MGMA), 2011


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The Doctor's Office as a Union Shop

by David J. Lefell, MD

As new health-care laws turn physicians into service workers, why wouldn't they organize?



David J. Leffell, MD, is a practicing physician and is former CEO of the Yale Medical Group and a professor at the Yale School of Medicine.
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As the country moves toward the effective start date of the Affordable Care Act in 2014, the operational and economic elements of this vast legislation are becoming clearer. Yet one likely outcome of the act that will directly affect the quality of patient care, and could affect its cost, has gone virtually unnoticed and unreported: the increasing trend for physicians to become employees, rather than self-employed. This development represents a potentially radical factor in the transformation of health care—the doctor as union worker.

Physicians have historically practiced either in small groups or alone. Unlike hospitals, which operate under the rubric of large regulatory agencies, physicians have been much more difficult to regulate and monitor. For cost control to be effective, the professional autonomy and independent clinical judgment of the physician and other providers must in some measure be sacrificed to standardization. This can't be accomplished by overseeing thousands of doctors in thousands of offices and medical complexes, each conducting its own symphony.

The Obama administration, by intent or accident, has effectively driven a major change in the status of physicians. By reducing the reimbursement for certain office-based specialists while enhancing related payment to hospitals, the administration is compelling more and more physicians—many of them with an any-port-in-a-storm fatalism—to seek employment with health systems or large physician groups.

Another factor lubricating the path to physician employment is generational: Doctors now in training appear willing to forsake income for a better quality of life and are less interested in the entrepreneurship required to run a private practice. They prefer regular hours and don't necessarily want to be responsible for patients after hours. The net effect is that in 2012 approximately half of physicians already were employed by large health-care entities. Some industry observers estimate that, over the next few years, health systems will employ close to 80% of all doctors.

The shift will be important for many reasons. The migration of physicians into large, regulated entities is essential if the practice of medicine is going to be transformed into the corporatist-government model that is the only way health-care costs can be controlled. The number of failed cost-control experiments in this country—remember the HMO experiment?—is dizzying. None has worked.

The change in the nature of physician employment will have effects never before experienced in America. As the effects of the Affordable Care Act come into focus, it becomes clear that when the majority of physicians

are no longer self-employed—and barring any legislation to the contrary—their new employed status will provide doctors with the right to collective bargaining.

Leaders of the organized-labor movement already view service workers with nonexportable jobs as the last best hope of labor unions whose membership is at an all-time low. The truth is that physicians are now becoming service workers. They are well-educated and expensive to train, and their decisions have substantial significance in the lives of others. But doctors essentially provide a service, one that cannot be outsourced to India or China.

If doctors unionize, that raises an immediate question about their right to strike—the key lever in collective bargaining. That's a question for another day. For now, it's enough to contemplate what will occur when the practice of medicine becomes detached from its past as a profession—when doctors may in time come to see themselves not solely as healers but as workers, units of labor, in a system that is committed to delivering care to the greatest number.

When doctors occupy a service niche like the chambermaid in Las Vegas or the school teacher in Chicago, the expectations and compensation of the physician-worker will be defined in ways that may make the benefits of collective bargaining appear very attractive.

Americans don't expect the quality of their care or access to it to decline as health-care costs drop. But quality of care and access will require significant attention in a reformed medical system. As has happened in other countries that have charted the course we are now on, a new reason for lack of access may at times be: "Office closed, doctors on strike." MM

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Physicians Seek a More Personalized Approach in Retainer-Based Practice

by Jim Braibish, APR

Benefits include stronger physician-patient relationship and greater emphasis on prevention.

The opportunity to provide more personalized care and help patients with prevention is drawing a small but growing number of physicians to retainer-based or "concierge" practice.

In this approach, patients pay a flat fee for unlimited office visits and 24/7 access to the physician by phone and/or email. Same-day appointments are available. Tests, specialist care, and hospitalization are additional.

David Katzman, MD, was the first in St. Louis to convert to retainer practice in 2003. In practice with Jennifer DeLaney, MD, they each see about 600 patients a year compared to what would be 5,000 in a conventional practice.

"I converted to personalized medicine because I could not treat my patients in the manner I desired," Dr. Katzman said. "In the traditional setting I found the visits were hurried due to the volume of patients I was seeing. It was difficult to establish a strong relationship with my patients, which to me is the real reward of being a doctor."

Like many but not all retainer practices, Dr. Katzman opted out of Medicare and insurance contracts, but patients can use insurance on an out-of-network basis.

A search of local and national websites and media reports shows more than 25 St. Louis-area physicians practicing under some form of retainer-based approach. Nationally, it is estimated that fewer than 1,000 physicians have a full concierge practices that do not take insurance, according to the *American Medical News,* while estimates range up to 3,500 or more when including those that also take insurance and/or Medicare.

Internist Richard Bligh, MD, also started his retainer practice in 2003. "I was in a large group practice seeing 40-50 patients a day. I couldn't put any emphasis on prevention and counseling," he said. "Now I enjoy medicine much more. We do a much more aggressive prevention profile, including advanced cardiac testing. We educate patients about diet and exercise."

Dr. Bligh also attends to his patients who are hospitalized, adding that he brings a greater knowledge of the patient's history than the hospitalist.

For family practitioner Glennon Fox, MD, it is about the physician-patient relationship. "This practice format encourages and deepens the physician-patient relationship. Hour-long appointments offer the time to determine more information about the patient and his or her needs. The small patient panel allows for same-day and next-day availability for acute needs."

Dr. Fox adds that he begins to consider patients as family. He has been practicing under the retainer model since 2004.

One of the newest converts to retainer medicine is Robert Saltman,



Jim Braibish, APR, Braibish Communications, is the Managing Editor for St. Louis Metropolitan Medicine magazine.
Contact: jbraibish@sbcglobal.net
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MD. After practicing internal medicine and endocrinology for 25 years, he and partner Daniel Gaitan, MD, changed the internal medicine portion to retainer in 2011. Endocrinology patients continue to receive specialty treatment but not primary care.

They accept Medicare and private insurance in-network. The retainer covers services including longer appointments, comprehensive preventive examinations, and 24-hour access to the doctor. He now has 440 retainer patients.

"The advantage for physicians is a completely different level of care for patients, the kind of care we were trained for and what attracted us to medicine," Dr. Saltman said. "There truly is time to direct the care for very complicated patients, to personally follow up on interventions, and to personally talk to patients when they call in for problems. It gives you a tremendous sense of satisfaction and returns the joy of practicing medicine."

What Types of Patients Are Attracted?

Physicians say retainer practices attract patients from all socio-economic backgrounds who want more time with their doctors and strive to live more healthy lives.

"My practice generally attracts those who care about their health and want a meaningful relationship with a doctor who cares about them," Dr. Katzman said. "They want easy access to me and the office. I think patients like this sort of practice because they know their doctor and staff, and know that they will receive timely attention when a need arises."

Dr. Fox added, "Our practice format works well for families with young children who need quick response to problems, for patients with medical issues requiring close observation and management, and for anyone who would like to have time to talk with a physician about multiple questions without needing to make multiple appointments."

Fears that some patients would abuse the unlimited access have proven unfounded. Dr. Saltman said, "Many assume that patients will constantly call for unnecessary issues. Nothing could be further from the truth. Patients are reassured they can reach us easily during office hours. I get very few calls after hours."

Dr. Bligh said, "People have been very respectful and do not use the access inappropriately. I actually have fewer calls than I did before."

They also dispute the notion that concierge practice is mainly for the wealthy. "We have patients from all socio-economic circumstances," Dr. Fox said. "Our patients who do not have health insurance find that they can get their primary-care services less expensively through this practice than through urgent-care centers or emergency rooms."

Regarding the cost of the retainer, many equate the patient's cost of enrolling with a retainer practice to the cost of a latte per day.

Evolution of Retainer Practices

As the number of retainer practices grows, variations have evolved. One is the "hybrid" practice which sees both retainer and traditional patients, and accepts Medicare and insurance.

Some physicians are working with several national companies to help convert their practices. Dr. Saltman utilized Signature MD of Santa Monica, Calif. In return for a percentage of each patient's retainer, Signature offers an array of services starting with comprehensive demographic analysis and patient survey and helping to manage the conversion process. Signature MD provides a conversion resource at the physician's office for 90 days to meet with patients and explain the benefits of the program, said Matt Jacobson of Signature MD. The company also conducts an outbound mail and telephone campaign. On an ongoing basis, Signature MD manages retainer billing operations, provides regulatory and legal guidance, maintains the physician's website, and promotes the practice through online advertising and corporate outreach.

Another vendor, MDVIP of Boca Raton, Fla., announced in November 2011 that it had 500 affiliated physicians. As of this writing, MDVIP's website shows eight St. Louis-area internal medicine physicians affiliated: William Guyol, MD; Edward Heidbrier, MD; Patrick Majors, MD; C. Scott Molden, MD; Anna Niesen, MD; Timothy Pratt, MD; Paul Stein, MD; and Kevin Weikart, MD. MDVIP is owned by Procter & Gamble, according to *American Medical News.*

Concierge Choice Physicians of Rockville Centre, N.Y., has 200 affiliated physicians. Other companies include Personal Medicine International, Inc. of San Francisco, Concierge Medicine Direct of Durham, N.C., and PartnerMD of Richmond, Va.

First Stop Health of Chicago (www.fshealth.com) offers a new variation combining concierge with telemedicine. For membership fees ranging from $240 per year for an individual with infrequent medical needs to $600 annually, First Stop offers 24-hour telephone consultation from a team of on-call 250 physicians, plus support from personal health-care advocates and access to a website featuring directories and ratings of local health-care providers and health information.

Ethical Concerns Raised

Concerns have been raised that, should retainer medicine become more prominent, it could limit access to already strained primary care. In a Sept. 3 *American*



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Medical News ethics forum, members of the Saint Louis University Bander Center for Medical Business Ethics wrote, "In addition to paying a retainer, most patients will want to maintain insurance to cover medications, specialist care, surgical procedures and expensive tests. This can put retainer-based medicine beyond the reach of many or at least require a significant change in spending priorities."

A November 2011 article in the *Annals of Internal Medicine* argues, "But even if it were granted that social justice required society to provide health care to all and social justice were recognized as a core professional virtue, it would not follow that primary caregivers should interpret the demands of social justice as requiring them individually to care for some minimum number of patients."

If the social justice argument were carried through, the article continues, primary care physicians could be condemned for working less than full-time, going into hospital medicine or changing careers entirely. The forces behind the decline of primary care are much larger than retainer medicine, the article says.

The AMA has adopted a code of ethics for concierge physician practices. Key points include:

- Be clear about financial terms and do not pressure patients.
- Do not promote the retainer practice as providing better diagnostic care and therapeutic services and provide the same standard of care for concierge and non-concierge patients.
- During the transition to concierge, make it easy for patients who do not opt for the retainer to transfer to other physicians.
- If you are still billing to insurers, clearly define what is and is not covered under the concierge fee, and comply with all relevant laws, rules and contractual requirements.
- All physicians have a professional obligation to care for those in need regardless of ability to pay.

The AMA also offers a resource guide for physicians considering concierge practice.

Retainer physicians believe they offer a viable alternative for patients.

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- American Academy of Private Physicians: www.aapp.org.

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Hundreds of New Doctors Have No Jobs

Where Shall We Put All of Our Students?

by Charles Van Way, III, MD

"Prediction is difficult, especially about the future."
-Neils Bohr, Physicist



Charles W. Van Way, III, MD, FACS, FCCP, FCCM, MSMA member since 1989 and Missouri Medicine Contributing Editor, is Professor of Surgery, the Sosland/Missouri Endowed Chair of Trauma Services, and the Director of the Shock Trauma Research Center.
Contact: cvanway@kc.rr.com
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The physician shortage is now upon us, although we have denied it for these past 30 years. Almost since the ink dried on the 1983 report by the Graduate Medical Education National Advisory Committee (GMENAC), which predicted a physician surplus, we have been training too few physicians.[1] Congress even capped the number of training positions in 1996, ensuring that, eventually, we will run out of residencies for our graduates. The AAMC, the Association of American Medical Colleges, held to the "too many physicians" party line since the 1980s. It has now reversed itself, calling for 30% more students in American schools. The AAMC speaks only for allopathic (MD) schools. As discussed below, the osteopathic (DO) schools have taken a different course over the last 20 years. Current predictions of the physician shortage by 2020-25 have reached as high as 200,000.[2] We are now making a major effort to expand health care to all segments of the population. Where will the doctors come from?

Other entities besides allopathic medical schools have done their best to make up for the shortfall. Osteopathic schools in particular have grown dramatically. Given the shortage, that's a really good thing. According to an AMA report from 2009, there were 4,400 students in the first year class, with 5,300 projected for 2012.[3] Allopathic schools are now ramping up their numbers of graduates. Slowly, but from a larger base. But there is a serious limiting factor in expanding schools. Calculating from the current total enrollment for osteopathic students (19,000) and allopathic students (78,000), there are about 48,000 students in their clinical years.[4] This represents a significant increase over the last decade. There are a limited number of teaching hospitals. Both medical and osteopathic schools are finding it difficult to find places to train their students.

Non-American Schools

Another collective entity, which has grown remarkably, is non-American schools, specifically the proprietary English language schools in the Caribbean. There are currently 39 of these.[3] According to verbal testimony at the AMA Annual Meeting last June, the largest, Ross and St. George's, accept 900 and 750 students respectively each year. The overall effect of these schools can be seen in the steadily increasing number of United States citizens who are applying for the certification through the Educational Commission for Foreign Medical Graduates (ECFMG). As of 2011, the country with the greatest number of its citizens applying for ECFMG certification was the United States.[5] That number has increased linearly for the last 20 years. The instructional model of the Caribbean schools is two years in the islands followed by two years in American teaching hospitals. The schools must secure commitments from American

hospitals to train their students. They can afford to pay considerable sums for such privileges. Tuition at these schools runs to about $1,000 per week - $50K to $60K per year. In 2007, an agreement between the American University of the Caribbean and two New York hospitals went badly, and made its way to Federal court.[6] It provides a window into the economics of the transactions. The deal called for a compensation of around $340 per student per week. Testimony established that such places would cost the University $700 per student per week outside the contract in question. In 2008, New York's Health and Hospitals Corporation signed a 10-year contract with St. George's University School of Medicine to provide places for that school's medical students in their 11 public hospitals.[5] The contract was for $100 million, which works out to $400-425 per student per week, on a very long-term contract.

There are nine medical schools, allopathic and osteopathic, in the New York area. They are, understandably, concerned about finding places for their medical students. And their students are concerned. At the AMA Annual Meeting last June, the AMA Medical Student Section brought up Resolution 302, "Securing Quality Education Sites for US-Accredited Schools."[8] Testimony on the resolution made it quite clear that this problem is not limited to New York, but was also found in New England, New Jersey, California, Texas, and Illinois (Chicago). Students testified that they were required to travel considerable distances to their clerkships, being crowded out of the hospitals in which they had expected to do their clinical training.

But can't someone do something, you say? The LCME (Liason Committee for Medical Education), which accredits allopathic schools, does indeed have regulations limiting competition between a school's students and outside students. The rules don't apply, and cannot be enforced, if the hospital simply withdraws from its medical school affiliation. Given enough money, that's exactly what some hospitals are doing.

Residency Slots

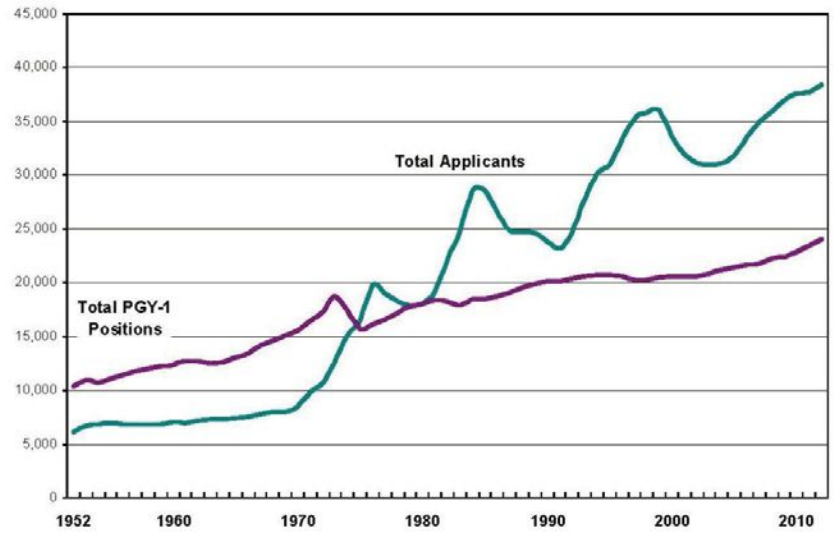
Residencies are another problem. After they graduate, where are all of these new doctors going to go? Your average Caribbean graduate, having paid upwards of a quarter of a million dollars for his or her MD, is unlikely to settle for a job as a paramedic. Neither, for that matter, are many American graduates. And yet, we have run out of places in residencies. Now, we are long past having enough slots to train everyone who wants a residency position. Figure 1 shows the total number of individual applicants versus the total number of places in residencies.[9] Applicants began to outnumber positions in the 1970s. This was, of course, mostly because of the numbers of international graduates applying. But today, even American graduates are unable to find positions.

The graph in Figure 1 shows a very odd thing. Residency positions increased until about 1990, and then remained stable for 10-15 years. When Congress instituted the cap in 1996, it actually legislated something that had already happened. After about 2003, the number of residency positions began slowly to rise. The number of PGY1 positions offered in the 2012 match was 26,700, which is a new high, and considerably higher than in the 1990s. However, if we add 16,500 MDs, 2,400 DOs, and 4,300 Caribbean graduates, there are about 23,000 new graduates in the match who are U.S. citizens. We are now graduating enough U.S. citizens, between U.S. schools and other schools, to fill almost all of our places in residency. But we don't want to forget international graduates who are not U.S. citizens. Many still apply to come to the U.S., and we accept significant numbers of them into residency. We do so because many of them are highly qualified, frequently with years of training after medical school, often with specialized expertise. Many international graduates compete successfully for residency places.

The net result is that not every U.S. graduate gets a place. Here are the figures for the 2012 NRMP match. For allopathic graduates, 16,500 applied, and 800 went unmatched. For osteopathic graduates, 2,400 applied, and 700 were unmatched. The picture for graduates of non-U.S. schools was more dismal. For U.S. citizens who graduated from international schools, there were 4,300 applications, and only 2,100 matched. After a very expensive education, half of them are unable to find residency slots. For non-U.S. citizens from international schools, the picture is worse. There were 6,800 applicants, and 2,800 matched. But at least they have a home to return to. One highly revealing figure is this. There were 1,300 previous graduates of U.S. allopathic schools who applied. These are, for the most part, American MDs who have been unable to get categorical residency positions, or are trying to change residencies. Only 560 of them matched, less than half. These figures are somewhat too pessimistic, because there are a fair number of positions filled outside the match. But it's still a grim picture.[10] The results of the 2013 match aren't final, but it appears that 528 graduates failed to find jobs, either in the main match or the post-match. That's 3% of the graduating class, not very different from 2012.

The Federal government doesn't recognize the problem. Health care reform pretty much ignores medical education and residency training. Daniel Henninger, in an article in the *Wall Street Journal*, referred to doctors as the "lost tribe" of healthcare reform.[11] All parties in Washington want to cut residency training funds. Both the President's budget and the Simpson-Bowles Commission proposed to severely cut Medicare funding for residency programs. Expansion of residency slots wasn't even mentioned. Only the fact that Congress refuses to pass any budget at all has saved residencies. It seems an article of faith inside the Beltway that physicians will magically appear where they are needed. Faith is a Good Thing. But faith alone will not train enough physicians for the newly-reformed healthcare system. A shortage of 200,000 physicians is projected by the 2020s.[12] But if we won't expand residencies, it won't matter how many we put through medical school.

Figure 1
Total Applicants, Total PGY1 Positions
From National Resident Matching Program, http://www.nrmp.org/data/index.html[10]



Conclusion

Should we conclude that our medical education system is a mess? Perhaps "mess" is too strong a term. Let us just use that all-purpose term, and say it is in "crisis." We have too few students coming out of our schools to provide the next generations of physicians. We have allowed a large proprietary and unaccredited medical education industry to grow up offshore, and we are now hard put to find places to teach our own students, much less places in which to expand our own schools. And we refuse to talk about whether graduates of Caribbean schools are trained to U.S. standards, other than to require the ECFMG examination from them. We have failed to expand residencies, and we now have the unbelievable situation in which U.S. graduates of U.S. schools are unable to find residency training. And – oh, yes – we've jacked up the cost of medical education so far that 85% of our graduates are in debt. The average debt is between $150K and $180K, depending on whether the student is in a state school or a private school. This burdens our new doctors with crippling debt, and influences strongly their choice of specialty training. That is, when they can find residency training.

We should be ashamed of ourselves. At the AMA, one speaker on Resolution 302, Dr. Kenneth Mattox of Texas, called for a new "Flexner report" to help us to reform medical education. He's right.

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KCUMB
KANSAS CITY UNIVERSITY OF MEDICINE AND BIOSCIENCES

From Simulators to Tablet Technology: KCUMB Leaps into the Future

by Marc B. Hahn, DO

KCUMB is also stepping into an elite group of medical schools that plan to fully integrate tablet technology into their curriculums.

This is an especially exciting time to be part of Kansas City University of Medicine and Biosciences.

KCUMB has always worked to provide its students with state-of-the-art facilities and resources to appropriately complement their educational experiences. From the sophisticated human patient simulators in the Kesselheim Center for Clinical Competence and the spacious study areas inside the new D'Angelo Library, to the nearly two-dozen flat-screen monitors in the Anatomy Laboratory and the recently renovated Wheeler Osteopathic Clinical Skills Laboratory, KCUMB's well-equipped campus is designed around the needs of our students.

In addition to significant facility upgrades and recent building additions, KCUMB continues to make investments to enhance the campus. Many of these new initiatives will be unveiled later this summer as the University releases its ten-year Campus Master Plan.

KCUMB is also stepping into an elite group of medical schools that plan to fully integrate tablet technology into their curriculums. The University is currently in the process of distributing Apple iPads and iPad minis to faculty and students, something that will not only enhance the learning process and increase the institution's sustainability efforts, but also provide students with a technological edge.



Marc B. Hahn, DO, MSMA member since 2012, is Executive Vice President for Academic and Medical Affairs, Provost and Dean of the College of Osteopathic Medicine.
Contact: MHahn@kcumb.edu

At the same time that the University is making significant investments in its future, KCUMB's Board of Trustees and administration recently announced a one percent reduction in tuition for the upcoming academic year, demonstrating we are cognizant of the challenges created by student debt. During a time when most U.S. graduate and medical schools are raising tuition by three to four percent or more, KCUMB's Board of Trustees and administrators believe this step is necessary in order for the University to be a leader in student-centered medical and health sciences education.

Our concern over medical student debt allows our graduates to continue to choose training in all specialties, especially primary care. The realities of the ever-changing health care landscape can, at times, make the choice to pursue primary care a difficult one; therefore, we want our academic programs to be a meaningful benefit to our graduates.

The University is also striving to add millions of dollars in new funding of scholarship endowments. By increasing our scholarship endowments, the University has been able to offer additional merit-based and diversity scholarships to more than double the students who received scholarship aid.

A History of Student Commitment & Community Support

Founded in 1916, KCUMB has been a fixture in the Kansas City community for nearly a century. Approximately 1,000 students attend the University's two colleges – the College of Osteopathic Medicine and the College of Biosciences – on our beautiful 21-acre campus near downtown Kansas City, Mo.

KCUMB's College of Osteopathic Medicine is one of the oldest osteopathic medical schools in the United States and the largest medical school in Missouri. In fact, KCUMB yields the second-largest number of physicians for the state. Specifically, KCUMB-COM graduates account for 40 percent of the practicing osteopathic physicians in the state. In addition to our doctor of osteopathic medicine degree, KCUMB-COM students may choose a concurrent



Incoming first-year osteopathic medical students take the Oath of Commitment in August 2012 during KCUMB's annual White Coating Ceremony in Weaver Auditorium. In 1997, KCUMB became the first medical school in the Kansas City area to host a white coating ceremony for its incoming students, and students often choose to include family and friends who are physicians in the event by asking them to help them don their white coat.

KCUMB at a Glance

2012-2013 Enrollment:

- Total medical school enrollment: 1,012
- 57.5 percent male; 42.5 percent female

Degree Offerings:

- Doctor of Osteopathic Medicine
- Master of Arts in Bioethics
- Master of Science in Biomedical Sciences
- Doctor of Osteopathic Medicine / Master of Arts in Bioethics
- Doctor of Osteopathic Medicine / MBA in Healthcare Leadership (in conjunction with Rockhurst University's Helzberg School of Management)

dual-degree path, earning a master of arts in bioethics or a master of business administration in health care leadership (awarded by Rockhurst University's Helzberg School of Management, through a unique partnership between the two universities).

The College of Biosciences offers a stand-alone master of arts in bioethics and a master of science in biomedical sciences, with both programs designed to fulfill the Kansas City area's growing need for well-trained professionals in their respective fields.

At KCUMB, students are our focus. Not only do we strive to create an environment conducive to learning, but we also welcome student participation in the decision-making process and encourage open communication amongst all constituencies. We are dedicated to fulfilling our mission, which centers on improving the well-being of the community we serve.

As evidence of this commitment, KCUMB-COM graduates help fill critical primary care positions at a higher rate than graduates of most other medical schools. As communities across the country face severe physician workforce shortages, especially in primary care fields – family medicine, internal medicine and pediatrics – KCUMB-COM graduates are meeting that need. Of the 949 KCUMB-COM graduates currently practicing in Missouri, 72% are working in primary care and 41% practice in rural areas of the state.

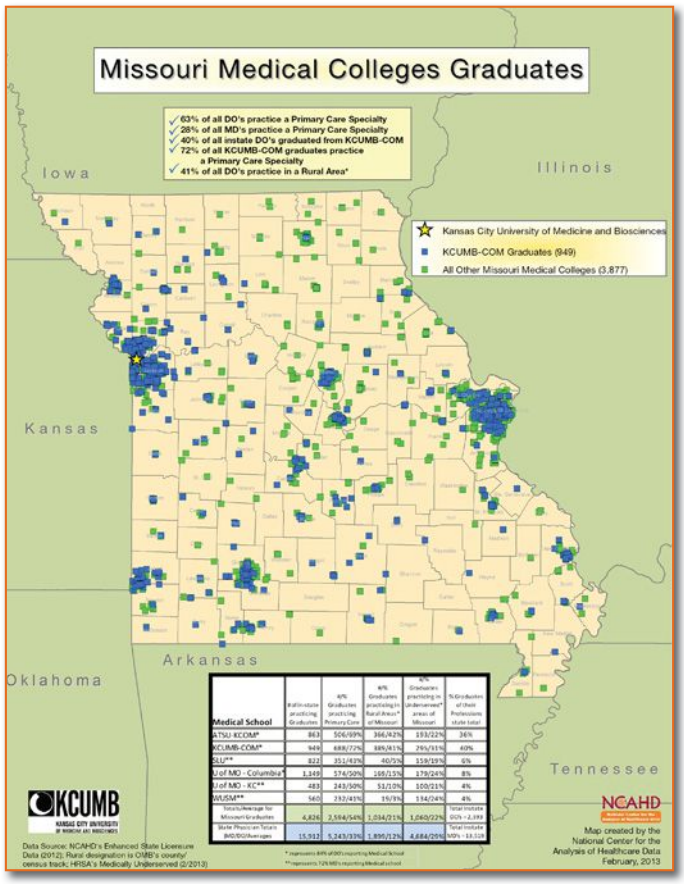
Of course, KCUMB is equally as proud of its history in graduating military physicians. Nearly 10% of the Class of 2013 was commissioned into the U.S. military upon graduation. In fact, a KCUMB-COM graduate, Harry Walter, DO (COM '65), actually became the first osteopathic physician in the military when he was commissioned into the U.S. Air Force in July 1966, opening the door for thousands of osteopathic physicians to serve their country in the decades since.

The University attracts high-caliber students each year. In addition to academic excellence, the makeup of each class reflects a diversity of accomplishments, talents, interests and backgrounds. Our students also demonstrate a commitment to the principles and practice of the osteopathic medical philosophy, which values a holistic approach and places emphasis on preventive medicine.

While KCUMB recognizes the quality of existing students, it is always striving to find ways to attract the best and the brightest. We are also committed to increasing diversity at our institution – students, faculty and staff. KCUMB recognizes that a diverse scholarly community helps prepare graduates for the cultural and ethnic diversity that exists in the communities they will serve.

KCUMB has a proud heritage of serving its community, something that we hope to continue in the years to come. Since 1996, the University's second-year osteopathic medical students, under the supervision of faculty and alumni, have provided tens of thousands of free health screenings to children in need through the University's "Score 1 for Health" program. The program provides care for children who otherwise might not have access, while our also students gain valuable early clinical experiences.

Over the next few years, KCUMB will also work toward expanding the quantity and quality of its research contributions. In addition to expanding the amount of research we conduct related directly to osteopathic medicine, we will seek collaborative opportunities within the Kansas City community, exemplified by partnerships the Kansas City Area Life Sciences Institute; Frontiers: The Heartland Institute for Clinical and Translational Research, a network of scientists from across the Kansas City region and the state of Kansas working on translational research; and Children's Mercy Hospital.



Of Clinical Importance

Beginning with students' first days on campus, KCUMB-COM puts the patient at the center of the learning process. The University's innovative curriculum integrates clinical relevance with a solid foundation in the basic sciences.

We emphasize the importance of the physician-patient relationship. Students take part in early hands-on clinical experiences that prepare them to become more effective physicians. The University also offers clinical enhancements, such as patient simulation and standardized patient encounters, which teach vital clinical communication skills.

During the third and fourth years of study, our students receive advanced clinical training in a wide variety of medical settings, both in the Kansas City area and throughout the United States. Students work under the guidance of clinical faculty, transforming their classroom knowledge into real-world clinical experience.

KCUMB is dedicated to embracing new ideas that will provide the best educational opportunities possible for our students. The 2012-2016 Strategic Plan lays forth the framework for our efforts, and KCUMB is committed to enhancing student success, strengthening research initiatives, exploring new ways to connect with our community, promoting sustainability and creating a more diverse campus community. As KCUMB prepares to celebrate our 100th anniversary in 2016, we look back with pride on the University's many accomplishments. At the same time, we look forward to a bright future for the next generation of osteopathic physicians, researchers and bioethicists who will positively impact the health and well-being of Missouri, and the nation. MM

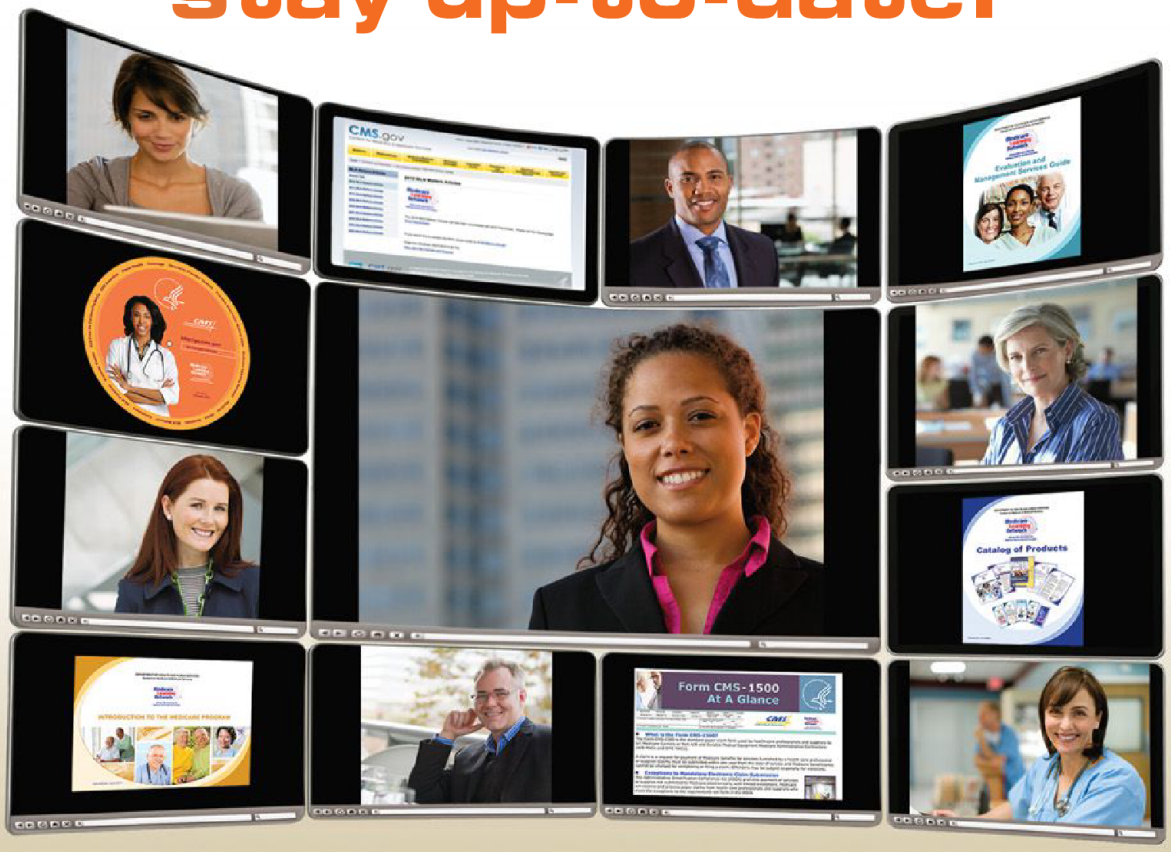


Norbert Seidler, PhD, professor and chair of biochemistry, works with students inside his laboratory at the Dybedal Center for Research on the KCUMB campus. Dr. Seidler's research interests include Alzheimers Disease, anesthetic preconditioning, post-operative cognitive disfunction and chemical chaperones. In addition, he recently wrote a book, "GAPDH: Biological Properties and Diversity," which reveals new findings on the multiple functions of a particular enzyme, glyceraldehyde 3-phosphate dehydrogenase (GAPDH). His article on this subject is featured on page 236 of this issue of *Missouri Medicine*.

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A Physician's Duty to Warn Others

by Greg Minana, JD & Justin Stephens, JD

Could a physician face civil liability for failing to warn of the dangers posed by a patient who later commits violence?



Greg Minana, JD, (left) is a partner, and Justin Stephens, JD, is an associate in the St. Louis offices of Husch Blackwell LLP. The firm serves as outside general counsel to the MSMA.
Contact: Greg.Minana@huschblackwell.com

Over the past several months, our nation has endured several acts of violence that resulted in tragedy. Several of these horrific acts – including the Sandy Hook Elementary School shootings, the Aurora, Colorado, movie theatre shootings, and the attempted assassination of U.S. Representative Gabrielle Giffords – were carried out by individuals who had shown signs of behavioral disturbance in the days and weeks leading up to the incident.

Prior to the Aurora, Colorado, movie theatre shootings, James Holmes had been seeing a psychiatrist and (according to at least one report) the psychiatrist had warned University of Colorado officials about Holmes, although no action was taken because he later withdrew from the school's graduate program. Similarly, just a few months before he attempted to assassinate Representative Giffords, Jared Lee Loughner was expelled from the college he attended due to his erratic behavior during class, which had prompted one classmate to presciently express concern that Loughner might commit a mass shooting during class.

For many physicians, particularly psychiatrists, these horrific incidents have raised questions concerning the balance between doctor-patient confidentiality and the need to disclose confidential patient information when a patient signals that he/she might present a risk of violence toward himself or others. In addition to clinical concerns, these issues raise several legal questions. Could a physician face civil liability for failing to warn of the dangers posed by a patient who later commits violence? If there is a legal duty to disclose confidential patient information, when does that duty arise and how is it discharged? Does the duty to warn trump doctor-patient confidentiality in all cases? This article will discuss those issues.

The leading case nationally on these issues is *Tarasoff v. Regents of University of California*, 551 P.2d 334 (Cal 1976), a landmark California case which sparked litigation in nearly every state. Unfortunately, the law that has emerged from that litigation is laden with inconsistencies concerning when a duty to warn will arise. Since *Tarasoff*, some states have enacted legislation to address these inconsistencies, but Missouri has not. Moreover, Missouri's judiciary has addressed these issues on just a few occasions. Accordingly, Missouri case law does not provide clear answers to the above questions.

Nevertheless, the few cases in which the Missouri judiciary has addressed the physician's duty to warn do provide some guidance to practitioners who face the unenviable task of assessing patient dangerousness and the need to warn others of such dangerousness, balanced against confidentiality and HIPAA privacy protections.

In *Bradley v. Ray*, 904 S.W.2d 302 (Mo. App. 1995), the plaintiff brought an action on behalf of Kelly,

a child, against the psychiatrists who counseled Kelly's step-father for his prolonged and ongoing sexual abuse of Kelly. According to the plaintiff's petition, the step-father had been sexually abusing Kelly since 1980, when Kelly was four-years old. When Kelly's mother learned of the abuse in 1988, she arranged for the psychiatrists to provide counseling to the step-father. Shortly after the psychiatrists began counseling the step-father, the psychiatrists terminated the counseling. The plaintiff's petition alleged that the psychiatrists were aware that the step-father was abusing Kelly, but failed to report it to any law enforcement authorities during the counseling or upon termination of their services. According to the plaintiff, Kelly continued to be abused as a result of the defendant's failure to report the abuse.

As a matter of first impression, the *Bradley* court held that the psychiatrists owed a duty to Kelly to warn appropriate authorities that the step-father, their client, presented a serious danger of future violence to Kelly, who was an identified victim. In so holding, the court stated:

"When a psychologist or other health care professional knows or pursuant to the standards of his profession should have known that a patient *presents a serious danger of future violence* to a *readily identifiable victim* the psychologist has a duty under Missouri common law to warn the intended victim or communicate the existence of such danger to those likely to warn the victim including notifying appropriate enforcement authorities."

The *Bradley* holding has limited application – for a duty to warn to arise, the health care professional must know or should know that a patient: 1) presents a serious risk of future violence; and 2) that is targeted at a readily identifiable victim. In *Bradley*, this standard was met because the defendant healthcare professionals were specifically retained to counsel the step-father regarding his ongoing violence (in the form of sexual abuse) toward a readily identifiable victim (his step-daughter).

While the *Bradley* court enunciated the general circumstances under which a duty to warn will arise, it left several questions unanswered. For instance, it offered little guidance on how the duty to warn can be satisfied. Moreover, *Bradley* does not identify the specific information that should be included in a warning from a physician. In this regard, the court stated only that the physician "must warn the intended victim or communicate the existence of the danger to those likely to warn the victim, including notifying appropriate enforcement authorities." Thus, the *Bradley* holding suggests that the physician should warn those in a position to thwart the potential violence and should include the information that will allow them to do so. In the context of child abuse, this may mean notifying the police and social services of the potential victim and of the nature of the abuse threatened, so that the authorities may be in a position to intervene to prevent the anticipated violence.

What Should You Do?

- If a physician does suspect that a duty to warn has arisen, he/she should consider the nature, format, and scope of the warning.
- For purposes of establishing that a warning was given, a physician should consider issuing the warning in writing or otherwise documenting the warning.
- If a threat is imminent, a physician may not have time to issue the warning in writing. In such cases, the physician, when time allows, should still document in writing that the warning was given.
- Physicians should also consider documenting the reasoning and logic in deciding to issue the warning.
- When in doubt about the specific type of danger posed by the patient, a physician should not speculate or offer gratuitous suggestions regarding how best to thwart the danger.
- A physician should not make dichotomous or percentage-probability predictions regarding whether a patient will or will not act violently.

In reaching its decision, the *Bradley* court relied upon *Sherrill v. Wilson*, 653 S.W.2d 661 (Mo. 1983). In Sherrill, the plaintiff sued various physicians because a mental patient, after being released on a two-day pass from his court-ordered confinement, killed the plaintiff's son. Unlike the plaintiff in *Bradley*, the plaintiff in Sherrill did not proceed on a failure to warn theory. Instead, the plaintiff argued that the defendant physicians were negligent for releasing the patient when they knew of his dangerous proclivities and for failing to recapture the patient when he did not return from his two-day pass. The Missouri Supreme Court held that the physicians did not owe a duty to protect the general public. Because the plaintiff's son was a member of the general public – and not a readily identifiable victim like Kelly in the *Bradley* case – the Court upheld the trial court's dismissal of the plaintiff's petition.

Another Missouri case, *Virgin v. Hopewell Center*, 66 S.W.3d 21 (Mo. App. 2001), illustrates the limitations of the "readily identifiable victim" rule announced in *Bradley*. In *Virgin*, the plaintiff was injured in a head-on

automobile collision with a patient who had been diagnosed with bipolar disease, manic, with psychotic features and paranoia, and who had previously told her psychiatrist that she had a "death wish" when she drove. The plaintiff filed a lawsuit against 14 of the driver's health care providers, alleging that they were negligent for failing to warn the innocent driver, her family, her close associates, the police, and the Department of Revenue that the patient should not drive a motor vehicle.

The appellate court affirmed the dismissal of the action. In reaching this conclusion, the court took great care to distinguish the facts in *Virgin* from the facts in *Bradley*, which involved a specific person who had been identified as a target of the patient's abuse. Relying on *Sherrill* and the limitations of the duty to warn recognized in *Bradley*, the Court determined that "Appellant's request that 'this Court recognize a potential duty to warn a class of foreseeable potential victims (i.e., motorists, like Appellant) . . . runs contrary to Missouri law."

The *Virgin* court also stressed the importance of the confidential nature of the doctor-patient relationship:

"[A] finding of no duty furthers the public interest in maintaining the physician-patient privilege. The policy behind this privilege is to protect the patient by allowing him to make full disclosure without fear that the information will be used against him. The purpose of the privilege is to enable the patient to secure complete and appropriate medical treatment by encouraging candid communication between the patient and the physician, free of fear of the possible embarrassment and invasion of privacy engendered by an unauthorized disclosure of information. Establishing a duty in the instant case would erode, to say the least, the physician-patient privilege, as well as subvert the purpose and policy behind it."

Taken together, *Bradley* and *Virgin* establish that foreseeability of harm alone is not sufficient to create a duty to warn. Rather, for a duty to arise, the patient must present a foreseeable danger to a *readily identifiable victim*.

Thus, a physician should seriously evaluate any danger or threat that a patient poses to a specific individual. The most obvious sign that a patient poses such a danger is where the patient expressly threatens harm to a named individual. Under certain circumstances, a duty to warn will arise even where the patient fails to convey to the physician an intent to harm a specific individual. For instance, where a physician becomes aware that an unstable patient with a history of violence toward a specific individual has purchased a gun and begun stalking that



individual, a duty to warn may arise. Moreover, where the physician, like the physicians in the *Bradley* case, becomes aware of a history of violence that is *ongoing*, a duty to warn may arise. Unfortunately, because Missouri law on these issues is unclear, it is difficult to formulate definite rules or guidelines that apply broadly to a clinical practice. Rather, whether to disclose patient information to protect a third party is a situational evaluation that considers the individual patient, potential victim, and the danger posed.

If a physician does suspect that a duty to warn has arisen, he/she should consider the nature, format, and scope of the warning. For instance, for purposes of establishing that a warning was given, a physician should consider issuing the warning in writing or otherwise documenting the warning. If a threat is imminent, a physician may not have time to issue the warning in writing. In such cases, the physician, when time allows, should still document in writing that the warning was given. In addition to documenting the warning itself, physicians should also consider documenting the reasoning and logic in deciding to issue the warning. Moreover, when in doubt about the specific type of danger posed by the patient, a physician should not speculate or offer gratuitous suggestions regarding how best to thwart the danger. Finally, a physician should not make dichotomous or percentage-probability predictions regarding whether a patient will or will not act violently.

Notably, the HIPAA Privacy Rule does not prevent a health care provider from disclosing necessary information about a patient to law enforcement or other persons, when the provider believes the patient presents a serious and imminent danger to himself or others. As such, if a duty to warn under *Bradley* has arisen, a physician should be able to exercise that duty without violating the HIPAA Privacy Rule. The provisions allowing for disclosure of protected information may be found in the Privacy Rule at 45 CFR § 164.512(j).

Disclosure

The information contained in this article should not be construed as legal advice or legal opinion on any specific facts or circumstances. The contents are intended for general informational purposes only, and readers are encouraged to consult their own attorney regarding specific legal questions. MM

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Glacial Pace of Approval is Killing Us!

Part IV
by John C. Hagan, III, MD

Bureau Blind Sides the American Public

The FDA: Incompetent? Stupid? Doesn't Give a Damn? Or All the Above?

I use ophthalmology as an example but all fields of United States medicine and surgery are falling decades behind the rest of the developed world. This tragedy is because of the unconscious able delays, unaffordable cost and an inept and arcane bureaucracy at the Food & Drug Administration (FDA).

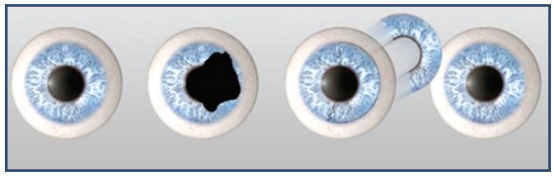
As the article by Stephen G. Slade, MD, (March/April 2013 *Missouri Medicine*) laments U.S. ophthalmologists are unable to use lasers, intraocular lens, medical devices, medications that have been used successfully, some for decades, by European ophthalmologists. Often these are made by U.S.-based companies that realize the U.S. is one of the least desirable markets for innovative drugs and devices.

How do you deal with a Federal agency that would prefer citizens to die, go blind, live in disability and pain, rather than crank up their glacial processes? It seems of little interest to Congress and the President. The power and predation of U.S. trial lawyers and the patronage of the politicians their hundreds of millions of dollars of election contributions buy only compounds the problem.

This is a partial list[1] of the devices not available to U.S. ophthalmology: Wavelight Allegretto Wave Eye-Q Laser, iDesign Wavefront Imaging Device for the Star S4, Amaris Laser System, ReLEx smile procedure with the VisuMax, corneal collagen cross-lining for treatment of keratoconus (huge problem), advanced intra-ocular lens: Mplus, FineVision MicroF, Visian ICL Toric, Artisan iris-clip IOL, light adjustable lens, artificial iris, Kamira, and Raindrop Near Vision corneal inlays.

The FDA: their way or the highway. Thousands of Americans blinded by their might!

Artificial iris prosthetics are not routinely available in USA to repair iris trauma as shown in second figure.



Collagen crosslinking with riboflavin has been shown to reduce and arrest the progression of keratoconus and thereby prevent a corneal transplant. Routinely used for over a decade outside USA.



Reference

1. Koury CB. US Ophthalmologists' Wish List. Cataract & Refractive Surgery Today 2013;13(2): 61-66



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Should **Ophthalmologists** Test Hearing & Sell Hearing Aids?



Our series in the January/February issue of Missouri Medicine by Steven M. Silverstein, MD, Martin E. Anderson, MD, Anthony A. Mikulec, MD and Charles M. Lederer, MD drew the attention of members who wrote in for comment. The comments continue in this issue, as well as Dr. Silverstein's response.

Any patient who can make it to my office could also make it to one of the two ENT offices that are in our complex. For any service that we currently provide, we can pretty well look the patient in the eye and tell them we can provide that service at a level competitive with anyone in the community. That is generally a good standard in deciding to offer any given service. There is no way honestly that I could in good faith look a patient in the eye and make that statement with respect to hearing services when there are two audiologists in our complex and many more in our area. It isn't like we live in a geographically remote area that is underserved medically and patients have limited access.

Just because you can provide a service and it is not blatantly illegal, doesn't necessarily mean you should do so or it is ethical.

William L. White, MD, Ophthalmology
Kansas City, Missouri
MSMA Member Since 1995

A Fair Hearing: Listen Up - It's the New Paradigm

When asked to write the 'PRO" column favoring integrating hearing services into an ophthalmology practice, I knew that it would receive pushback; most shifts in major medical paradigms do. This occurred when ophthalmologists integrated optical retail services into their practices; when optometrists were welcomed into ophthalmic practices, and when ophthalmologists were amongst the first to market and advertise their services. There was tremendous argument on both sides of these issues which now are commonplace and in standard practice around the country. Much of the resistance comes from lack of understanding and fear that these changes will adversely affect quality of patient care, the profitability of the other physicians or both. An in-depth conversation with a highly respected, now retired, ENT physician in Kansas City revealed that he was one of the first to incorporate hearing/audiology services in his ENT practice. For this he received considerable criticism. Now these practices are routinely provided by most ethical ENT practices.

Nationally, there are currently 140 ophthalmic practices that have integrated hearing services, with two to three new practices each month adding to this total. The state licensing of the hearing specialists/audiologists employed and the quality of the equipment used to perform hearing tests are exactly the same as those in ENT offices, or audiologists who own their own practices, or are employed by large retail chains. Under Obama's Affordable Care Act, primary care is now required to at a minimum review vision and hearing.

And ophthalmologists are not alone. There are many primary care physicians around the country that have set up a hearing testing facility within their practices. In these instances neither the primary care physician nor ophthalmologist are acting as a pseudo-ENT. Most do not get involved in the evaluation or diagnosis at all. Our patients are initially informed that we are not 'ear doctors' and we will refer them to trusted ENT colleagues if the results of their testing warrants. Before building a hearing center, we rarely referred patients to an ENT physician. Last year, we referred 40 patients, and 10 patients in the first quarter of 2013. Most tested patients require no further evaluation, nor do they need hearing aids. Most of the patients we test would not self-refer to an ENT, audiologist nor be referred by their primary care physicians. Our center represents an entry point for a largely neglected or over-looked cohort of patients.

The result of our testing might disclose:

1. Tested No Hearing Loss. Upon completion it is noted that that patient has hearing levels acceptable for their age and there is no further action.

2. ENT Referral: The licensed hearing professional is trained and certified under state guidelines to determine the need for an ENT referral. When a patient answers key questions consistent with a need for a medical referral, they are immediately referred.

3. Treatable Loss: When a patient would benefit from the latest advancements in hearing instrumentation the licensed hearing professional provides those options.

At no time is the Ophthalmologist looking in ears or treating any form of hearing loss. Patients who do not address concurrent diminished vision and hearing health can suffer from withdrawal, depression and in some instances, a higher mortality rate. As physicians, we often recognize conditions outside our area of expertise and make timely and appropriate referrals. Ophthalmologists are in an ideal position to find other health problems, such has hearing disorders, because older adults visit eye care practices three times more per year than any other healthcare provider. It is this opportunity to find otherwise undetected hearing loss or ENT pathology that was the premise for adding hearing services to our ophthalmic practice.

Is there a revenue opportunity that supports the added clinical care and no cost screening/diagnostic work up? Yes, there is. It is modest by any standard. It was the suggestion and request of a number of our patients that led to the integration of hearing services into our practice. As I learned more of the overlap of conditions (macular degeneration, glaucoma, and diabetes) that we as ophthalmologists treat which includes a high proportion of patients with hearing deficits, this integration made even more sense. I would welcome ENT colleagues performing on their patients simple eye screening such as visual acuity or tonopen intraocular pressures to identify potential undiagnosed ophthalmic pathology.

We must not be afraid of ethically incorporating ancillary services into our respective practices which will benefit our patients; nor should we be embarrassed about modestly profiting from them.

Steven M. Silverstein MD, FACS
Silverstein Eye Centers, Kansas City, Missouri
MSMA Member since 1992

Urologists Believe PSA Test Remains a Valued Tool to Detect Prostate Cancer Early

The American Association of Clinical Urologists (AACU), an organization representing specialists who manage prostate cancer and urologic health, issued the following policy statement today concerning early detection of prostate cancer.

The American Association of Clinical Urologists (AACU) is concerned that recently published guidelines on screening for prostate cancer could unintentionally leave physicians and the general public with the impression that early detection of prostate cancer is no longer needed. The AACU wishes to express its position on the importance of early detection of prostate cancer and the role of PSA screening.

Prostate cancer is the second leading cause of cancer death in American men. Thus, early detection of prostate cancer is vitally important. Although PSA testing has some limitations as a screening method, it remains a useful tool to help identify prostate cancer in its early stages. Since the introduction of PSA testing and heightened prostate cancer awareness over the past 20 years, there have been significantly fewer advanced prostate cancers at diagnosis and a reduction in deaths attributed to prostate cancer."

The revised prostate cancer screening guidelines released by the American Urological Association on May 3, 2013, emphasize the importance of continued PSA testing for men between the ages of 55 and 69 and all men at increased risk including African-Americans and those with a family history. For asymptomatic men below age 55 or above age 69 with average risk factors, individualized decisions about the benefits and potential harms of PSA testing need to be discussed between the patient and his physician.

We have made great progress in national prostate cancer awareness initiatives and in reaching out to men at high risk. The treatment of prostate cancer has improved for all stages, and death from prostate cancer is declining. For many men, early detection is clearly needed, and PSA-based screening is currently the best test available. Physicians and their patients are encouraged to have the discussion to determine whether the test is right for them.

Mark Austenfeld, MD,
President, American Association of Clinical Urologists
Justin Albani, MD
Missouri Medicine Urology Editorial Board
North Kansas City, Missouri
MSMA Member since 2006
Frank Albani, MD, Urology
Liberty, Missouri
MSMA Member since 1977

Open Letter to a Missouri Senator

Dear Senator Chappelle-Nadal,

As a practicing physician who had an opportunity to observe the comments on the proposed HB 112 on Tuesday, April 30, I wanted to share with you some important facts regarding the impact of this bill and tort reforms on the practice of medicine.

In order to assist you in your continued search for facts and information on this topic, I would like the opportunity to offer my perspective on this proposal, as this bill directly impacts me as a provider and consumer of health care.

As you noted, HB 112 proposes a cap on only noneconomic damages for medical malpractice lawsuits. This has absolutely no bearing on the ability of a patient's right to have a fair trial by jury, nor to limit the potential award given to a plaintiff for economic damages. Several times today during your testimony, you alluded that somehow this bill would preclude your constituents' right to a trial by a jury, and that is simply false. Additionally, you mentioned several times in your discussion that this bill would somehow not allow a 'wronged individual' to seek recompense for damages for a 'patient's lifetime,' giving the example of the cerebral palsy injury or the patient who had the wrong hand or leg removed. In ALL of these examples that you gave, that injured patient would certainly have the right to have a jury determine a lifetime of potential lost wages that could be awarded to the patient, at a value that would reflect current inflationary rates, and there is NO limit to what this award would be.

The 'cap' that this bill is referring to ($350,000) is simply on non-economic damages, as this is impossible to define, impossible to predict, and thus makes absolute coverage by an insurance carrier impossible to achieve. This problem was illustrated quite well by your colleague, Senator Sifton (D-1st District, St. Louis County) who aptly noted that 'no insurance carrier can cover 99.9999% of physicians with the possibility of an award of infinity,' as this would bankrupt the system after one award.

The importance of the cap, is not to restrict a patient's right to trial, which it in no way does, nor to prevent justifiable recompense to a damaged patient, but to keep awards into a realm of reason that serve the needs of the plaintiff and the health care system. If trial attorneys were honest with you, as Senator Justus (D-10th District, Jackson County) noted today, lawyers demand 25-40% of the awarded amount at the time of a verdict. Thus, it is certainly to their advantage, and their livelihood to 'go for broke' and aim for the 'sky is the limit' attitude in seeking awards. Without a cap, what is to stop this attorney for seeking millions of damages, for the real purpose of simply seeking

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to fill his or her pockets with cash, rather than seeking true justice. The motivation for removing these caps is for building individual attorney wealth, not for providing for the damaged client. This is at the expense of everyone involved, from the health care provider, the hospital, the insurance carrier, and even the patient, himself or herself, as the bulk of the award is going to the attorney rather than the deserving patient.

In your comments today you mentioned several times that this cap should be somehow adjusted for the cost of inflation. This cap is on non-economic damages. How does one correct for inflation on 'pain and suffering' or stress from a medical error? Does this cost increase over time?

In your comments, you said that you are committed to equality for all of your constituents and all people. By not supporting HB 112, ironically, you are furthering inequality for access to health care among your own constituents. By focusing on the one in one million 'never-events' that you referred to multiple times, and the deserved awards, you are admitting that you would rather protect the possibility of this occurrence rather than the certain probability of not providing for adequate health care for the other 999,999 constituents/patients in your district.

Let me explain: with the uncertainty of significant judgments to be awarded for ANY cases, medical malpractice insurance will continue to skyrocket. With this continued increase in expense, physicians in your district and our state will no longer be able to afford insurance and will thus no longer be able to provide care in your district or our state. This will lead to an exodus of doctors and a loss of health care providers in your community, and thus, a significant decline in the health and quality of life for your constituents. Several times in your comments today, you noted that you favored a 'free market system.' Are you not in favor of stimulating job growth and industry in your state? Are you such a capitalist that you would rather see Missouri decline at the expense of its eight neighboring states so 'the market forces can take effect?" It is well known that all states provide incentives to corporations to spur their local economy through tax breaks, grants, and other incentives. Are you opposed to this being done in your community as well, and would rather other states and municipalities received these awards, so your 'free market system would thrive and your constituents would suffer?' The cap on economic damages really should be viewed simply in this light.

The 'crisis' that you continue to note that you 'just don't see' is right in front of you.

You appropriately admit that you are not a doctor, nor an attorney. I applaud you for taking the time to do your research on the issues, but you are still missing the forest through trees, as you do not seem to understand what is before you. Even with the caps in place, the disparity for medical malpractice based on location is already alarming. In my own personal experience as a urologist, which is a far less risky specialty (in contrast to neurosurgery or obstetrics) the difference between practicing in Missouri is approximately $30,000 per provider, per year compared to ~ $11,000 for practicing in Kansas, a state with caps on economic damages. This is a staggering difference and is compounded by EACH provider. For a small business such as mine with four physician providers, this is a difference of at least $76, 000 a year. This is money that could be used to hire more staff, see more patients, or even be used to hire another provider.

With the loss of tort reform, this number is surely to rise even more so. This is projected to be such a problem that many groups across the state bordering other states such as St. Louis and Kansas City, are actually advising their prospective applicants who are looking for a job in Missouri to move to Kansas! Is this what you want with your interest in a 'free market economy?' We all want a strong, vibrant, and healthy Missouri, and without caps on noneconomic damages, we risk losing all of those things.

With each day that passes since the ruling on July 31, 2012, from the Supreme Court that struck down reasonable limits on non-economic damages in medical malpractice lawsuits, physicians will continue to leave the state for a more physician-friendly locale, leaving Missourians with the possibility of their 'one in a million jackpot' award without a physician to win it from, as there will be none left to provide the health care and commit the mistakes of which you speak.

Please strongly consider the implications of all the issues surrounding HB 112, and support tort reform to provide reasonable limits on non-economic damages in medical malpractice cases to retain the seasoned physicians we currently have and recruit those young physicians looking to join our great state.

Justin Albani, MD
Missouri Medicine Urology Editorial Board
North Kansas City, Missouri
MSMA Member since 2006

Editor's Note

The difference between "economic" and "non-economic" damages was explained to this Senator at least six times, by my count, and she still didn't get the difference. She also said several times that "Never Events" was a legal term. It is not; it is a quality of care term. After listening to her drone on for close to two hours, I fled the Senate chamber gallery noting she was as clueless as when she stood up; but that was the whole point of the trial lawyer engineered filibuster. MM



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ONE MEDICINE

Collaborative Research on Human & Animal Disease for the Betterment of Both

by Craig L. Franklin, DVM, PhD

MU is one of the few universities with a school of medicine, college of veterinary medicine, and several strong departments ranging from biology to engineering, whose outstanding research is devoted to the life sciences.



Craig L. Franklin, DVM, PhD, dACLAM, is Professor, Department of Veterinary Pathobiology, University of Missouri and coordinator of this One Medicine theme issue.
Contact: franklinc@missouri.edu

"Between animal and human medicine there is no dividing line – nor should there be. The object is different but the experience obtained constitutes the basis of all medicine."

-Rudolf Virchow (1821-1902)

The theme of this issue of *Missouri Medicine* is animal modeling with an emphasis on ongoing activities and unique resources at the University of Missouri (MU).

MU is one of the few universities with a school of medicine, college of veterinary medicine, and several strong departments ranging from biology to engineering, whose outstanding research is devoted to the life sciences. As a result, MU is uniquely suited to advance 'One Medicine,' a concept recognized by Virchow and Sir William Osler, and now the lodestar of collaborative biomedical research.

Through its Office of Infrastructure Programs (within the Division of Program Coordination, Planning and Strategic Initiatives, Office of the Director), the National Institutes of Health funds several animal resources (http://dpcpsi.nih.gov/orip/cm/index.aspx). MU is home to three such resources: the Mutant Mouse Regional Resource Center (MU-MMRRC http://www.mu-mmrrc.com), the Rat Resource and Research Center (RRRC http://www.rrrc.us), and the National Swine Resource and Research Center (NSRRC http://www.nsrrc.missouri.edu).

Moreover, MU maintains a number of other animal model-based resources including, but not limited to the National Cancer Institute's Comparative Oncology Trials Consortium (COTC https://ccrod.cancer.gov/confluence/display/CCRCOPWeb/Home), the Research Center for Human Animal Interaction (http://rechai.missouri.edu/), the Christopher S. Bond Life Sciences Center (http://bondlsc.missouri.edu), the Laboratory for Infectious Disease Research (http://rbl.missouri.edu), and the Comparative Medicine Training Program (http://cmp.missouri.edu).

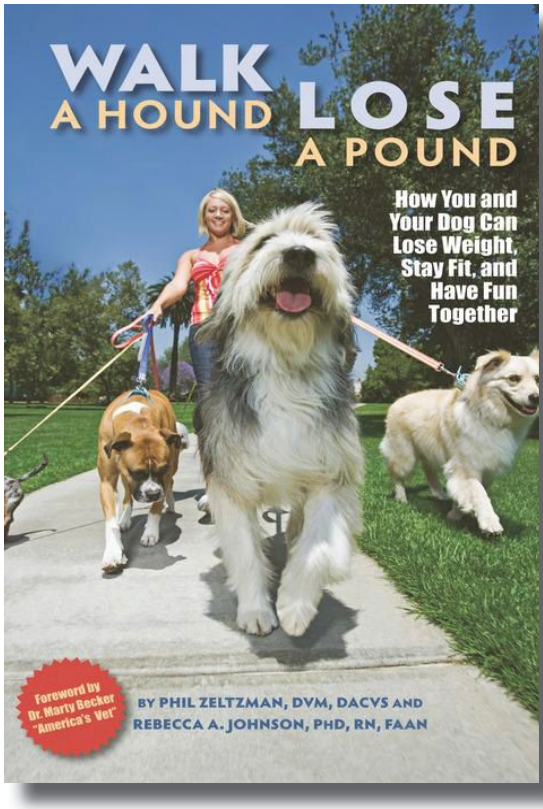
In a multi-department collaboration we present a collection of manuscripts that exemplify the broad range of comparative medicine initiatives at MU. Authors include faculty and residents from MU's School of Medicine, College of Veterinary Medicine, and School of Nursing. For a history of animal models and a brief look into the

future, readers are referred to the manuscript by Ericsson et al. Bryda builds on the discussion of rodent models for disease and describes the MMRRC and RRRC, critical centralized repositories for the preservation and distribution of rodent models that serve biomedical researchers across the globe. Walters and Prather change species and describe the growing use of swine in biomedical research with a focus on how the NSRRC is using new genetic engineering tools to create swine models with distinct advantages over historical rodent models. Henry and Bryan introduce the concept of One Medicine which promotes the study of naturally occurring diseases in companion animals for the benefit of both animal and human patients. This is best exemplified by activities of the COTC, which facilitates nationwide studies of and therapeutic trials for cancer in domestic animals. The definition of One Medicine is broadened by Johnson to studies of the human-animal bond, which provides great benefit to both human and animal health.

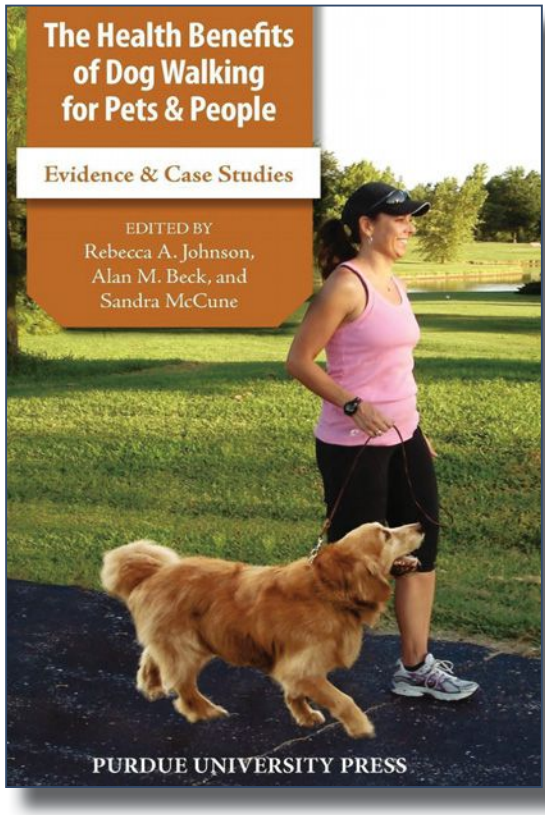
A common buzzword in today's research is translational medicine. To this end, Choudhary and Ibdah discuss the translation of data from animal models to the human condition, which drives progress of research along the continuum from basic biomedical research findings into clinical practice. Finally, Alvarado and Dixon describe the role of laboratory animal veterinarians as a bridge between the humane use of laboratory animals and the advancement of scientific and medical knowledge. MM

Human/Animal Interaction

Two recent resources for promoting pet owners' exercise with their companion animal are books co-authored/co-edited by the author of "Promoting One Health: MU Research Center for Human/Animal Interaction"



Zeltzman, P. & Johnson, R. A. Walk a hound, lose a pound: How you and your dog can lose weight, stay fit and have fun together. West Lafayette, IN: Purdue University Press; 2011. Available Amazon.com



Johnson, R. A., Beck, A. M., & McCune, S. The health benefits of dog-walking. West Lafayette, IN: Purdue University Press; 2011. Available Amazon.com

Promoting One Health: The University of Missouri Research Center for Human/Animal Interaction

by Rebecca A. Johnson, PhD, RN

Pets, especially dogs, have been shown in rigorous studies to improve both the mental and physical health of most of their owners.



Rebecca A. Johnson, PhD, RN, FAAN, FNAP, is Professor and Director, Research Center for Human Animal Interaction, College of Veterinary Medicine, and the Millsap Professor of Gerontological Nursing, MU Sinclair School of Nursing, University of Missouri.
Contact: rajohnson@missouri.edu

Abstract

The University of Missouri's College of Veterinary Medicine is home to the Research Center for Human-Animal Interaction. This center uniquely addresses a growing area of research that focuses on how the human-animal bond impacts health in people and animals. This article highlights the One Health basis for the center, several research projects, and future goals for the center.

Introduction: One Health Defined

There is considerable evidence that there has been an interrelationship between humans and animals since well before the domestication of animals. In varying degrees, the health of humans and of animals was then, and continues to be, interdependent. In particular, humans relied on animals for food, protection, and warmth. The concept of One Health is based on this premise and has resulted in a movement between human and veterinary medicine promoting cross-disciplinary collaboration to address not only illnesses common across species, but also interventions to facilitate health as more than just the absence of illness.

The American Veterinary Medical Association has arrived at the following definition:

"One Health is the collaborative effort of multiple disciplines - working locally, nationally, and globally - to attain optimal health for people, animals, and our environment. Together, the three make up the One Health triad, and the health of each is inextricably connected to the others in the triad. Understanding and addressing the health issues created at this intersection is the foundation for the concept of One Health."[1]

In recognition of the importance of long-standing cross-species interconnectedness, in recent years there has been considerable growth in human-animal interaction research. One specific area in this field is human-companion animal interaction. This interaction commonly takes place in four contexts: pet ownership; animal assisted activity in which specially trained and registered therapy animals and their handlers visit patients in acute and long term care settings; animal assisted therapy in which an animal is incorporated by a licensed professional as part of a patient-specific treatment plan; and service animals commonly dogs trained to perform specific tasks to facilitate independent living of their owner.[2]

Health Benefits Abound, Especially for Dog Owners

Pet ownership benefits human health in a number of ways, and to greater degrees in particular populations. In adults, research demonstrated that the presence of a pet has been associated with better performance on mental tasks.[3] Pets are commonly identified as nonjudgmental members of families.[4] Pet ownership has been associated with greater exercise levels (particularly dogs and in older adults); dog walking was associated with sustained physical functioning over a three-year period,[5] and fewer patient-initiated physician visits.[6] Dog ownership has been associated with better lipid panel outcomes[7,8] and pet owners have been found to be more likely to survive one year after myocardial infarction than non-pet owners controlling for age, severity of illness and comorbidities.[9] Older pet owners were found to be less depressed than non-pet owners.[10] This outcome is important for preventing the downward spiral in functional ability, mood, and social engagement that may lead to nursing home placement.



The goal of PALS (Pet Assisted Love and Support for Seniors) is to improve the quality of life, and to bring healing to the team: the volunteer, the animals, and the older adults who benefit from this program.

Human animal interaction and pet ownership have been found to be beneficial in relation to obesity prevention and treatment. Obesity is now a major public health problem given that there are over 79 million obese adults in the U.S. and 12.5 million children and adolescents. This condition is ranked as the leading cause of preventable death and resulted in annual national health care expenditures of over $147 billion in 2008. Missouri is one of nine states with an adult obesity rate of over 30% (http://www.cdc.gov/vitalsigns/AdultObesity/index.html#). The problem also occurs in companion animals. An estimated 34% of dogs are overweight or obese.[11] Existence of this problem on both ends of the leash suggests an opportunity for health care providers to engage the human-dog relationship to promote physical activity and one health across the two species.

Commitment to owning a dog has been found to promote exercise through dog walking as owners meet the needs of their dog for exercise and in doing so, benefit themselves. Australian dog owners walked 18 minutes per week more than non-owners and met physical activity recommendations of 150 minutes per week.[12] In the United States, adults who walked dogs accumulated a minimum of 30 minutes of walking per day in bouts of at least 10 minutes.[13] One trial found that obese adults with pets increased their moderate physical activity over those who did not have a pet.[14] Older adults who walked shelter dogs were found to have significantly increased walking speeds when compared with those who walked with a human companion.[15] Stress reduction commonly associated with exercise was demonstrated in one study in which older Japanese adults experienced increased parasympathetic neural activity. This activity was sustained while dog-walking and was cumulative over succeeding walks.[16] These findings suggest that dog ownership may be one way to facilitate healthy physical activity patterns benefitting both owners and their dogs. Two recent resources for promoting pet owners' exercise with their companion animal are books co-authored/co-edited by the author of this paper: (See sidbar on page 196.)

Animal Assisted Activity

Animal assisted activity appears beneficial in anxiety-inducing disease states or treatment protocols. It is thought to provide distraction and stress relief, particularly in settings in which patients may feel isolated and need additional interaction and companionship (e.g. in hospitals and nursing homes).[17] Nursing home residents who had dog visits were significantly less lonely than those not having visits.[18] Companion animals have been found to facilitate social interaction. People are more likely to interact positively with others when an animal is present.[19] Increased positive social interaction occurred between nursing home staff, residents and staff, and residents with other residents when a dog was present.[20] Indirect interaction with animals has also been found to be of benefit for nursing home residents. Patients with Alzheimer's disease sat for longer periods and ate significantly more food when watching

fish swim in an aquarium placed in front of them during meals.[21] Hospitalized patients reported less pain and used fewer analgesics during and after an animal visit.[22] In patients with heart failure, anxiety, and epinephrine levels decreased during and after an animal visit.[23]

Animal Assisted Therapy

Animals are used in rehabilitation settings to facilitate patients' progress with specific therapy goals. In this and other therapeutic settings (e.g. psychotherapy), licensed professionals (e.g. psychologists, physical and occupational therapists and social workers) include interaction with animals in therapy protocols. Children with autism were better able to stay on task with their therapist with a therapy dog present.[24] In other modalities such as in therapeutic horseback riding, patients increased their balance, and improved their gait through specific activities while riding specially selected and trained horses.[25] Animal Assisted Therapy has increased; however, in order to ensure that such programs persist and continue to be adopted, randomized clinical trials are needed to define less equivocal and more replicable outcomes.



Service dogs perform specific tasks to assist their owners such as opening doors, turning on lights, or retrieving objects.

Service Animals

In contrast to pets, service animals live and work with their owners to facilitate independent living. These animals (generally dogs) are federally protected by the Americans with Disabilities Act and are permitted to accompany their owner wherever that person goes as long as the dog does not create a disturbance or unsafe situation through unruly or aggressive behavior. The dogs perform specific tasks to assist their owners such as opening doors, turning on lights, or retrieving objects. Presently, service dog roles are being expanded to alleviate post-traumatic distress symptoms (PTSD, e.g. in military veterans) through tasks such as alerting their owner to someone coming up from behind, going ahead around blind corners to signal the owner that it is safe to proceed, and creating personal space by standing in front of the owner in a crowded situation. The Veterans Administration has recently released a policy indicating that it will not provide financial support for veterans' PTSD service dogs due to a lack of published research demonstrating their efficacy http://www.stripes.com/va-says-no-service-dogs-benefits-warranted-for-ptsd-sufferers-1.188166. However, veterans continue to seek and obtain PTSD service dogs to assist them in daily life.

One Health Human Animal Interaction Work

The Research Center for Human Animal Interaction (ReCHAI) was established in 2005 at the University of Missouri, College of Veterinary Medicine, as a collaborative center with the Sinclair School of Nursing. ReCHAI's mission is "Studying and promoting the health benefits of human-animal interaction (HAI)." ReCHAI plays a vital role in international initiatives to promote research, practice, and education in human animal interaction through the International Association of Human Animal Interaction Organizations (IAHAIO), a global umbrella association of over 40 organizations conducting varied work in HAI. The author of this paper is currently President of this Association. In July, 2013, IAHAIO will hold its triennial conference in tandem with the 150th annual convention of the American Veterinary Medical Association. This will create unprecedented opportunities for collaboration and information sharing across human health and veterinary medical fields.

ReCHAI conducts both research and community programs. One example of a community program, the TigerPlace Pet Initiative, aims to enhance pet ownership among older adult residents of TigerPlace, an aging-in-place retirement residence originated by the Sinclair School of Nursing. ReCHAI provides older adults with support needed to keep their pets via a pet care assistant. This assistant visits pet owners at least three times each week to walk dogs (for those who are unable to do this), clean cat litter boxes, and provide other assistance as needed (e.g. administering medications to pets). We maintain an on-site veterinary medical exam room which is used by

our faculty veterinarian who makes monthly house calls on the pets, and also gives presentations for the older adults and facility staff on matters pertaining to pet health. The program includes a fund for providing foster care for pets until their adoption when their owners pre-decease them. This program facilitates One Health by providing older adults who own pets support to help them keep their pets and benefit from the known positive outcomes of pet ownership. In addition to increasing TigerPlace residents' happiness, this program also provides early detection of health problems in the pets, which enables prompt intervention, facilitating health of the animals.

Similar programs could be implemented in other retirement facilities by linking the facility with a local veterinarian willing to engage in this type of primary and preventive care for older adults' pets. An auxiliary or volunteer corps could be formed to help older adults with the tasks done by the pet care assistant at TigerPlace. ReCHAI is called upon to advise other facilities wanting to establish similar pet-owner facilitating programs. This includes recommending procedures to address animal behavior problems (e.g. protective dog behavior toward staff working with older adults), pet overfeeding, and concerns of residents who do not like pets.

Since 2005, ReCHAI has conducted 13 studies including five which are currently underway. The center is a research training site for doctoral students across disciplines, professional veterinary medical students and undergraduate students completing capstone or practicum experiences. ReCHAI's research investigates topics that include: alleviating US military veterans' post traumatic stress through shelter dog obedience training, relieving anxiety of abused children during forensic interviews by placing a trained service dog with them during the experience, exploring the role of the family dog in families with children who have autism, and identifying the effect of training shelter dogs in basic obedience on prison inmates' rehabilitation. The studies are funded by grants from external sources including but not limited to the National Institutes of Health, the Missouri Foundation for Health and several other foundations.

Future Directions and Goals

Future goals for ReCHAI are to expand its funding base through endowments, gifts, and additional research grants; and, to enable additional research, community programming, and student learning opportunities. A further goal is to develop pre and post-doctoral training fellowships in HAI and One Health through cross-disciplinary collaboration. Any reader interested in finding more information about the research and programs of the MU Research Center for Human-Animal Interaction can find it on the webpage at http://www.rechai.missouri.edu.

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Disclosure

None reported.

MM

A Brief History of Animal Modeling

by Aaron C. Ericsson, DVM, PhD, Marcus J. Crim, DVM & Craig L. Franklin, DVM, PhD

Animal models play a critical role in translational research and advancement of human and animal health.



Aaron C. Ericsson, DVM, PhD, Marcus J. Crim, DVM, and Craig L. Franklin, DVM, PhD, are in the Mutant Mouse Regional Resource Center, Comparative Medicine Program and Department of Veterinary Pathobiology, University of Missouri.
Contact: franklinc@missouri.edu

Abstract

Comparative medicine is founded on the concept that other animal species share physiological, behavioral, or other characteristics with humans. Over 2,400 years ago it was recognized that by studying animals, we could learn much about ourselves. This technique has now developed to the point that animal models are employed in virtually all fields of biomedical research including, but not limited to, basic biology, immunology and infectious disease, oncology, and behavior.

"Ought we, for instance (to give an illustration of what I mean), to begin by discussing each separate species-man, lion, ox, and the like-taking each kind in hand independently of the rest, or ought we rather to deal first with the attributes which they have in common in virtue of some common element of their nature, and proceed from this as a basis for the consideration of them separately?"

-Aristotle (384 -322 BC)
"On the Parts of Animals"

Early History of Animal Modeling

The use of animals as models of human anatomy and physiology began in ancient Greece (see Table 1). These first recorded instances of comparative science were very observational, their purpose being to better understand human ontogeny and physiology. Fortunately, many of the findings of prominent thinkers like Aristotle were documented and conveyed to other countries via trade routes, and animal modeling soon became a research tool of both European and Arab physicians. While this early period saw great discoveries, there were still many misconceptions about the workings of the body, and it was not until the Renaissance (fourteenth through seventeenth centuries) that animal modeling contributed to a true paradigm shift in our understanding of human physiology.

During the mid-sixteenth century, a few astute physicians such as Servetus and Lusitano deduced that blood followed two connected but distinct circuits through the body, i.e. pulmonary and systemic circulation. In the late sixteenth and early seventeenth centuries, William Harvey (1578-1657) assiduously studied and compared the anatomic and functional properties of the heart and vasculature in multiple species including eels and other fish, chicks, and pigeons. Based on these investigations, he penned several seminal texts including *De Motu Cordis* in which he describes with great accuracy, and in great detail, the human circulatory system. He also pioneered

Table 1. Early Milestones in Animal Modeling

Years	Researcher(s)	Milestone
6th c. BCE	Alcmaeon of Croton	Determined that the brain is the seat of intelligence and sensory integration based on studies using dogs
4th c. BCE	Aristotle	Studied embryogenesis and ontogeny in chicks
3rd c. BCE	Erasistratus	Studied the cardiovascular system in live animals and deduced that the heart functions as a pump
2nd c. CE	Galen of Pergamum	Studied cardiovascular and neuroanatomy extensively using live animals
12th c.	Avenzoar	Practiced surgical techniques on animals before applying them to humans, e.g. tracheotomy
17th c.	William Harvey	Studied anatomy of several species of live animals and provided accurate and detailed descriptions of the function of the cardiovascular and other systems

the theory of epigenesis, i.e. that embryos originate and develop from a single cell, based on his observations of embryonic chicks (recommended for developmental studies by Aristotle in Book II of *The Generation of Animals*). Of note, Harvey was careful in his selection of model species, in order to exploit certain properties of the animal such as heart rate and poikilothermy ("cold-bloodedness").

The careful selection of the most informative species for an animal model is still very important, but it also presents a unique challenge for investigators. Scientists must consider not only financial feasibility and previous experiments utilizing a given species, but also the unusual biological characteristics of a species and the available palette of imaging and molecular techniques available for that species. The choice of a naturally occurring species model, sometimes called the comparative method, was perhaps most famously and succinctly stated by the 1920 winner of the Nobel Prize in Physiology and Medicine, August Krogh, in 1929, "*For a large number of problems there will be some animal of choice or a few such animals on which it can be [most] conveniently studied.*"[1] One recent example is the use of the nine-banded armadillo in studies of leprosy due to the armadillo's unique susceptibility to *M. leprae.*[2]

Animal Models in Modern Biomedical Research

By the beginning of the twentieth century, the use of animal modeling had increased dramatically and, while some individuals still questioned the ethics of their use, animal modeling, particularly in rodents, had become the *de rigeur* method of demonstrating biological significance. However, all research animals at this time were outbred and as the use of animals became more experimental, rather than observational, researchers soon appreciated the confounding factor of genetic variability in their research. Through the efforts of many forward-thinking individuals such as William Castle, Clarence Little, Halsey Bagg, and Leonell Strong, this problem was addressed via inbreeding of mice to the point that genetically identical mice became available for experimental use (see Table 2). This provided a steady source of research subjects that bred to maturity very quickly and with limited variability from litter to litter and year to year. As more and more inbred strains of mice and rats were developed, it was soon appreciated that there were inherent differences between strains in basic biological parameters, as well as susceptibility to induced and spontaneously occurring diseases. Many of these were complementary strains bred in parallel providing susceptible and resistant strains that are otherwise genetically similar, such as the non-obese diabetic (NOD) and related strains.[3] Thus, strain selection is one of the most important considerations in animal modeling, particularly in rodents.

If natural models were not available or feasible, the ability to manipulate the genome of a model species allowed for the creation of animals uniquely susceptible or resistant to a certain model. So, as advances were made in the field of genetics, scientists became increasingly adept at manipulating the as yet unsequenced genome of mice. The 1980s saw an explosion in this technology with the advent of transgenic mice carrying additional genetic material, and knockout mice in which genetic material is deleted. Recently, our ability to manipulate the mouse genome has become increasingly refined with developments such as tissue-specific methods of

knocking out genes such as the Cre-Lox system,[4] methods of turning on or off gene transcription *in vivo* using tetracycline- or tamoxifen-induced systems,[5] and methods of identifying or removing entire cell lineages *in vivo* via fluorescent protein- and diphtheria-toxin receptor-knockin mice respectively.[6, 7] Additionally, researchers have used similar technologies to generate transgenic rats,[8] cats,[9] dogs,[10] rabbits, pigs, sheep,[11] goats, cattle, chickens,[12] zebrafish,[13] and non-human primates,[14] to name just a few. While the ability to generate targeted gene knockouts in other species has lagged behind, knockout rats were successfully created in 2009 using a zinc finger nuclease-based technique distinct from that used in mice.[15]

Table 2. Recent Milestones in Animal Modeling

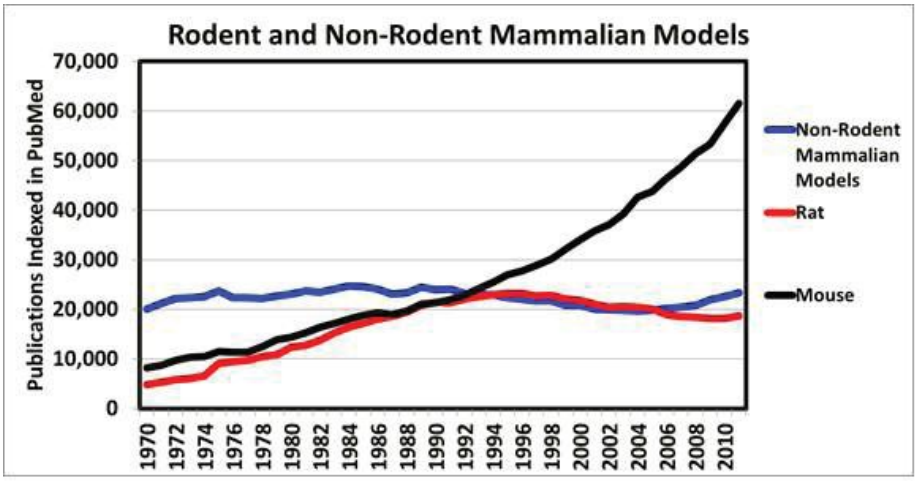
Years	Researcher(s)	Milestone
1902	William Castle	Begins breeding mice for genetic studies
1909	Clarence Little	Begins inbreeding mice to eliminate variation
1920s	Frederick Banting	Isolated canine insulin and effectively treated diabetic dogs
ca. 1930	Little and MacDowell	First fully inbred mouse (20 brother × sister matings) achieved
1940s	John Cade	Studied the use of lithium salts as an anticonvulsant in guinea pigs and translated his findings to treatments of depression
1976	Rudolf Jaenisch et al.	Developed first transgenic mouse
1980s	Several	Extensive testing of drug safety and dosing regimens for HIV performed in rhesus macaques
1987	Capecchi, Evans, and Smithies	Developed first knockout mouse
1997	Wilmut and Campbell	First animal cloned from an adult somatic cell, Dolly the sheep
2002	Several	Mouse genome sequenced
2004	Several	Rat genome sequenced
2009	Aron Geurts et al.	Developed first knockout rat

The mouse continues to be the powerhouse for biomedical research (see sidebar page 206). Undoubtedly, the most important change over the last 25 years is the spectacular escalation of the laboratory mouse in research, which stands in glaring contrast to the declining role of most non-rodent mammalian models (see Figure 1). By comparison, use of the rat has plateaued, as targeted genetic manipulations proved more difficult in this species. The creation of the first knockout rats may help to explain the very recent up-tick in rat model-based biomedical publications. However, with the rising capacity to modify the genomes of laboratory species other than the mouse, the face of biomedical research is now changing. Genetically malleable species such as swine and the zebrafish are increasingly out-competing once common model organisms like the guinea pig, rabbit, and ferret (see Figure 1). These important trends reveal both 1) the dramatically increasing utility of certain model species relative to others, and 2) the refinement of animal research via use of the lowest ordered vertebrate possible to accomplish a given scientific objective.

Additionally, the recognition of the impact of the gastrointestinal and dermal microbiota led to the birth of an entirely new research era – gnotobiotics. Through the use of Caesarian birth, flexible-film isolator cages, and irradiated food, mice can now be maintained in completely germ-free conditions or colonized with one or more defined bacterial species. A combination of eight commensal aerobic and anaerobic bacteria called Altered Schaedler's Flora (ASF) is commonly used as the known intestinal microbiota.[16] However, with the recent development of robust methods of fingerprinting the entire gut microbial community such as Denaturing Gradient Gel Electrophoresis, Automated Ribosomal Intergenic Spacer Analysis, and deep sequencing, researchers are capable of quickly and reliably monitoring the composition of the gut microbiota and thus moving away from more reductionist models such as ASF. While the development of inbred rodent strains allowed for the control of host genetics, the development of research animals harboring complex but defined microbiota allows for control of microbial genetics known to impact host physiology. Moreover, gnotobiotics can also be applied to non-murine species, so this field is likely to continue to evolve.

Future of Animal Modeling

What does the future hold for animal models? As biomedical research funding agencies continue to



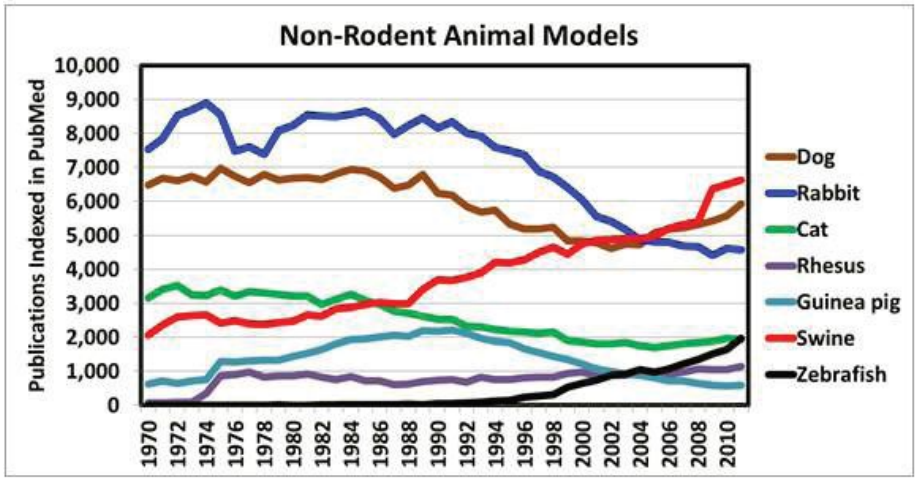


Figure 1
Pubmed search results by publication date, 1970 through 2011. Search terms for each species included the scientific name and the common name for each species; except that only the scientific name was used for mouse and rat. "Non-rodent mammalian models" includes the dog, rabbit, cat, rhesus macaque, guinea pig, swine, chimpanzee, and ferret.

emphasize rapid and robust translatability of studies, it is likely that animal modeling will move more and more towards models that most appropriately mimic human conditions, using multiple models to ensure robustness of data and new genetic and metagenomic tools to develop and refine "humanized models." With advancements in genetic engineering in non-mouse species, we are also likely to see new models generated for diseases where mouse models have not adequately replicated the human condition. For example, genetically engineered mouse models of cystic fibrosis develop intestinal diseases similar to those seen in humans with this disease, but fail to develop the devastating pulmonary complications. To circumvent these deficiencies, a swine model was recently generated and early data suggest that the latter better replicates pulmonary disease.[17] Other examples include the study of naturally occurring diseases in domestic species that optimally mimic disease such as the study of osteosarcoma progression and response to therapy in dogs.[18] This concept, referred to as One Medicine, promotes the sharing of resources, knowledge, and effort toward the common goal of improving the health and well-being of all species and is proving to be a powerful adjunct to traditional laboratory animal models.

Humanized models such as transgenic animals expressing human genes are also rising to the forefront. A classic example involves the insertion of the gene encoding the human major histocompatibility locus, HLA-B27 into rats.[19] Individuals with this MHC haplotype have increased susceptibility to several autoimmune conditions. Similarly, rats with this transgene are more susceptible to autoimmune disease and as a result, this model has proven indispensable to studies of MHC-related disease susceptibilities. This concept was expanded by coupling targeted mutations in endogenous murine genes with the introduction of

transgenes of mutated human genes. Newer models continue this process through combinations of multiple mutations that provide refined models that better recapitulate disease.

Humanization of models has also involved creating mice with entire human systems. To this end, mice with human "immune systems" were generated as early as 1988 by implanting either fetal lymphoid tissue or peripheral blood leukocytes into mice with spontaneous severe combined immunodeficiency. These mice, along with several refined versions have demonstrated their usefulness in studies of hematopoiesis, basic immunology, infectious disease, and autoimmunity.[20] The concept of creating human "organs" in mice has also made its way into other systems such as the liver, where humanized mice are proving invaluable in studies of drug metabolism and viral hepatitis.[21]

Taking concepts of gnotobiology one step further, researchers have recently begun reconstituting germ-free mice and rats with microbiota isolated from human fecal samples.[22, 23] These and other studies have yielded surprising discoveries regarding the role of microbiota in host physiology and well-being, in the gastrointestinal tract as well as other less intuitive disease models.[24, 25] These studies at the forefront of animal modeling take into account not only the variability present within the individual model organism but also the variability present within the superorganism, i.e. the host and its associated microbiota, allowing for control of important variables that were once often overlooked.

The combination of these concepts will likely lead to increased genetic engineering and humanization of non-rodent species, and coupling of this data with one medicine-based studies of domestic animals and human clinical trials. Thus it is likely that animal models will continue play a critical role in translational research and advancement of human and animal health.

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Disclosure

None reported.

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New York Times Article Misleads on the Value of Mouse Models

by Catherine E. Hagan, DVM, PhD

In February 2013, the *New York Times*[1] covered a study published in a prestigious research journal, the *Proceedings of the National Academy of Sciences* (PNAS).[2] The sensational headline was "Mice Fall Short as Test Subjects for Humans' Deadly Ills." The study compared gene expression data in white blood cells from both humans and mice under conditions of trauma, burn, or sepsis.

A detailed response to the *Times* article was posted by Mark Wanner[3] on a blog at the Jackson Laboratory, a non-profit organization that conducts mammalian genetics research to advance human health. His rebuttal highlights the main problem with the PNAS study - it compares heterogenous human data to a single mouse strain, which is the equivalent of one mouse, given that animals within an inbred strain are genetically identical. Furthermore, the strain used has long been known to be resistant to bacterial infections.

The general public may be left with the impression that research using mice has been a waste of years of research and billions of dollars of funding. Headline scanners and casual readers may miss a key sentence: "The study's findings do not mean that mice are useless models for all human diseases."[1]

The hyperbole in the *Times*' article underscores the importance in distinguishing the various opinions of scientists from conclusions that are supported by actual data. In the original PNAS article, the study conclusions are more conservative, suggesting that genomic studies in the dawn of this new era of molecular medicine could complement or decrease the need for mouse models in drug discovery and development. That is a reasonable statement. The authors then claim their data support prioritization of genomic studies such as theirs over mouse studies. They set up a "straw mouse," using a model that one would not expect to recapitulate human sepsis - an infection-resistant strain - and then knock it down, citing the lack of correlation of its gene expression data compared to humans.

Though the media overstated the study's findings, it revitalized an important conversation about the strengths and limitations of mouse models. For understanding the role of genes in whole animals, the mouse is the best model. The *Times* article ultimately conceded the potential contributions of mice, stating "Researchers said that if they could figure out why mice were so resistant, they might be able to use that discovery to find something to make people resistant."[1] Funding agencies clearly recognize that medical progress will most likely occur through diverse funding portfolios that include both basic research using animal models and clinical research in human patients.



Catherine E. Hagan, DVM, PhD, is an Assistant Professor, Department of Veterinary Pathobiology, University of Missouri.
Contact: haganc@missouri.edu

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The Mighty Mouse: The Impact of Rodents on Advances in Biomedical Research

by Elizabeth C. Bryda, PhD

What is not always appreciated is the extraordinary impact that laboratory mice and rats have on biomedical research.



Elizabeth C. Bryda, PhD, is with the Rat Resource and Research Center, Department of Veterinary Pathobiology, University of Missouri.
Contact: brydae@missouri.edu

Abstract

Mice and rats have long served as the preferred species for biomedical research animal models due to their anatomical, physiological, and genetic similarity to humans. Advantages of rodents include their small size, ease of maintenance, short life cycle, and abundant genetic resources. The Rat Resource and Research Center (RRRC) and the MU Mutant Mouse Regional Resource Center (MMRRC) serve as centralized repositories for the preservation and distribution of the ever increasing number of rodent models.

Perceptions of Mice and Rats: An Introduction

Mention mice and rats to most people and images of unsanitary conditions and urban decay come to mind. Rats have been vilified as the carriers of the infected fleas that led to the dreaded Black Plague that decimated Europe, North Africa and Central Asia in the fourteenth century. It has been suggested recently that an apology is in order and that other influences, not rodents, were to blame.[1] More recently, infected mice have resulted in Hantavirus outbreaks including the recent scare in Yosemite National Park where many campers contracted the deadly virus from mice living in the cabins.[2]

For many people, exposure to rodents consists of seeing them used as food for snakes or birds of prey at the zoo, or having to deal with unwanted rodents invading their dwellings. A kinder image of rats and mice sometimes appears in literature – think of the rodents in E.B. White's beloved books: the adventurous mouse Stuart in *Stuart Little* or the gluttonous rat, Templeton, of *Charlotte's Web* fame. Recall the heroic cartoon character Mighty Mouse who always "saved the day" and of course, the best known mouse of all, Disney's Mickey Mouse.

What is not always appreciated is the extraordinary impact that laboratory mice and rats have on biomedical research. They

are often the preferred animal model for studies of human disease and the standard species of choice for pre-clinical trials.

Comparative Medicine Research

Comparative medicine is built on the ability to use information from one species to understand the same processes in other species. Basic biomedical research involves the characterization of genes/proteins, the study of anatomical and physiological functions and the characterization of normal and pathological states in a variety of animal species. This knowledge is then applied to understanding these same processes in humans. Likewise, information gained in the field of human medicine can be mined to advance veterinary medicine because of the commonalities among species that form the basis of comparative medicine.

Laboratory rats and mice provide ideal animal models for biomedical research and comparative medicine studies because they have many similarities to humans in terms of anatomy and physiology. Likewise, rats, mice, and humans each have approximately 30,000 genes of which approximately 95% are shared by all three species.[3-6] The use of rodents for research purposes has economic advantages: mice and rats are relatively small and require little space or resources to maintain, have short gestation times but relatively large numbers of offspring, and have fairly rapid development to adulthood and relatively short life spans. For example, mice have a gestation period of approximately 19-21 days; can be weaned at three to four weeks of age, and reach sexual maturity by five to six weeks of age, allowing large numbers of mice to be generated for studies fairly quickly.

The use of rodents also provides advantages related to the wealth of genetic information available to scientists. The human genome was sequenced in 2001,[4, 5] with those of the mouse and rat following in 2002 and 2004 respectively.[3, 6] The availability of the complete nucleotide sequences for all three species has enabled genome-wide comparisons across species which have been critical for the identification and characterization of genes. The ability to use sophisticated molecular genetic techniques to manipulate the genes in mice and more recently rats, allows genes to be "knocked out" (no expression) or expressed at designated times of development or in select tissues in order to better understand their normal function and/or role in disease.

Mice as Models to Study Human Disease: Hereditary Deafness

The identification of genes responsible for hereditary deafness provides an excellent example of the utility of mice for studying human disorders. In humans, hearing loss is the most common sensory deficit, with congenital deafness occurring in one per every 1,200 to 2,000 live births. [7] Over a hundred different genes are involved in non-syndromic hearing loss.[8] The mouse has been instrumental in identifying and characterizing a large number of these genes.

Traditionally, it has been difficult to study the genetics of hearing loss and deafness in humans due in part to the lack of large families or large numbers of affected individuals for studies, the issue of genetic heterogeneity (the phenomenon in which a single genetic disorder, in this case deafness, can be due to mutations or defects in a number of different genes), and the general inability to perform detailed anatomical analysis on human ears, particularly inner ears. Especially problematic is the difficulty in ascertaining what damage is due to inherited factors versus environmental factors such as exposure to loud noise or infections.

The mouse allows investigators to circumvent all of these problems. Genetically identical inbred strains of mice carrying a single mutated gene are particularly valuable in identifying gene function. Many mice carrying mutations related to hearing loss have been identified over the years because of the often obvious phenotype (physical characteristics) of a deaf mouse: failure to respond to noise as indicated by the lack of Preyer's reflex (ear flick), unusual head tossing and circling (literally running around in a circle) behavior. This latter characteristic is the manifestation of the vestibular defects that are

common in mouse deafness mutants. Unlike with humans, mice can be purposely bred to specific mates in order to generate many offspring with the desired genetic make-up (genotype). Because the mice are raised in controlled, pathogen-free environments, the effect of environmental factors can be highly controlled. Thus, we can attribute any hearing deficits completely to the genetic mutation. Because of the identical anatomical structures, findings in the mouse can be directly correlated to the expected pathology in humans. Lastly, using comparative genomic techniques, identification of a gene responsible for deafness in the mouse allows the equivalent (orthologous) gene to be identified in people. Beyond these studies to identify genes important in auditory development and function, the mouse strain can serve as a model to further explore the biological function of the gene and better understand its role in the auditory system. To date, over 55 non-syndromic human deafness genes have been identified[9] and in every case, a corresponding mouse mutant serves as a model for that particular form of deafness (http://hearingimpairment.jax.org/models).

Advantages of Rats in Biomedical Research

Since mice are small in size and generally cost less to maintain, and because the tools to genetically manipulate their genomes have been available since the 1980s, mice are often the first choice as a rodent model. However, there are many areas of investigation where rats are preferred, including cardiovascular research, behavioral studies and toxicology.[10]

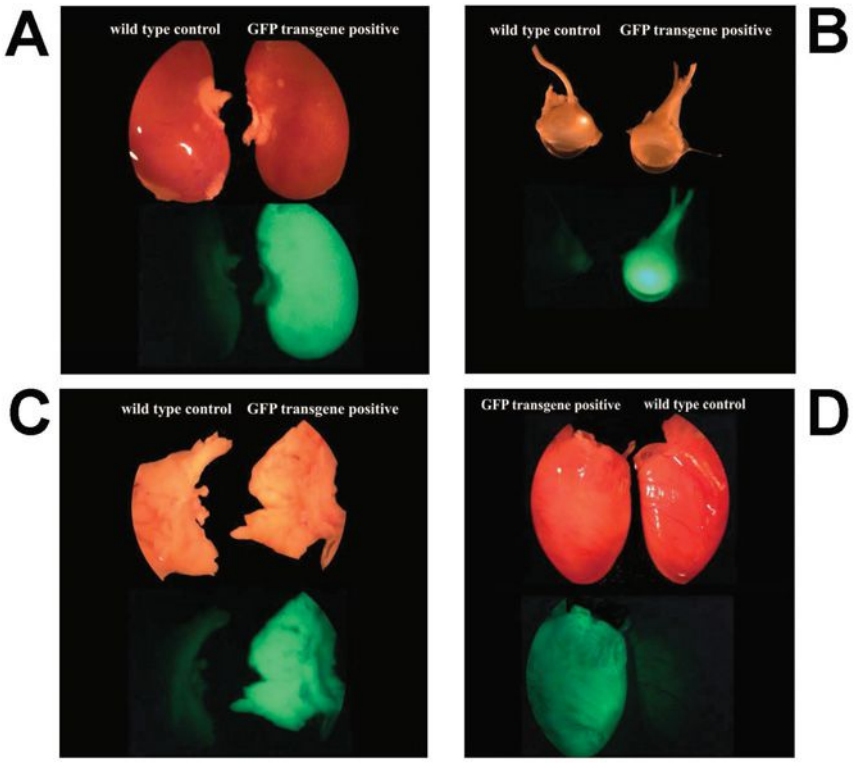
Cardiovascular disease is the leading cause of death and morbidity in developed countries (http://www.who.int/cardiovascular_diseases) and it is typically multifactorial (caused by combinations of genetic and environmental factors).[11] Rats are often the preferred rodent model for cardiovascular research where their larger size is an advantage, especially for facilitating surgical procedures and other types of testing. Many unique strains of rats have been generated that model the complex nature of human obesity, diabetes, and cardiovascular disease and therefore in this case, rats provide excellent animal models for the study of these diseases.[12,13]

Rats are commonly used for behavioral studies because they are much more social than mice and their behavior better mimics behavior seen in humans. For example, expansion of a three-base pair sequence in the FMR1 gene is responsible for Fragile X syndrome, the most common cause of inherited intellectual disability in humans.[14] This expansion leads to methylation of the FMR1 gene, essentially shutting it down such that the gene is not expressed.[15] Defects in this gene are a known genetic cause of autism.[16] When the FMR1 gene is knocked out in mice, they exhibit elevated social interactions.[17] However when the same gene is knocked out in rats, they become less engaged in social play and emit fewer vocalizations during play sessions. These social impairments more closely parallel social behavior symptoms seen in humans with FMR1 mutations. Affected rats also display compulsive chewing behavior. Compulsive and repetitive behaviors are core symptoms in autism spectrum disorders (http://www.sageresearchmodels.com). Thus, in this case, the rat is the more appropriate rodent model.

Choosing the Best Species

In the past, the use of the mouse often eclipsed that of the rat because of the availability of better molecular techniques to manipulate the mouse genome. Recent advances in genetic tools to create knockout rat models promise to eliminate these barriers and may lead to an increase in the use of rats for a wider variety of biomedical research. Ultimately, the choice of rodent model depends on which species more closely recapitulates the symptoms and disease process seen in humans. It is clear that rats are not simply huge mice and that each species has advantages and disadvantages that often depend on the particular process or gene being studied. From a translational medicine standpoint, it is particularly critical to choose the appropriate model because a tremendous amount of money is

Figure 1
Example of fluorescence seen in EGFP rat strains. Pictures of organs from SDTg(GFP)2BalRrrc (RRRC:0065) animals (images on right of each panel) and wild type controls (images on left of each panel). Upper images for each panel are under bright light, bottom images for each panel are under fluorescent light. Panel A: kidney; Panel B: eye; Panel C: lung; Panel D: heart.



spent testing drugs and therapies that ultimately fail at various stages of pre-clinical and clinical trials. One reason for this is that results obtained in animal trials do not always accurately reflect outcomes in humans.

It has been estimated that new drugs take an average of 15 years to go from discovery to market at an average cost of $900 million.[18] Based on a report from the Tufts Center in 2001, it is estimated that of 5,000-10,000 compounds that enter the development pipeline, 250 will make it to preclinical trials and of those, only five will move into human clinical trials. Of those five, on average, only one will actually make it to market. The investment losses of money and time associated with the four failed drugs is huge. Interestingly, a retrospective study of several best selling drugs found that the mouse knock out phenotypes of the targets of these drugs correlated well with known drug efficacy. The therapeutic effect observed in the knock out model was often a good indicator of success in the clinic.[19] This supports the notion that establishing a more specific and sensitive preclinical trial paradigm based on the best animal models will reduce drug development costs and more importantly, reduce the risk to human subjects in clinical trials.

Rodent Resource Centers

The use of rodents in biomedical research continues to rise and the number of unique strains and models is increasing tremendously as individual investigators and large federally funded multi-group projects generate increasing numbers of genetically engineered mice and rats.

The University of Missouri has the unique distinction of being the home of three National Institute of Health (NIH)-funded animal resource centers: The Rat Resource and Research Center (RRRC), the MU Mutant Mouse Regional Resource Center (MMRRC) and the National Swine Resource and Research Center (NSRRC). The RRRC and NSRRC are the only Centers of their kind in the United States. The MMRRC is part of a consortium of four regional centers located throughout the U.S. The purpose of the two rodent-centric Resource Centers is to serve as repositories for rat and mouse strains/stocks that are important for use in biomedical research. The Centers 1) import these important animal models, 2) cryopreserve

embryos and/or sperm as a means to store and bank the models, and 3) serve as distribution centers to send the animals or cryopreserved materials to investigators worldwide who use these models in their research.

These repositories came into existence as a means to centralize the storage and distribution of important rodent animal models. The time and money used to create genetically modified animal models and characterize them is quite large; it is therefore important for them to be readily available to the scientific community for further research. The Resource Centers take the burden from the individual investigators of preserving the strains and shipping the animals to other researchers. Importantly, the Resource Centers use strict quality control measures to ensure that the genetics and clean health status of these models are monitored and maintained at the highest standards.

Currently, the most highly requested rats that are distributed by the RRRC are strains that contain a genetic modification consisting of the addition of a fluorescent reporter gene (enhanced green fluorescent protein or EGFP) within their genome. The consequence of this genetic addition is that every cell in these rats expresses the green fluorescent protein, allowing them to be readily observed by fluorescence microscopy (see Figure 1). These strains are particularly useful for transplantation and immunological research. Regenerative medicine, adoptive cell transfer and identification of genetically modified cells after gene therapy in vivo require the ability to track donor cells in host tissues and the EGFP rat strains facilitate these types of studies. In 2012, the RRRC received requests for EGFP rat strains from 24 academic institutions, research institutes, and for profit companies located not only in the United States but worldwide.

Future of Rodent Models in Biomedical Research

Rats and mice will continue to play a central role in biomedical research. Increasingly sophisticated manipulations of rodent models, including the creation of so called "humanized" rodents that carry human genes, cells, tissues, or organs may lead to improved and refined models for developing therapeutics for human disease. The power of comparative medicine and the use of mice and rats will continue to provide a powerful tool for advancing the understanding of both normal and disease processes across species and facilitate the transition of research from "bench to bedside" to improve human health.

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Disclosure

None reported. MM

Advancing Swine Models for Human Health and Diseases

by Eric M. Walters, PhD & Randall S. Prather, PhD

Although the pig is the relative 'new kid' on the block, pig models of human disease will continue to have a significant impact on the scientific community.





Eric M. Walters, PhD, (left) and Randall S. Prather, PhD, are in the Division of Animal Sciences and National Swine Resource and Research Center, University of Missouri.
Contact: walterse@missouri.edu

Abstract

Swine models are relatively new kids on the block for modeling human health and diseases when compared to rodents and dogs. Because of the similarity to humans in size, physiology, and genetics, the pig has made significant strides in advancing the understanding of the human condition, and is thus an excellent choice for an animal model. Recent technological advances to genetic engineering of the swine genome enhance the utility of swine as models of human genetic diseases.

Introduction

Pigs are an ideal animal model for human health and diseases because their anatomy and physiology are similar to humans and because the porcine genome is three times closer than the mouse genome to that of the human.[1] Moreover, the recently completed swine genome sequence (Sus scrofa Build 10) will help advance the pig as an animal model[2] by facilitating the manipulation of genes. The pig has previously gained acceptance from the medical community for studies in organ transplantation, surgical training of medical students, and the development of novel techniques and medical devices. More recently, naturally occurring and genetically modified pig models have gained acceptance from the biomedical community as animal models for human health and diseases. This shift from the classical rodent model to the pig model for certain diseases has been largely due to the failure of several rodent models to recapitulate the physiology of the disease. One prominent example is cystic fibrosis. When the mutation that causes cystic fibrosis in humans is introduced into mice, the mouse does not recapitulate any of the human disease symptoms; however the recently developed pig model appears to fully mimic the human condition.[3-6]

Domestic swine have been selectively bred for centuries to produce animals with desired characteristics. Altering these characteristics to be more useful to researchers can be done quickly with genetic engineering, or altering the DNA sequence. The integration of foreign DNA into the genome provides a method to rapidly produce animals with a desired characteristic. In 1985, Hammer produced the first transgenic pig through microinjection of the foreign DNA into the pronuclei of the pig zygote.[7] In addition to this method there are several other methods that can be used to produce transgenic pigs including the current standard method of somatic cell nuclear transfer

(SCNT).[8] SCNT can be used in combination with simple transgenesis, as well as advanced genetic manipulations to create knock-ins and knock-outs. More recently, there have been advances in genetic manipulation of cells that will allow more cell-based transgenesis such as Zinc Finger Nucleases and Transcription Activator-Like Effector Nucleases (TALENs) that will enhance the production of swine models for human health and diseases.

The Pig: An Animal Model

The classical rodent models have proved to be very important for understanding the basic biology of genes and proteins involved in human health and disease, but with limited ability to recapitulate some human diseases, their usefulness is restricted. In addition to cystic fibrosis, murine models of diseases such as Spinal Muscular Atrophy (SMA)[9] and Parkinson's disease[10] are inadequate and swine models may prove to be superior.

The pig has many advantages as a non-rodent biomedical model because of the wealth of information about husbandry, logistical support, and reproductive management. Pigs reach sexual maturity at about six to eight months of age (domestic) and have a relatively short gestation period (~four months) resulting in multiple births. Pigs are also not seasonal breeders so mating can occur year round. There are several genetic backgrounds of both domestic and miniature pigs that thrive in a variety of environmental conditions. The anatomical structure and function of the cardiovascular system, the gastrointestinal tract, and the pancreas of the pig are very similar to humans making them ideal models for investigating diseases related to these systems. Pigs have some notable difference when compared to humans. The pig lymph node is inverted compared to the human lymph node with follicles central to a peripheral medulla.[11] Besides anatomy, genetic analysis has identified naturally occurring swine models for a variety of human health conditions such as hypercholesterolemia, puerperal psychosis, human melanocytic proliferation, and polycystic ovarian syndrome.[12-16] In addition to the spontaneous pig models, genetically engineering the pig genome has allowed us to advance the understanding of genes, proteins, pharmacological "pharming," and to develop organs for xenotransplantation.

Another potential use of the pig as an animal model is in the field of toxicology and drug discovery. With the physiologic similarities between pigs and human, the pig is becoming the non-rodent species of choice for toxicological studies. Examples are assessment of the effects of putative endocrine-disrupting compounds and drug discovery. Advantages of the pig to toxicology studies include: 1) they have a similar response to several varieties of drugs; 2) tissue and body fluid samples can be collected during the dosing period prior to euthanasia; 3) oral and parenteral dosing is similar to humans; and 4) the use of pigs eases some of the increasing societal pressure about using primates and dogs as animal models. The challenges to using swine as a model for toxicological studies include requirements for more experimental reagent, higher costs of purchase, and the requirement for more space which increases per diem costs and is not possible in some animal facilities. Some of these concerns can be addressed with the use of miniature pigs, and development and utilization of novel techniques such as xenografting procedures, proteomics, and metabalomics.



Currently there are 29 different lines of pigs (wild-type and genetically engineered) available for request from the NSRRC.

Genome and Transgenesis

The swine genome is estimated to be ~2.7 GB (about 7% smaller than the human genome), and is comprised of 18 autosomes and two sex chromosomes. The lineage of the pig and human genome (in comparison to the human and mouse) has a lower rate of nucleotide substitution with the exonic sequences showing the slowest evolution followed by the 5' untranslated regions and 3' untranslated regions, respectively.[1] Having the sequenced pig genome will be advantageous in developing biomedical models where differences exist between the pig and human. An example of this is Spinal Muscular Atrophy (SMA). Humans have two survival motor neuron genes (SMN1 and SMN2), while the pig only has a single gene for SMN. With this knowledge of the pig and human genomes, investigators made appropriate adaptations to best recapitulate SMA in the pig.[9] This was achieved by adding a transgene for human SMN2 and subsequently disrupting swine SMN to simulate a disrupted SMN1 in humans with SMA.

Table 1
NSRRC Swine Availability

Strain Name	Modification(s)	Gene(s)	Application(s)
Truline® Hampshire	none	wildtype	background for genetic modification
Truline® Duroc	none	wildtype	background for genetic modification
Truline® Landrace	none	wildtype	background for genetic modification
Truline® Large White	none	wildtype	background for genetic modification
Minnesota Mini	none	wildtype	immune system ontogeny and regulation, xenotransplantation, xenoimmunotherapy of cancer
Ossabaw	none	wildtype	background for genetic modification, obesity, diabetes, cardiovascular, Polycystic ovarian syndrome
GGTA1KO/hDAF	transgenic targeted knock-out	α-1,3-galactosyltransferase knockout; human decay-accelerating factor	xenotransplantation research
GFP NT5	transgenic	enhanced green fluorescent protein	cell tracking
FAT-1	transgenic	express a humanized *Caenorhabditis elegans* gene, fat-1, encoding an n-3 fatty acid desaturase	research in the areas of reproduction, cardiovascular, immune system, depression and cancer
Yucatan	none	Wildtype	small porcine model as background for genetic modification
NIH Mini g/g	none	MHC SLA $^{g/g}$	research in the areas of immune system, and xenotransplantation
NIH Mini c/c	none	MHC SLA $^{c/c}$	research in the areas of immune system, and xenotransplantation
NIH Mini a/a	none	MHC SLA $^{a/a}$	research in the areas of immune system, and xenotransplantation
GFP NT92	transgenic	enhanced green fluorescent protein	cell tracking
Rhodopsin	transgenic	rhodopsin P23H substitution	retinitis pigmentosa research
FVIII	tri-transgenic	human coagulation factor VIII; human alpha-antitrypsin; propeptide cleavage enzyme (PACE)	hemophilia research
FIX	tri-transgenic	human coagulation factor IX; human alpha-antitrypsin; von Willebrand factor	hemophilia research
GFP NT92-Yucatan	transgenic	enhanced green fluorescent protein	cell tracking
Tie2-eNOS	transgenic	endothelial nitrate oxide synthase	cardiovascular, exercise physiology
Tie2-Catalase	transgenic	human catalase	cardiovascular, exercise physiology
PSMA1-GFP	transgenic	GFP-Proteasome Fusion Protein	proteasome research
Multi-Xeno	transgenic	α-1,3-galactosyltransferase knockout; human decay-accelerating factor (CD55); CD39; CD59 and thrombomodulin	xenotransplantation
NLS-CAG-eGFP	transgenic	nuclear localized signal-CAG- enhanced green fluorescent protein	cell tracking
CAG-Tomato	transgenic	CAG-Tomato	cell tracking
AFP-CD	transgenic	alpha fetoprotein promoter driving cytosine deaminase	liver research
ALB-TK	transgenic	albumin promoter driving thymidine kinase	liver research

Currently, there are many ways to produce genetically modified animals, however in the pig the most effective method is SCNT. [8] The first transgenic pig to model a human health condition[17] was produced in 1996. Since that time, several transgenics, knock-ins and knock-outs have been produced (for further details see these reviews[8,18]). Somatic cell nuclear transfer provides us with an advantage over previous methodologies in that it allows gene targeting versus random insertion. The exact genetic modification can be determined prior to creating the animal. Gene targeting is a valuable tool for in vivo studies of gene expression, signaling pathways, and developmental biology and more advanced cell based transgenic techniques such as a Cre/Lox-P system and Zinc Finger Nucleases to avoid embryonically lethal targeting events are now amenable to swine genetic engineering.[8] When designing the mutation to be made, the completed pig genome will allow us to have prior knowledge about alternative splice variants, isoforms, or locations in the genome where genetic modification can occur that have no effect on the animal (so called "safe harbors"). Comparative genomic analysis will help identify conserved cross-species genes and regulatory elements that can be utilized in the development of genetically modified pigs.

Swine Resources

There are many resources available for the pig as a biomedical model. With the release of the completed swine genome (Sus scrofa Build 10), there are several genomic resources available for the pig (ftp://ftp.ncbi.nih.gov/genbank/genomes/Eukaryotes/vertebrates_mammals/Sus_scrofa/Sscrofa10.2/ or www.ncbi.nlm.nih.gov/genome/guide/pig/). In 2003, the National Institutes of Health established the National Swine Resource and Research Center (NSRRC) (www.nsrrc.missouri.edu) at the University of Missouri. The goal of the NSRRC is provide the infrastructure to ensure that investigators have access to swine for their biomedical research through production of new genetically engineered pigs and reagents from animals already available. The NSRRC serves as a central resource for reagents, information, and training related to use of swine models in biomedical research. Investigators can donate swine models to the NSRRC for maintenance, production and distribution to the entire scientific community. Currently there are 29 different lines of pigs (wild-type and genetically engineered) available for request from the NSRRC as listed in Table 1 and the website. Furthermore, the NSRRC produces three to four new models for investigators each year.

Summary

Although the pig is the relative 'new kid' on the block, pig models of human disease will continue to have a significant impact on the scientific community. With a sequenced porcine genome[19] and advancements in genetic manipulations, the pig has become an optimal model for many human diseases. However, their greatest impact is likely yet to come with increasing recognition and use of these models by the biomedical research community.

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Disclosure

None reported.

MM

Not Lost in Translation: How Study of Diseases in Our Pets Can Benefit Them and Us

by Carolyn J. Henry, DVM & Jeffrey N. Bryan, DVM, PhD

Infectious diseases, cancer endocrinopathies, toxicities, and immune-mediated diseases are just some of the disorders that share causes and clinical signs across species.



Carolyn J. Henry, DVM, MS, DACVIM, is in the Department of Internal Medicine, Hematology/Oncology Division and Department of Veterinary Medicine and Surgery. Jeffrey N. Bryan, DVM, PhD, is in the Department of Veterinary Medicine and Surgery. Both are at the University of Missouri.
Contact: HenryC@missouri.edu

Abstract

Practice-changing medical discovery requires preclinical and clinical assessment be carried out using appropriate disease models. There is growing awareness of companion animals with naturally-occurring disease as such models. They offer significant advantages over more traditional *in vivo* models of induced disease. This review describes current efforts to promote translation of discoveries between human and veterinary medicine in order to more rapidly and efficiently make progress in improving the health of all human and animal patients.

Case Presentation

The patient sat in the exam room, uneasy in the hospital surroundings as I delivered the diagnosis: osteosarcoma. The family stared in disbelief as we reviewed the images together and their questions reflected the unfairness of the situation. Why him? Why so young? As I began to talk about treatment options, prognosis, and quality of life issues, the young patient was noticeably detached from the conversation—unable to comprehend the issues with which his family was already grappling. When presented with the option of clinical trials, some organized through the National Cancer Institute, there was a mixed reaction: concern about trying something unproven and hope that this new treatment would provide a better outcome; not just in this case but for those diagnosed in years to come. Eager to pursue the most cutting-edge therapy, the family agreed to speak with the Clinical Trials Coordinator that afternoon. They would leave the hospital weighing options to be discussed further when results of staging procedures were known. Complicating all of this was the fact that the patient was uninsured.

Introduction

This is a difficult situation all too familiar in pediatric practice. However, in this case the patient was a 45-kg Rottweiler and the hospital is the Veterinary Medical Teaching Hospital at the University of Missouri. But before you dismiss the story as irrelevant to your medical practice, consider the

following: pet dogs are at approximately ten-fold risk of developing naturally-occurring osteosarcoma compared to people; genetic mutations involved in development of osteosarcoma are shared across species; therapy studies conducted using pet dogs with osteosarcoma have led to advances in limb-sparing procedures for people; and current clinical trials for canine osteosarcoma include investigation of inhalant chemotherapy, small molecule inhibitors, and novel immunotherapy approaches (http://www.vetcancertrials.org).[1-3] Many of these have direct translational application to human oncology.[4]

The Comparative Oncology Trials Consortium

The University of Missouri was one of the eight original institutions selected for inclusion in the National Cancer Institute's Comparative Oncology Trials Consortium (COTC) (https://ccrod.cancer.gov/confluence/display/CCRCOPWeb/Home), the goal of which is to design and execute clinical trials in dogs with naturally-occurring cancer to assess novel therapies for translation to human patients.[5]

Since its inception in 2003, the Comparative Oncology Program, and specifically the COTC, has initiated 18 trials and has grown to 20 member institutions in North America. All member institutions must meet strict staffing criteria and have both CT and MRI imaging equipment, a dedicated clinical trials coordinator, tissue banking capability, radiation therapy on site, and demonstrated expertise in electronic data reporting.

The first trial conducted through COTC (COTC001) evaluated a targeted AAV-phage vector designed to deliver tumor necrosis factor (RGD-A-*TNF*) to $\alpha_V\beta_3$ integrins on tumor vasculature endothelium. This dose-escalation trial enrolled cohorts of three dogs (n = 24) to determine the optimal safe dose (5×10^{12} transducing units administered intravenously) of RGD-A-*TNF*.[6] A unique feature of this trial that would have been impossible in a human clinical trial was the ability to demonstrate selective targeting of tumor-associated vasculature and sparing of normal vasculature via serial biopsy of both tumor and normal tissue. Why would someone seek to enroll their pet in a clinical trial? The answer sometimes lies in the fact that health insurance and prescription plans are uncommon for veterinary patients and standard-of-care is less well-defined. Thus, treatment options for veterinary patients can vary widely and financial constraints are often the determining factor when medical decisions are made.

The upside to this economic dilemma is that clinical trials investigating new treatment options are often a win-win for pet owners and clinical researchers. The incentive to pet owners is three-fold: 1) trial funding means that pet dogs are treated at minimal expense to the owners, 2) trials offer cutting-edge therapy not available elsewhere, and 3) the opportunity to contribute to "the greater good" is attractive in terms of both altruism and the chance to turn individual misfortune into opportunity for future patients. The value of the latter cannot be overestimated. The sense of empowerment provided by turning a frightening diagnosis into an opportunity to advance the field of oncology in ways that could have tangible benefits for humans and animals affected by cancer is highly motivating for many people enrolling their pets in veterinary clinical trials.

In the case of the COTC001 trial, pre- and post-treatment biopsy of normal and tumor tissue confirmed targeting of the $\alpha_V\beta_3$ integrins on tumor vasculature. Repetitive dosing in a cohort of 14 dogs using the defined optimal dose was well tolerated and led to objective tumor regression in two dogs (14%) and stable disease in six dogs (43%). The study findings were used to inform decisions in design of ongoing Phase I clinical trials in humans. Other COTC studies that are currently underway are facilitating protocol optimization and elucidating mechanism of action for novel anti-cancer therapies that will undoubtedly enter human clinical trials if success is demonstrated in canine models of spontaneously-occurring cancer.

The key to successful translational studies is the appropriate choice of disease model and who better to choose that model than Mother Nature? While the phrase "cancer researcher" has traditionally conjured visions of laboratory personnel assessing tumor response in rodents with artificially-induced tumors, animals with naturally-occurring cancer offer distinct advantages. Rodent models of human cancers either develop within an incompetent immune system as xenografts or arise artificially homogeneic in knockout models. They lack heterogeneity, progress rapidly, and may not recapitulate the tumor microenvironment found in human cancers to the degree that spontaneously occurring cancer in companion animals does. The internal and external environments in which cancer develops in pets share similarities with those of people. The environments encompass everything from exposure to carcinogens to fluctuations in hormone levels. Given the abundance of

examples where cures in rodents have not translated to effective therapies in people, this side-step of medical discovery into the field of companion animal medicine offers a logical new path.

Beyond the applications of canine disease models to cancer drug development, the field of comparative medicine extends into many other disciplines including neurology, infectious disease, immunology, cardiology, orthopedics, and ophthalmology to name just a few. Researchers at the University of Missouri's College of Veterinary Medicine have gained international recognition as leaders in the study of animal models of retinal degeneration, asthma, degenerative neurological disease, and osteoarthritis. Mizzou researchers have modified existing technology to validate these animal models with comparative genomics and epigenomics, flow cytometry, ex vivo immunological evaluations, and bioengineering.

The concept of comparative medicine is gaining interest of late, both in the scientific literature and in the lay press. In articles from the *New York Times* to the *New England Journal of Medicine* this past year, authors have given examples of medical discoveries that have crossed species boundaries, benefitting patients of the two-legged and four-legged varieties.[7,8] In her newly published book, "Zoobiquity, What Animals Can Teach Us About Health and the Science of Healing," cardiologist Barbara Natterson-Horowitz coins the term "zoobiquity" to describe what she calls the "fusion of veterinary, human and evolutionary medicine."[9] She describes the tremendous potential for advancement of medical science if barriers between physicians, veterinarians and evolutionary biologists are broken down, stating "we are uniquely situated to explore the animal-human overlap where it matters most urgently - in the effort to heal our patients." Admittedly, when veterinarians use the phrase "patient" to refer to a pet presented for medical care, our physician counterparts do a double-take. But the reality is that precisely the same technology and treatment options found in local hospitals for human patients are available at academic and referral institutions for veterinary patients. In certain specialties such as veterinary oncology, drugs marketed for use in people are routinely prescribed for use in pets, as comparable veterinary-labeled drugs do not exist. Ignoring that the patient is a dog or a cat, the underlying etiology and pathology are similar, demanding the same diagnostics and drugs.

Viewing diseases with this lens, the similarities become obvious. Infectious diseases, endocrinopathies,



Efficient and rapid scientific discovery through comparative genomics are enhanced by clinicians and researchers sharing knowledge between human and veterinary medicine.

toxicities, and immune-mediated diseases share causes and clinical signs across species. Most canine patients come from large "families" of siblings/littermates, often with defined pedigree information available through kennel clubs such as the American Kennel Club. This facilitates the genetic mapping of disease susceptibility traits by breed, enhancing the power of comparative studies to elucidate underlying genetic causes. If one breed is uniquely susceptible to Disease X and another breed rarely affected, comparing the genomics of these two breeds to the rest of the population often defines the underlying etiology for Disease X, as well as giving clues as to how to manage or mitigate it.

Compatibilities in Genomic Studies

The field of genomics was bolstered in 1989 when the National Center for Human Genome Research was established in response to the charge to map the human genome as part of the International Human Genome Project. With sequencing of the human genome completed in 2003, biomedical research has experienced the opening of a floodgate of opportunities for discovery in areas as broad and varied as understanding genetic mechanisms of disease to developing a more sustainable food supply. Fast forward to 2005 when the completion of a genome sequence of the domestic

dog expanded the horizons of comparative medical genomics. Opportunities for efficient and rapid scientific discovery through comparative genomics are now limited only by the imagination of clinicians and researchers and the shared knowledge between human and veterinary medicine. An inherited cancerous disease in German Shepherd dogs, renal cystadenocarcinoma and dermatofibromatosis, is found to be caused by a mutation in the gene for folliculin, bearing a striking clinical similarity to the human disease, Birt-Hogg-Dube syndrome.[10] A form of progressive retinal atrophy (Leber's congenital amaurosis type 2) that leads to blindness shortly after birth shares a similar genetic mutation between dogs and people. Using gene therapy to restore the RPE65 protein that is lost through the mutation restored vision in affected dogs and led to subsequent successful therapy in people.[11,12] Veterinary neurologists, geneticists, and physicians at the University of Missouri have worked together to identify the genetic cause of degenerative myelopathy in dogs that is analogous to human amyotrophic lateral sclerosis (aka, Lou Gehrig's Disease).[13] NIH funding for a University of Missouri-led therapy trial in affected dogs was announced in September 2012. Clearly, the pace of scientific discovery and medical innovation has quickened and we are well positioned to lead the way in this critical endeavor.

One Health/One Medicine

Few sites in the U.S. can boast the atmosphere of creative, innovative and collaborative research found at the University of Missouri. The phrase "One Health/One Medicine" refers to the sharing of resources, knowledge and effort toward the common goal of improving the health and well-being of all species. This One Health/One Medicine concept is a key component of the MU's strategic plan. The presence of a School of Medicine, School of Nursing, College of Veterinary Medicine, University Hospital and Clinics, Center for Clinical Research, Life Sciences Center, and tremendous strength in basic science research, biomedical innovation, and bioinformatics makes MU an ideal setting in which to translate medical discovery from idea to clinical implementation efficiently and at a pace to have a real impact on patients in our lifetime. This translational approach is being extended to other sites throughout the State. University of Missouri is partnering with other Missouri academic centers, the Kansas City Area Life Sciences Institute, the Institute for Conservation Medicine, the St. Louis Zoo, and the "Animal Health Corridor" extending west along I-70 and connecting MU veterinary and human medical researchers and clinicians with animal health companies and academic institutions in Kansas City.

We are also reaching outside of the state to Kansas State University's College of Veterinary Medicine and the University of Kansas to speed clinical translation of novel diagnostic and therapeutic approaches. We are rapidly moving towards a day when the patient in the examining room with osteosarcoma will receive better news of individualized therapy developed in comparative trials. Through One Health/One Medicine efforts, whether the patient is human or canine will matter less than the underlying, shared disease mechanisms for therapy decision making.

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Disclosure

None reported. MM

Internal Medicine IM@MU University of Missouri - Columbia

Animal Models in Today's Translational Medicine World

by Abhishek Choudhary, MD & Jamal A. Ibdah, MD, PhD

Recent advances in molecular technology are leading to the development of superior animal models and providing unprecedented opportunities to test both gene and pharmacological therapies prior to clinical trials in humans.



Abhishek Choudhary, MD, (above) and Jamal A. Ibdah, MD, PhD, are in the Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of Missouri School of Medicine.
Contact: ibdahj@health.missouri.edu

Abstract

Translational medicine drives progress of research along the continuum from basic biomedical research findings into clinical practice. Animal models play a central role in the above continuum. The recent explosion in molecular biology and generation of human physiological system in animals has led to an increasing use of in vivo animal models in today's translational medicine.

Translational Medicine: Introduction

Early Definition of Translational Medicine

Discovering new treatment and prevention of disease depends on a research continuum from basic biomedical research findings into clinical practice. Various methods and strategies have developed to bridge the gap between the discoveries generated in laboratory and implementing those findings in human clinical trials. The term "translational research" appeared in early 1990s but was used in the context of bench research involving molecular genetics and immunology spanning basic and clinical research.[1]

"Bench to Bedside" Definition of Translational Medicine

In basic and clinical research literature, multiple attempts have been made to define 'Translational Science' or 'Translational Medicine' or 'Translational Research.' The National Institutes of Health (NIH) offered the following definition:

"Translational research includes two areas of translation. One is the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans. The second process of translation concerns research aimed at enhancing the adoption of best practices in the community. Cost-effectiveness of prevention and treatment strategies is also an important part of translational science."[2]

Translational research according to the above NIH definition is continuous process with the ultimate goal of improving patient health by moving, efficiently and expeditiously, laboratory research discoveries into clinical human trials and finally to the patient bedside. The first stage of translational research also known as T1 in literature is a bridge between laboratory research and human clinical trials in which findings generated in laboratory though the means of animal models, cell culture and molecular studies can be used and forwarded for application in human clinical trials. The next stage in the continuum is considered as T2 which moves results from clinical trials eventually to clinical practice with the ultimate goal of improving community health (see Figure 1).

Broad Multidirectional Definition of Translational Medicine

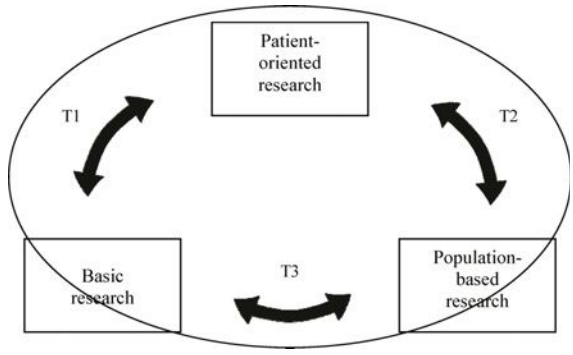
Recently, an argument was made that the concept of translational

research demonstrated in Figure 1 defines translational research too narrowly.[3] Rubio et al.[4] added a T3 arm with a new definition for translational research such that it is defined as multidirectional integration of basic, patient oriented, and population based studies leading to ultimate goal to improve public health (see Figure 2). T1 research involves bidirectional interaction between basic and patient oriented research for better scientific understanding with T2 coordinating between patient-oriented and population research for improvement of patient outcome, and finally T3 interacting between population and basic research for understanding human health and disease. Figure 2 demonstrates a dynamic interplay between basic, patient oriented, and population research with bidirectional arrows.[4] Basic research is often considered as the first step of the translational process and as per the American Cancer Society it provides the foundation of clinical research and involves laboratory studies, including animal models.[5]

Figure 1
The first stage of translational research (T1) is often carried out using animal models, cell cultures, or other experimental systems. Clinical research in the figure encompasses human subject research studies that involve direct interaction between investigators and human participants. The second translational process (T2) takes results from studies in humans and applies them in clinical practice with the ultimate goal of improving community health.



Figure 2
Model for translational research, as proposed by the Evaluation Committee of the Association for Clinical Research Training (Adopted from reference 4)



Use of Animal Models in Translational Medicine

Introduction to Animal Models

The history of animal models goes back more than a millennium, when animals were used for experimental surgery. The first textbooks on anatomy were based on dissection on pigs and apes, not on human cadavers. Use of animal models is well known for some of the greatest discoveries in history. William Harvey's great work on circulation[6] and Louis Pasteur's work in microbiology[7] are few examples of use of animal model for great discoveries. Nowadays, the main use of animal models is for translational medicine and that role is considered the central point in the multidirectional paradigm of translational research.

Examples of Animal Models in today's Translational Medicine

Translational research is primarily developed through the use of animal models. Examples in cancer research include xenografting, in which human cancer tissue is transplanted into nude mice (immunosuppressed to avoid rejection) allowing cancer development to be studied in vivo. Subsequently, the focus has shifted to development of "human physiological systems" within the mouse model. One of the steps in the development of humanized models is the production of mice with targeted mutations in genes to knock out further immune response. Human hematopoietic stem cells are then engrafted into these mice to colonize the bone marrow and differentiate into the multiple cell lineages that constitute a human immune system. These models are used in various research fields including immune, infectious and oncology research and are considered central to recent and future advances in translational research, including pharmaceutical development and personalized medicine. In a recent study by Thomas et al utilizing cultured hepatocellular cancer cells from a humanized mouse model, an experimental combination therapy was found to be effective in reducing tumor burden.[8] The above observation led to an investigator-initiated Phase 1B-2 dose escalation trial with combination drugs in patients with HCC.[8]

In addition, selective breeding, genetic modification, and advances in molecular imaging have provided a better understanding of disease processes and insights into possible interventions that were not possible previously. For a long period of time, neurodevelopmental disorders

such as autism and fragile X syndrome were considered medically untreatable. However, selective breeding and creating mouse models for behavioral phenotypes, such as the BTBR T+tf/J mouse model, have made it possible to better understand the behavioral phenotypes and design potential pharmacological interventions with the possibility that a single targeted pharmacological intervention may alleviate multiple diagnostic behavioral symptoms of autism.[9] The robustness of such data increasingly contributes to the translation of biomedical breakthroughs from preclinical studies to clinical applications. For instance, a protein known as Sema3A was found to facilitate bone regeneration in mice by simultaneously reducing bone destruction and increasing bone synthesis, and could lead to a new class of dual-action therapeutic agents for osteoporosis in humans.[10]

Use of mice is invaluable for translational research because of the ease of genetic manipulations to produce mice models for human disease. A trans-NIH initiative, the Knockout Mouse Project (KOMP), was conceived in 2003 with the aim of "knocking out" each of the genes in the mouse genome to create multiple new lines of knockout mice.[11] This project will make knockout mice available to researchers through live mouse models, embryonic stem cell clones, or frozen embryos and sperms with the goal of developing better models of human disease.

Although mice may be considered as a standardized translational device, various other animal models including primates are being developed and available for translational research and drug discovery.[12] Similar to the Knockout Mouse Project (KOMP), the National Primate Research Centers (NPRCs) established Working Groups (WGs) for developing resources and mechanisms to facilitate collaborations among non-human primate (NHP) researchers as well as to develop Genome Banking. The Genetics and Genomics Working Groups are developing resources to advance the exchange, analysis and comparison of non-human primate genetic and genomic data across the National Primate Research Centers.[13]

Limitations of Animal Models in Translational Medicine

Similar to human clinical studies, use of animal models for translational research with the goal of translation of bench research to clinic has few limitations. Involving young and healthy animals for research always carries a risk of selection bias.[14, 15] Natural dissimilarities between physiological and pathological system of various animal models and humans is one of the challenges of translation of bench research to clinical practice. Various remedies and approaches are underway to circumvent these differences. This includes work at the genetic, molecular, cellular, and clinical scale to understand the link between these elements within animals and humans. The ultimate goal of translating data between species via interdisciplinary approach will require techniques and expertise from mouse genetics, stem cell science, clinical research, comparative genomics, pathology, and medicine.

Conclusion

In the present era, animal modeling is considered the backbone of understanding various disease pathophysiologies and provides enormous opportunities for novel, effective therapy for a wide spectrum of presently untreatable disease and injuries. Recent advances in molecular technology are leading to the development of superior animal models and providing unprecedented opportunities to test both gene and pharmacological therapies prior to clinical trials in humans.

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Disclosure

None reported.

MM

The Laboratory Animal Veterinarian: More than just a Mouse Doctor

by Cynthia G. Alvarado, DVM & Lonny M. Dixon, DVM

Laboratory animal veterinarians have become irreplaceable contributors to the advancement of medical and scientific knowledge through their involvement in collaborative and independent research that ultimately benefits both humans and animals.



Lonny M. Dixon, DVM, MS, DACLAM, (left) is Director at the Office of Animal Resources, and Cynthia G. Alvarado, DVM, is a resident in the Comparative Medicine Program. Both are at the University of Missouri.
Contact: DixonL@missouri.edu

Abstract

Use of animals in research is strictly regulated by federal laws that define how the animals can be humanely housed, studied, and sold. Veterinary care for these animals is also required. Laboratory animal veterinarians serve as a unique bridge between the humane use of laboratory animals and the advancement of scientific and medical knowledge.

Introduction

It is not common knowledge that laboratory animal veterinarians and their support staff work every single day monitoring the health and welfare of the animals used in biomedical research. The role of laboratory animal veterinarians as multi-disciplinary contributors to biomedical research has grown significantly over the past fifty years. This article will give our colleagues and the general public a glimpse into the realm of laboratory animal medicine and the role that veterinarians play to ensure the welfare of animals used in research while also contributing to discoveries that benefit both humans and animals.

The History of Laboratory Animal Medicine

The history and development of the veterinary specialty of laboratory animal medicine began in 1915, when a veterinarian, Simon D. Brimhall, VMD, was employed by the Mayo Clinic.1 As the first veterinarian appointed to a research animal management position at an American medical research institution, Dr. Brimhall's role at that time mirrored some of the same responsibilities of present day laboratory animal veterinarians: providing veterinary care to research animals, overseeing animal husbandry, managing animal facilities and breeding colonies, studying animal diseases, and performing collaborative and independent research. However, until the 1940s Dr. Brimhall continued to be one of only a handful of veterinarians involved in laboratory animal medicine.

In 1944, Congress passed the Public Health Service Act, which resulted in the post-war expansion of biomedical research by increasing funding to the National Institutes of Health (NIH). As the NIH grew to become the largest federal funder of biomedical research, the demand for veterinarians in research

also increased.[2] Although veterinarians of that time were well-versed in the care of common domestic and agricultural animals, their knowledge was minimal regarding proper husbandry, veterinary care, and diseases common in research animals, especially rodents. In an effort to formalize education, training, and research in laboratory animal medicine, a group of approximately 20 dedicated veterinarians sought approval from the American Veterinary Medical Association (AVMA) for a new specialty board. In 1957, the American Board of Laboratory Animal Medicine became the third veterinary specialty to be recognized by the AVMA. The Board, now known as the American College of Laboratory Animal Medicine (ACLAM), establishes standards for training and board certification in laboratory animal medicine, organizes continuing education opportunities, and promotes research in laboratory animal science and medicine.[2]

The History of Animal Welfare Regulations

Although biomedical research surged in the 1940s, federal laws regulating animal use were not passed until many years later. In 1965, *Sports Illustrated* featured the story of Pepper, a pet Dalmatian that was stolen from her family in Pennsylvania and was sold by her dognappers to a New York hospital where she died during an experimental surgery. Soon after, *Life* published an article exposing the neglectful treatment of animals by a Maryland dog dealer. These incidents prompted the public to lobby for legislation for the regulation of animal care, housing, sale, and use in research.[4]

In response, Congress passed the Laboratory Animal Welfare Act of 1966, which was renamed the Animal Welfare Act (AWA) in 1975. In its initial form, the AWA focused on the protection of pet dogs and cats. However, after numerous amendments, the AWA has evolved to become one of two key laws governing research animal care and use. The AWA requires licensing of all facilities using animals for the purposes of research, testing, or teaching in higher education and is enforced regardless of the source of funding. The AWA provides specifications for virtually all aspects of animal care including feeding and watering, sanitation, identification, ventilation, space/housing requirements, handling, transportation, recordkeeping, and adequate veterinary care. A special agency of the United States Department of Agriculture serves as the enforcement agency of the AWA and conducts unannounced yearly inspections at licensed facilities to monitor compliance.[4]

Another key law is the Health Research Extension Act of 1985. This act provides the legislative mandate for the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy), which is enforced at all institutions that receive funding from any of the eight Public Health Service agencies, which include the NIH, Centers for Disease Control and Prevention and the Food and Drug Administration. In accordance with PHS Policy, institutions must also comply with the guidelines set forth by the Guide for the Care and Use of Laboratory Animals (the Guide). The 220-page, 8th edition of the Guide was published in 2011 and provides specific guidelines for the care and use of all vertebrates. Though the AWA and PHS Policy share many similarities, the AWA does not cover agricultural mammals used in agricultural research, birds, or mice and rats bred for research, while the PHS Policy includes specifications for the care and use of all live vertebrates.[4]

Ensuring Animal Health and Welfare

To ensure that animals receive adequate veterinary care, both the AWA and PHS Policy require that all research facilities employ an attending veterinarian (AV) with experience in laboratory animal medicine.[5] Adequate veterinary care is defined as "what is currently the accepted professional practice or treatment for that particular circumstance or condition."[4] In addition to ensuring the well-being of research animals, the duty of the AV is to ensure that the animal care and use program at the institution has the appropriate equipment, facilities, and trained personnel necessary to provide adequate veterinary care. The AV also has the responsibility to provide guidance to researchers and their staff regarding any aspect of animal use including humane handling, anesthesia, analgesia, and euthanasia.[5] The regulations also require that all research animals are observed daily for general health and that emergency veterinary care be available at all times.[4]

In addition to the AV, most large institutions find it necessary to employ additional clinical laboratory animal veterinarians to work under the AV to provide for the daily care of their research animals. These veterinarians serve as the designee of the AV, who has the authority within the institution to suspend or terminate animal use at any time if it is not operating within the standards of the AWA or PHS Policy.[4]

Both the AWA and PHS Policy also require that the AV be a voting member of the Institutional Animal Care and Use Committee (IACUC). Required at all institutions using animals covered by the AWA or PHS Policy, the responsibility of the IACUC is to ensure compliance with federal regulations by overseeing the care and use of animals at the research institution.[4] To meet this responsibility, the IACUC reviews and approves animal use protocols, which outline in detail how a researcher intends to use animals in a study. As experts in animal care and medicine, laboratory animal veterinarians are frequently consulted by IACUCs to ensure that animal use protocols are in compliance with animal welfare regulations and current standards of animal care.

Training and Certification in Laboratory Animal Medicine

The first residency training program providing veterinary care to research animals for veterinarians was funded by the NIH at Wake Forest University's Bowman Gray School of Medicine in 1959.3 The first formal training program in the uniformed services began in 1960 at the United States Air Force School of Aerospace Medicine.3 Currently, there are over 45 ACLAM recognized training programs, which range from two to four years in length. Some programs offer residency training in conjunction with additional coursework or extensive research training, resulting in a Master of Science or PhD degree. ACLAM-recognized residency training programs are designed to prepare veterinarians for ACLAM-board certification by providing an environment for didactic and clinical training in laboratory animal biology, pathology, medicine and surgery as well as animal husbandry, resource management and responsible animal use. These residency programs allow trainees to become familiar with the numerous regulations and policies relating to the welfare of animals used in research. Trainees are also encouraged to be involved in collaborative or independent research.

Currently, licensed veterinarians interested in board-certification in laboratory animal medicine must have completed either an ACLAM-recognized residency training program or have six years of relevant, full-time experience in laboratory animal medicine. In order to ensure that candidates have a working knowledge of the scientific method, they must serve as first author on a hypothesis-based research paper published in a peer-reviewed journal. In addition, admission into the College requires passing the ACLAM board certification examination.[3]

The ACLAM board examination tests knowledge regarding the biology, husbandry, and clinical medicine of species commonly used in research. Currently, 60-70% of animal-related questions are based on species used most commonly in research, which include mice, rats, rabbits, non-human primates, dogs, and pigs. Other species, such as cats, frogs, ferrets, guinea pigs, zebrafish, and invertebrates make up the remainder of animal-related questions. Candidates must also have a solid knowledge base regarding the research uses for these animals and possess proficiency in research facility design and management, animal welfare regulations, and research methods and equipment. A contemporary knowledge of advancements in the biomedical research field and laboratory animal medicine is also required to pass the exam, which may include questions based on recent articles from selected peer-reviewed journals. Once candidates have passed the board examination they are awarded the title of "Diplomate of the American College of Laboratory Animal Medicine" (DACLAM).[3]



The Public Health Service Policy on Humane Care and Use of Laboratory Animals requires that all research animals are observed daily for general health and that emergency veterinary care be available at all times.[4]

Careers in Laboratory Animal Medicine

After completion of residency training, many veterinarians trained in laboratory animal medicine may chose to remain in a clinically-oriented career, working as an institutional AV or clinical veterinarian in academia or industry. These veterinarians enjoy practicing veterinary medicine in a field with a wide range of animal species, including transgenic animals or those with other genetic mutations. For example, on a typical day a laboratory animal veterinarian's patients may include a genetically engineered mouse, a 500-lb transgenic pig, or a herd of sheep used for antibody production.

In addition to providing veterinary care to research animals, another duty of a clinical laboratory animal

veterinarian includes researcher support. Veterinarians are frequently involved with training and assisting researchers and their staff in specialized techniques and procedures and providing assistance with experimental design and protocol writing. Clinical veterinarians may have additional responsibilities, such as serving on the IACUC, teaching in higher education or training residents in an ACLAM-training program.

Other veterinarians trained in laboratory animal medicine may opt to pursue a career in research. Due to their training, these veterinarians are attractive as research collaborators due to their extensive knowledge of veterinary medicine and animal models of disease.



Laboratory animal veterinarians ensure the welfare of animals used in research while contributing to discoveries that benefit both humans and animals.

Laboratory Animal Medicine at the University of Missouri

Established in 1968, the Comparative Medicine Program (CMP) is the NIH-sponsored and ACLAM-recognized laboratory animal medicine residency training program at the University of Missouri (MU). In addition to providing training in laboratory animal medicine, the MU CMP also focuses on exploring the comparison of pathology and diseases in research animals to those of other species, including humans. Since the program began, more than 100 veterinarians have completed the program, of which 74 have become ACLAM diplomates. Of the 800 active ACLAM diplomates, the MU CMP has trained 62, which is approximately 8% of all active diplomates. The MU CMP allows veterinarians to combine their laboratory animal medicine training with a research program. Upon completion of the residency training program, relevant coursework, and research, a MS or PhD degree is conferred. As of 2012, there are 10 trainees in the MU CMP.

Unique components of the MU CMP include access to the NIH-funded Rat Resource and Research Center and the National Swine Resource and Research Center, the only centers of their kind in the country. The Mutant Mouse Regional Resource Center at MU is one of four in the US. These centers serve as repositories for cryopreservation, production, and characterization of genetically-engineered rodent strains and swine to ensure the continued availability of valuable genetically engineered animals to the biomedical research community. MU is also home to an animal biosafety level-3 research facility where select agents, such as *Bacillus anthracis* (anthrax) and *Yersinia pestis* (plague), are studied. In addition, MU is one of only six public universities in the country that have schools of medicine, veterinary medicine, engineering, law, and agriculture on one campus. This provides MU CMP trainees with extensive opportunities for interdisciplinary research collaboration.

Conclusion

Although rodents continue to be the predominant animals used in research, laboratory animal veterinarians are considered to be more than just "mouse doctors." They are recognized as valuable members of the research team as sources of extensive knowledge regarding laboratory animal medicine and the humane use of animals as research models.. Laboratory animal veterinarians have also become irreplaceable contributors to the advancement of medical and scientific knowledge through their involvement in collaborative and independent research that ultimately benefits both humans and animals.

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Disclosure

None reported.

MM

Adult Day Care: An Important Long-Term Care Alternative & Potential Cost Saver

by Richard E. Oliver, PhD & Meichele Foster

Physicians interested in learning more about adult day services can find an up-to-date list of licensed providers through the Missouri Department of Health and Senior Services.



Richard E. Oliver, PhD, is Dean, School of Health Professions, and Meichele A. Foster, MPA, is Assistant to the Dean for Strategic Opportunities, School of Health Professions. Both are at the University of Missouri.
Contact: Oliverr@health.missouri.edu

Abstract

As the number of elderly continues to increase dramatically, families are often faced with exploring how to secure needed care and assistance for a frail or functionally impaired relative. These decisions are often made in times of high stress and families frequently do not have the time needed to explore all potential care options. One important source of family support that is often overlooked or not even known to be a feasible option is adult day care. This article will help the reader gain better understanding of this important service and who might benefit from enrollment in such a program.

Introduction

Adult day care programs are an invaluable alternative to traditional long-term care placement, provide needed support to family caregivers and can often lessen health care expenses for consumers and the health care system.[1, 2] Programs are staffed by a full range of interdisciplinary professionals who provide clients with health monitoring, leisure activities, socialization opportunities and assistance with activities of daily living (ADLs). For caregivers, adult day programs offer respite, support group opportunities and access to supplementary networks and resources. In addition, these centers can reduce out of pocket health care expenses, lessen use of high cost centers such as emergency departments and delay institutionalization.[1, 2, 3]

Missouri has over 120 licensed programs, with a majority in the metropolitan St. Louis area. Adult day centers are regulated by the Missouri Department of Health and Senior Services and are subject to inspections similar to those for skilled nursing and residential care facilities. Care plans, current physician's orders for each participant and standards for quality care ensure program participants receive individualized medical oversight while in attendance. Missouri programs are required to provide assistance in ADLs, up to four hours of planned group activities each day, meals, and arrangements for any special dietary needs, and observation of health, functional and psychosocial status of program participants. Additional health services vary, but typically include regular vital sign monitoring, counseling, supervision of diabetic needs, assistance with bathing, medication set-up and

administration, connection to contracted therapy providers and transportation services.

According to the National Alliance for Caregivers and the AARP, there are an estimated 44 million Americans providing unpaid care to a family member or loved one. A substantial body of research shows that a majority of caregivers are unprepared for their role and generally have little to no support. [4,5,6] Resources like the Adult Day Connection (ADC), at the University of Missouri School of Health Professions, provide respite and are an alternative to placement in an assisted living or long-term care facility.

Case One Presentation

Roger is 77-years-old. Roger is two years post-ischemic stroke. He attends ADC two days per week while Betty, Roger's wife, runs errands and has time alone. Their children live in other states and Betty is his sole caregiver. Roger uses a wheelchair, has poor vision, impaired judgment, increased fall risk, is unable to verbally communicate effectively and requires medication several times each day. "Adult day care has been a lifesaver for us. I know I could not do this myself," says Betty.



A volunteer brings a puppy to the Adult Day Connection for socialization with participants.

While at the ADC, the staff monitor Roger's vital signs, observe for physical and cognitive changes, administer medications throughout the day and assist him with his toileting needs. In addition, Roger enjoys interaction with other participants, is served lunch, two snacks and benefits from physical therapy provided by the School of Health Professions' physical therapy faculty and students.

Daily assessment and observation help promote early detection for urinary tract infections, dietary and nutritional problems and diabetic related concerns. Even small changes are communicated to caregivers at arrival and pick-up times in an effort to encourage prompt medical intervention through their primary care physician.

For families like Roger's, the ADC provides a safe and engaging environment for him while Betty experiences much needed respite and enjoys a reprieve from her always watchful duties as a caregiver. Full-time caregivers like Betty are significantly more likely to experience depression, an increased risk of heart disease and less likely to engage in self preventive health behaviors.[7, 8, 9] It is estimated that elderly spousal caregivers (aged 66-96) have a 63% higher mortality rate than noncaregivers the same age.[10] One client's caregiver called the ADC "an oasis for the cared-for and caregiver alike." The ADC staff monitor client's physical and cognitive status and promptly alert caregivers to any changes. Early detection of health status changes and good communication with caregivers can lead to a quick trip to a primary care physician versus an alarming and expensive visit to the emergency department. The ADC staff are ever watchful of the caregiver's health and stress level. Constantly ready with additional resources and support, the center's staff are equally quick to act when caregivers show signs of distress or declining health. Betty reports that utilization of adult day services has helped to maintain Roger's general health and has enhanced quality of life for both.

Adult Day Care and Meeting Increased Demands Under ACA

The implementation of the Patient Protection and Affordable Care Act (ACA) has all providers searching for ways to efficiently and effectively control health care costs



Participants Diana and Leta enjoy a laugh during exercise program.

and maintain the highest quality care. Research suggests that adult day services can play a significant role in this discussion. According to the MetLife National Study of Adult Day Services, participants of adult day centers have higher incidents of chronic disease including hypertension (46%), physical disability (42%), cardiovascular disease (34%), diabetes (31%), mental illness (25%), and developmental disability (20%).[1] Programming and activities designed to address these pressing health issues are important to reducing health care costs. At the ADC, the center uses the evidence-based Arthritis Foundation exercise program on a daily basis for all participants and offers individualized workouts to address cardiovascular disease and diabetes. Medication management and nutrition counseling are provided by center staff and other rehabilitation services (physical, occupational, speech therapy and neuropsych services) are available through the MU School of Health Professions at no or reduced costs. In addition to maintaining or improving a client's general health, adult day services can delay placement into a long-term care facility. Community based options are in demand and boomers are readily choosing aging in place alternatives for themselves and their aging parents.[1]

Case Two Presentation

The ADC provided the optimal choice for Edna. Edna was 84 and lived with her daughter and son-in-law Sue and Bob. Edna had been diagnosed two years earlier with dementia and was no longer able to stay home alone. Sue and Bob both worked full-time. Edna needed help with ADLs, requiring staff assistance in the restroom and set up for grooming and meals. Her cognitive decline and low income qualified Edna to receive adult day services through the Missouri Medicaid program. Edna attended the ADC for 14 years before being placed in a long-term care facility.

Fourteen years ago, Sue could have selected a skilled nursing facility to provide Edna's care. The use of adult day services allowed Edna to remain at home and saved the state of Missouri considerable resources. The expense to Missouri's Medicaid program was substantially less than the cost of entering a skilled nursing facility. Based on the average daily rate for Missouri today, her semi-private nursing home bed would have cost $139 per day, compared to $70.20 per day of adult day services. This amounts to nearly $500,000 in savings to Missouri taxpayers. Unlike many caregivers, Sue and Bob reported they have not experienced negative financial setbacks due to lost wages or poor personal health or well being sometimes associated with being a full-time caregiver.[6, 11, 12, 13] As demonstrated at the ADC, Edna's delayed institutionalization yielded considerable cost savings. Adult day services are clearly at the intersection of cost effective care and the highest quality of life for these individuals.[1, 14, 15]

An important factor in ensuring the long-term viability of this care option is increased utilization. Area Agencies on Aging, family and friends and self-referral were the top three referral sources reported by adult day centers.[1] Enhancing the dialogue between adult day service providers, physicians and other healthcare providers to promote greater awareness and utilization of services is essential. Nationwide, fewer than 50,000 individuals use adult day services.[1] Of the 4,601 adult day center in the U.S., less than one-third report having a waiting list. According to the MetLife National Study of Adult Day Services, the Patient Protection and Affordable Care Act "provides potential new avenues of federal support for adult day services. This includes



Group activity and exercise at the Adult Day Connection.

the Community First Choice program which adds 6% additional funding to states for home and community based care. Pilot programs supporting Medicare funding for adult day services are also currently being evaluated."[1] Utilization is key to demonstrating cost effectiveness.

Currently, adult day programs accept private pay, long-term care insurance and Medicaid. There exists a substantial body of research highlighting adult day services benefits to individuals and their caregivers. Less is known about actual cost savings. The experience at the MU ADC suggests that utilization of the center does enhance quality of life as well as reduce use of high cost centers within the health care system, thereby, reducing health care costs.

How To Refer a Patient for Adult Day Care

Physicians interested in learning more about adult day services can find an up-to-date list of licensed providers at the Missouri Department of Health and Senior Services website, http://health.mo.gov/seniors/nursinghomes/pdf/ADC-licensed.pdf. The Missouri Adult Day Services Association (MoADSA) can also provide information about programs in your area; see http://www.moadsa.org/ for more information. State regulations require current physician's orders, including medications, diagnoses, activity limitations and restrictions, dietary modifications, and indicated therapies. Programs work with discharge planners and social workers to ensure a smooth transition into the day program, work out transportation arrangements, and secure assistance with funding if needed.

Ideally, as more citizens gain increased awareness of long-term options, the role of adult day health services on the continuum of care will be better understood and utilized in Missouri.

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Pain Management Mini-Series Part II

Chronic Opioid Drug Therapy: Implications for Perioperative Anesthesia and Pain Management

by Robert B. Fisher DO, Quinn L. Johnson, MD & Joseph L. Reeves-Viets MD

There is little question that daily opioid-maintained chronic pain patients are becoming more numerous and are coming to health care facilities for procedures and surgery with increasing frequency.







Robert Fisher, DO, (top) is Director of Chronic Pain and Assistant Professor of Anesthesiology of Clinical Anesthesiology. Quinn L. Johnson, MD, (left) is Interim Chairman, Department of Anesthesiology and Perioperative Medicine, and Director of Anesthesiology of the Missouri Orthopedic Institute. Jospeh L. Reeeves-Viets, MD, MBA, (right) is Director of Cardiovascular Anesthesia and Professor of Anesthesiology and Clinical Anesthesiology. All are at the University of Missouri School of Medicine.
Contact: johnsonql@health.missouri.edu

Abstract

In the U.S., there is a growing percentage of chronic pain patients requiring surgery. Chronic pain patients require careful evaluation and planning to achieve appropriate acute pain management. Peri-surgical pain management often requires continuation of previously prescribed chronic pain modalities and careful selection of multimodal acute pain interventions. This article will provide a broad overview of chronic pain, definitions, and current recommendations for the treatment of perioperative pain in patients maintained on opioid therapy.

Background

Chronic pain is usually defined as pain persisting six months or longer in a characteristic pattern or location, though criteria may vary with the approach to measurement, or the purpose of the study. Chronic pain with a special etiology may have different defining criteria.[1] For example, Post Herpetic Neuralgia is chronic pain for more than 120 days after the first appearance of the H. zoster/shingles rash. In the U.S. the Institute of Medicine of the National Academies estimated that chronic pain affects one hundred million Americans.[2]

The economic impact of chronic pain is difficult to gauge but is estimated as costing $61.2 billion dollars per year, which excludes the costs attributed to treatment. Interestingly, 76.6% of this lost work time was due to decreased worker efficiency not absence from work.[2]

A variety of noneconomic costs associated with chronic pain need to be considered. According to a 2006 American Pain Society survey, more than 77% of chronic pain patients suffer clinically significant depression, and more than half of chronic pain patients believe they have little or no control over their pain. Unfortunate and unintended corollaries to the noneconomic costs of pain attend the therapy itself. Estimates suggest that the total cost of prescription opioids diverted for nonmedical uses in the U.S. each year since 2005 exceeds the total value or cost of illegal opioids and cocaine smuggled into the country each year. Prescription analgesics have resulted in a large proportion of unintentional drug overdose deaths in the U.S. In 2007, prescription analgesics accounted for 12,000 of the 28,000 unintended prescription drug deaths reported.[3]

Management of Acute Pain in Chronic Pain Patients

Surgical pain had traditionally been viewed as an acute problem treated mainly with opioids in the recovery room. Recent arguments have been put forward that postsurgical or posttraumatic pain is best treated with a multimodal approach. This is especially true if the pain is severe and long-lived enough to interfere with or impede the recovery process.[4] This multimodal approach may include: systemic analgesics, anti-inflammatory agents, local anesthesia with other adjunct medications, use of heat/cold, electrical stimulation, drugs applied via cutaneous delivery systems and rehabilitation activities. Literature on multimodal pain management strategies report measurable benefits, including: reduced pain scores, decreased length of hospital stay, and in colorectal surgery, faster return of bowel function.[5] There is less support for the multimodal approach compared to conventional postoperative analgesia for surgery in other body sites, when the surgery is minor in nature, or is associated with minimal postoperative pain.

A major goal of the multimodal approach for inpatient procedures is to 'fast track' patients. This includes early mobilization, sense of patient control in regard to pain, rapid return of ability to eat, and minimization of stress responses to surgery to facilitate healing.[6] An estimated 34.7 million outpatient surgery visits were reported in 2006 in the U.S.[7] This trend toward outpatient surgery and shorter hospital stays for inpatient surgery over at least the past thirty years has resulted in the extension of 'fast track' protocols to outpatient procedures.

The actual number of patients using chronic opioids is difficult to estimate due to the variable and limited amount of data on patients with long-term opioid use. One study using a large U.S. population from 2009 included both cancer and noncancerous chronic pain patients indicated 0.65% utilized opioids for six months or longer.[8] A Dutch epidemiologic survey reported that 0.29% of population with non-cancer related pain reported opioid use regularly or continuously.[9] Another source reported long term opioid therapy usage rates in two large U.S. west coast health care plans ranged between 0.93 to 2.49% of adults.[10] The number of prescriptions for opioids has steadily increased starting in the early 1990s up to the present date. With the increased use of opioids in the U.S., it is reasonable to conclude that more patients being treated with opioids long-term are coming to surgery. One report on the epidemiology of ongoing opioid therapy estimates that 12% of surgical patients are chronic opioid users. Other studies conclude that frequency may be overestimated since the data on opioid-using patients is widely variable.[11] Regardless of the lack of quantitative data, every facility will be faced with a significant percentage of patients who are using opioids long-term and coming to surgery.

A significant challenge exists in how to improve perioperative acute pain management for chronic pain patients concurrently utilizing long-term opioid therapy. The first step is to identify any current long-term opioid medications. Significant information to obtain includes: which opioid is prescribed, the dosage, period of time it has been used and route of delivery. It is important to identify chronic pain patients using opioids for several reasons. It is likely that these patients will have increased tolerance, necessitating significantly higher doses to achieve satisfactory perioperative analgesia. In order to have a baseline for pain medications, the current medications along with their dosage will be used to calculate the equivalent doses that will be administered in the perioperative period. It is known that patients taking opioids daily for more than two weeks are likely to develop tolerance and require higher doses to maintain the same effect,[11] and it has been documented that the opioid tolerant patient requires much higher doses to achieve satisfactory acute pain management associated with trauma and surgery.[12,13]

Pain control should be assessed preoperatively and acute pain treated if possible.[14] Once the daily opioid dose is established, routes of delivery should be determined. The typical route is oral, but transdermal systems and subcutaneous or implanted spinal infusion pumps may be alternative routes of delivery. Manufacturers of transdermal buprenorphine and fentanyl consider their use contraindicated for post-operative pain management due to inflexibility in dosing which may result in delayed drug absorption postoperatively.[15,16] It is suggested that immediate release opioids at equianalgesic doses be given postoperatively when fentanyl patches have been removed.[17] At least one implanted spinal infusion pump manufacturer recommends leaving its parameters unchanged in the perioperative period to avoid interfering with a balanced analgesic regimen.

Preoperatively it is important to maintain patients on their chronic opioid analgesics in a fashion adapted to the perioperative situation requirements. Accurate estimations of total daily opioid use previously obtained from the patient's history are essential in order to provide

patients with at least 50% of their typical daily opioid dose in order to avoid opioid withdrawal. It is preferable that patients have their morning opioid dose, especially if they are on long acting drugs.[18] Although patients are typically instructed to be NPO for surgery, patients who chronically use opioids should be specifically instructed to take their morning pain medications. Patients who miss their typical morning opioids may receive an equianalgesic dose intravenously, factoring in the potency difference between IV and PO routes.

In managing patients on chronic opioids coming to surgery, thought should be given to diagnosis of tolerance, physical dependence, withdrawal, acute breakthrough pain and substance abuse. Mechanisms for tolerance have been attributed to increased sensitivity of NMDA receptors,[19] increased concentration of spinal dynorphin A[20] and decreased responsiveness of mu opioid receptors.[21] Possibly intertwined with tolerance is the phenomenon of opioid-induced hyperalgesia or the lowered pain threshold of patients exposed to opioids. This is present after chronic opioids but may also be present following acute opioid administration.[18] Physical dependence to opioids is a physiologic and pharmacologic condition that may occur in as little as two weeks of daily opioid use. With physical dependence, abrupt cessation of opioids or the reversal of their effects by opioid antagonists results in opioid abstinence or withdrawal.[22] While not necessarily life threatening by itself, withdrawal is extremely unpleasant and has a wide variation in duration. The withdrawal produces abdominal cramps, severe malaise, intensification of the suffering associated with existing pain, and adrenergic hyperactivity.[23]

Regardless of the anesthetic technique selected for the patient (general versus regional) the principle of utilizing at least 50% of the patient's daily opioid dose to avoid withdrawal should be followed. Regional anesthesia has not been shown to be superior to general anesthesia for chronic pain patients. There are no prospective studies that support the use of regional anesthesia as a technique to avoid a former chronic opioid user from resuming chronic opioid use postoperatively. Attempting to provide analgesia solely through regional opioids either intrathecal or epidural postoperatively resulted in withdrawal in some case reports.[24,25,26] Management combining systemic opioids with lipophilic epidural opioids has reportedly avoided this complication.[27,28,29] It is preferable to avoid administering opioid antagonists such as naloxone or partial agonist-antagonists such as nalbuphine to treat minor opioid side effects intraoperatively or postoperatively as this may bring on withdrawal and severe pain.

Intraoperative pain is variable, and patients on daily chronic opioid maintenance may require up to 20% above the usual daily opioid dose, factoring in the nociceptive potential of different procedures.[30] The character of postoperative pain may shift for instance from predominantly neuropathic to postsurgical nociceptive pain. The possibility of intraoperative withdrawal should be kept in mind. It typically presents as hemodynamic instability accompanied by autonomic hyperactivity, reflected as tachycardia and hypo- or hypertension. The pupils are frequently dilated and patients will often have gastric hypersecretion and sweating. One method of dosing the analgesics toward the end of the procedure includes reversing neuromuscular blocking agents and then titrating the analgesia to respiratory rate.

In the postoperative period, patients on chronic opioid therapy will likely have significantly higher analgesic requirements and report more intense pain. Breakthrough pain is more likely to be present in these patients postoperatively and subjectively be reported to be more severe. The expectation of a low pain threshold and increased need for procedural analgesia, coupled with the likelihood of more complicated post procedural analgesia management, make multimodal analgesia attractive.

The cornerstone remains maintenance of the preoperative daily opioid dose, combined with treatment of the acute post procedure pain utilizing multimodal therapies. Intravenous opioids delivered via patient controlled analgesia (PCA) are the most common approach, beginning as early as the post operative care unit. It is common to use PCA with a basal infusion in these patients because of their expected higher analgesic requirements. They are less likely to experience over-dosage with a basal infusion mode than in opioid naïve patients.[31]

Multimodal Adjuncts for Pain Management

Multiple studies have documented the opioid sparing effects of both upper and lower extremity nerve blocks in opioid naïve patients. Although there is little literature dealing directly with chronically opioid maintained patients, the benefits of nerve blocks are thought to be equally efficacious. Neuraxial blocks have been studied in chronically opioid maintained patients and the neuraxial opioid doses have been higher in this group compared to opioid naïve groups.[29,32] The neuraxial opioids that were most successful analgesics tended to be lipophilic, such as

fentanyl and sufentanil.[32] This may suggest that part of the analgesia is due to systemic effect of lipophilic epidural opioids, as it is generally accepted that they exert a portion of their analgesia systemically.[26] In any case, even these neuraxial opioid treated patients, as was previously mentioned, require systemic opioids to avoid potential withdrawal. Regional analgesia and neuraxial blocks, especially on the day of the procedure can make a positive contribution to the control of post procedure pain.

Non-opioid analgesics may prove useful in treating the post-operative acute pain in chronic opioid maintained patients when coupled with their daily opioid dose and opioids for perioperative pain. Non Steroidal Anti Inflammatory Drugs (NSAIDS) are frequently employed in pain management and have been shown to be of benefit in perioperative pain.[33,34,35,36,37] NSAIDs can be administered by a number of routes. Ketorolac, the most common agent available in the United States, can be given intravenously. It has a useful opioid sparing effect and an onset of action commonly 45 minutes after IV administration. It can be given at the start or near the beginning of the procedure so that it is exerting an effect in the PACU. Acetaminophen has a modest but useful analgesic effect and can be given perioperatively without impacting hemostasis or potentially wound healing. It is used perioperatively by multiple routes including more recently in the United States intravenously.

Ketamine has also proven useful in the perioperative management of chronic opioid-maintained patients. Ketamine has been utilized extensively to treat acute and chronic perioperative pain.[38,39,40] Ketamine has multiple pharmacologic effects, including direct analgesic effects, but its NMDA antagonist properties are the likely explanation for its ability to enhance the analgesic effects of opioids in patients who typically require much higher doses of opioids to attain satisfactory pain relief.[41,42,43] In opioid naïve patients, ketamine is demonstrated to have an opioid sparing effect with less pain, primarily on the day of the procedure,. Other experience showed that in cancer patients on high dose opioids, as well as perioperative patients maintained on chronic opioids, ketamine provided improved pain control and/or lowered opioid consumption.[41,42,43] Ketamine is usually given as a bolus intravenously early in the procedure. The usual bolus dose is 0.25-0.5 mg/kg, based on ideal body weight. It is generally accepted that the incidence of psychomimetic side effects in this dose range is uncommon. Infusions of ketamine subsequent to the bolus dose are less frequently used. The dose is 1 to 6 micrograms/kg/min. begun in the perioperative period and continued as needed for one to two days post procedure. One recent prospective study of 'opiate-dependent' lumbar spine surgery patients who were treated with bolus ketamine followed by intraoperative ketamine infusion reported significantly decreased morphine consumption at twenty four and forty eight hours post surgery compared to the non-ketamine placebo patients.[44] The bolus dose protocol enjoys fairly common clinical use due to its measurable effectiveness and ease of application to many perioperative situations involving chronic opioid managed pain patients. Intranasal ketamine for breakthrough pain in chronic opioid managed pain patients has been used extensively and successfully.[45] More recently intranasal ketamine has been effective in acute postoperative pain associated with dental molar extraction.[46] It may be useful for other acute post procedure pain.

Several other drugs, including oral dextromethorphan and gabapentin, have been used for perioperative pain with variable results. Clonidine and dexmedetomidine are advocated for use in chronic opioid maintained patients as they tend to attenuate opioid withdrawal while being modest coanalgesics. Dexmedetomidine has been used to attenuate symptoms of opioid withdrawal while weaning from parenteral opioids.[47]

Post-Operative Pain Management

Procedures associated with high levels of post-operative pain will frequently result in the patient requiring higher opioids doses than their preoperative daily opioid maintenance dose. These patients will tend to require IV and regional opioids longer than their non-opioid maintained cohorts. In patients who require post-operative IV opioids, conversion to oral and other chronic baseline routes precedes discharge. One useful method involves converting the daily IV opioid dose to its equivalent daily dose oral opioid, with 50-70% of this dose prescribed as a long acting opioid. The other 30-50% of the equivalent dose is given as short-acting opioids on an as-needed basis. As the surgical pain decreases the as-needed analgesic is tapered and discontinued. Converting to oral medication as soon as possible will facilitate patient discharge. In these situations the patient is likely to be on a larger daily opioids dose postoperatively. The managing physician may need to call on the patient's pain management physician for consultation. This also serves to bridge the patient back to the pain management physician's care. The consultation of a psychiatrist, or in the case of

a substance-using patient, an addictionologist may assist in the approach of these patients to their previous level of function. Without a doubt these patients add a level of complexity to the perioperative situation. There is little question that daily opioid maintained chronic pain patients are becoming more numerous and are coming to healthcare facilities for procedures and surgery with increasing frequency. They represent an ongoing challenge for the physicians managing them in the perioperative period to successful discharge.

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Disclosure

None reported.

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Role of extracellular GAPDH in *Streptococcus pyogenes* Virulence

by Kirsten A. Seidler & Norbert W. Seidler, PhD

***Streptococcus pyogenes* GAPDH becomes surface-localized by a currently unknown mechanism and on the surface of the pathogen it can wreak havoc.**



Kirsten A. Seidler (left) recently graduated magna cum laude (Class of 2013) from the University of Missouri with a Bachelor of Science degree in Biochemistry. Norbert W. Seidler, PhD, serves as professor and chair of biochemistry at Kansas City University of Medicine and Biosciences in Kansas City, Mo.
Contact: nseidler@kcumb.edu

Abstract

Pathogens generate molecules, or virulence factors, that enable them to colonize host tissues through several mechanisms, including adhesion to host tissues, or superior invasive capability. Some allow the pathogen to evade the host's immune system. Many of these molecules are proteins that are exported to the cell's surface or secreted. Curiously, GAPDH, which is a glycolytic enzyme, is also a virulence factor that has been shown to contribute to *Streptococcus pyogenes* pathogenicity by each of these mechanisms.

Introduction

Group A streptococci (conveniently abbreviated as GAS) represent a class of pathogenic microorganisms that cause a tremendous amount of human affliction. Importantly, GAS infections are considered highly communicable and a public health concern. The clinical presentations of GAS infections range from mild cases, such as pharyngitis and pyoderma, to more severe cases, such as rheumatic fever, rheumatic heart disease, and other invasive infections. Rheumatic fever occurs as a consequence of these mild GAS infections and represents an inflammatory disease in which antibodies created in response to the microorganism cross-react to one's own tissues. Rheumatic fever may lead to rheumatic heart disease through repeated bouts of carditis (i.e. inflammation of the heart muscle) that resolve with fibrosis. It is thought that immune response factors, which are under genetic control, may account for pathogenesis of rheumatic heart disease.

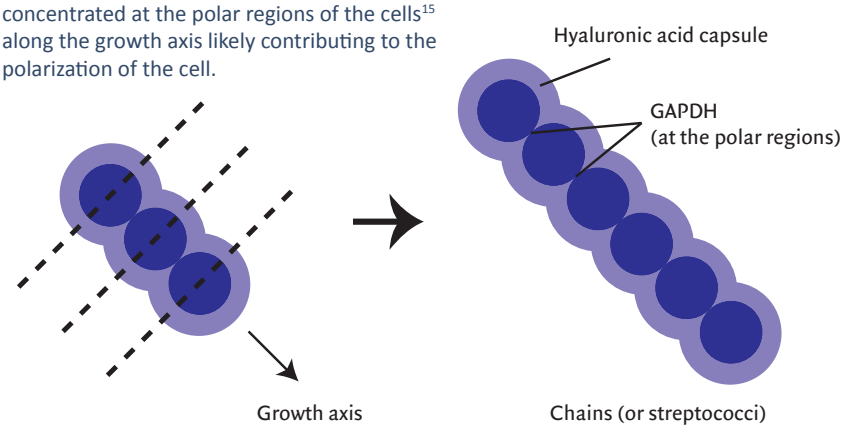
More than 700 million people have mild cases of GAS infection worldwide.[1] Severe cases, such as rheumatic fever and rheumatic heart disease, are responsible for an estimated 517,000 deaths per year globally. Rheumatic heart disease, which by far has the greatest impact on mortality and morbidity of GAS-related infections, contributes more than 282,000 new cases per year globally. Developing countries have the highest prevalence rate of rheumatic heart disease (i.e. 2 per 100 inhabitants).[2] The prevalence rate in the United States is approximately 3 per 10,000 children ages 5-14.[1] The annual number of deaths in the U.S. due to rheumatic heart disease, has fallen from 15,000 in 1950 to 3,100 in 2005-2008.[2] Furthermore, from 1996 to 2006, the rate of mortality due to either rheumatic fever or rheumatic heart disease dropped about 8%. Despite these encouraging statistics GAS-related infections remain a major public health concern.

Diagnosis

A reference manual (i.e. Communicable Disease Investigation Reference Manual) that was released by the Missouri Department of Health and Senior Services in 2002 states that invasive GAS infections may develop into any of the following clinical manifestations: pneumonia, bacteremia in association with cutaneous infection (e.g. cellulitis, erysipelas, or infection of a surgical or nonsurgical wound), deep soft-tissue infection (e.g. myositis or necrotizing fasciitis), meningitis, peritonitis, osteomyelitis, septic arthritis, postpartum sepsis (i.e. puerperal fever), neonatal sepsis, and nonfocal bacteremia. GAS infections in some instances may result in shock and multi-organ failure. The laboratory criterion for diagnosis is identification of *Streptococcus pyogenes* by culture. Penicillin is the antibiotic of choice for GAS infections. There are rapid 'strep' tests available that take approximately 15 minutes, utilizing proprietary antibodies to detect specific GAS polysaccharide antigens.

Figure 1
Morphology of Streptococcus pyogenes

The cells are spherical, asymmetrical, and exhibit polarity. Parallel dashed lines represent the equatorial axes of the cells. The direction of growth is indicated by the diagonal arrow and cell division takes place along a single plane. During cell division, the cells remain attached, resulting in chains of cells. GAPDH is concentrated at the polar regions of the cells[15] along the growth axis likely contributing to the polarization of the cell.



The primary care physician typically encounters 'strep throat' (the colloquial term for streptococcal pharyngitis). This condition, which may also involve the larynx, results in fever as well as sore throat. This infection aggravates the immune system; therefore, enlargement of lymph nodes is also common. Thirty-seven percent of children under the age of 18 that present with sore throat contain positive strep cultures.[3] Interestingly, 12% of children that do not exhibit any symptoms appear to have streptococcal microorganisms as part of their flora. In another study,[4] it is estimated that approximately 20% of asymptomatic children are positive for streptococcal microorganisms. These observations suggest that streptococcal microorganisms may in some way be avoiding immune surveillance.

Streptococcus represents a genus classification of bacteria. This genus is described as spherical Gram positive bacteria that can be seen as round cells grouped together in a chain like fashion (see Figure 1). The various species within the genus of Streptococcus are divided into three subcategories (i.e. α-, β-, and γ-hemolytic), based on the growth properties in culture. *Streptococcus pyogenes* is a β-hemolytic bacterium, meaning that in blood agar cultures, it completely lyses red blood cells. The lysis of red blood cells is due to the exotoxin, streptolysin (i.e. two types: streptolysin O and streptolysin S), that is also thought to participate in pathogenesis. *Streptococcus pyogenes* belongs to the Lancefield serogroup A, which defines this streptococcal microorganism as a Group A member.

What is GADPH?

GlycerAldehyde 3-Phosphate DeHydrogenase (GADPH) is a highly conserved glycolytic enzyme found in all living cells. It is an enzyme that is indispensable, meaning that its loss by genetic mutation is incompatible with life. The enzyme catalyzes the oxidative phosphorylation of the glycolytic substrate, D-glyceraldehyde 3-phosphate, to 1,3-bis-phospho-D-glycerate with the concomitant reduction of NAD^+ to NADH. This reaction is a pivotal step in glycolysis, which generates cellular energy.

While GAPDH has been known to function as a glycolytic enzyme since before 1950,[5] it was not until the last 25 years that the enzyme's amazing multi-functionality has come to light.[6] GAPDH plays a role in the structural organization of the cell, transmission of genetic information, and cellular signal transduction networks. And all of these functions are relevant to the life of human cells. The mechanism by which GAPDH affects these various cellular processes is associated with its ability to form functional complexes with diverse cellular components,

ranging from soluble actin to trans-membrane proteins. GAPDH in human cells is now known to be found throughout the cytoplasm as well as bound to cytoskeletal structures, each of the organelles, and the inner leaflet of the plasma membrane. These newly discovered functions of GAPDH include some fascinating findings about this protein in pathogenic microorganisms.

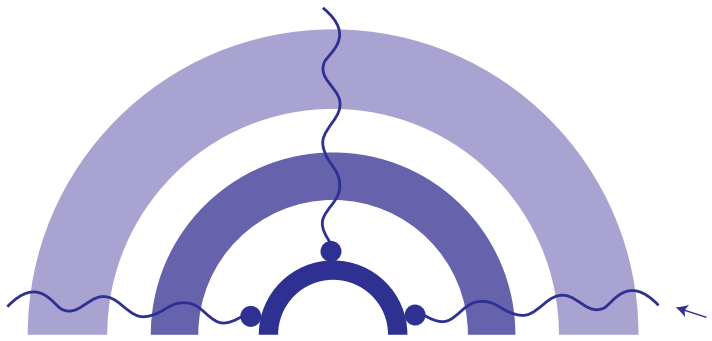
The microorganism *Streptococcus pyogenes*, like all cells, also contains GAPDH. In fact, the sequence of the streptococcal GAPDH is very homologous to the human GAPDH. Streptococcal GAPDH (UniProtKB/Swiss-Prot P0C0G7) is 59% similar and 49% identical to human GAPDH (UniProtKB/Swiss-Prot P04406) according to BLAST analysis (ncbi.nlm.nih.gov/blast). Curiously, streptococcal GAPDH is not only found in the cytoplasm, but it is found tightly bound to the external surface of this microorganism.[7,8,9] While this phenomenon (i.e. surface-localized GAPDH) occurs in many pathogenic microorganisms,[10,11,12,13] this article will only discuss the surface-localized GAPDH of *Streptococcus pyogenes*.

With the exception of a recent 2012 article that identified a surface-localized GAPDH on human macrophages that behaves as a transferrin receptor,[14] a surface-localized or secreted GAPDH has not been documented in human cells. The appearance of surface-localized GAPDH is a puzzling phenomenon. Streptococcal GAPDH does not contain a secretion signal sequence, nor a hydrophobic trans-membrane domain, nor a hexapeptide sorting motif[8]. It is considered an anchorless surface protein, though it is tightly bound. The manner by which the GAPDH is trafficked to the outer surface, and the way that it is attached to the membrane are still mysteries to be resolved.

In 1991, a streptococcal surface protein was first isolated that interacted with plasmin with high affinity and therefore the gene for this protein was designated, *plr* (for **PL**asmin **R**eceptor). The following year this plasmin-binding protein was identified as the streptococcal GAPDH.[7]

GAS contains several virulence factors. Some of the more well characterized virulence factors include the M protein, lipoteichoic acid (i.e. used for adherence), hyaluronic acid capsule (i.e. used as an immunological disguise), and invasins, for example, streptokinase and streptolysins (i.e. used to promote tissue invasion).

Figure 2
Cell surface structure of Streptococcus pyogenes
The peptidoglycan cell wall (shown as a arc) surrounds the plasma membrane (shown as the innermost arc). The hyaluronic acid-containing capsule (shown as the outermost arc) covers the cell wall with a gel-like coat. The peptidoglycan layer typically consists of repeating units of N-acetylglucosamine and N-acetylmuramic acid via 1,4 β-glycosidic linkages. Group A polysaccharide antigen contains N-acetylglucosamine and rhamnose. GAPDH binds to the M-protein attached to the pili (shown by the arrow).



Cell Surface Structure

Pancholi and Fishetti,[7] in 1992, identified the GAPDH protein as a major surface protein on this pathogen. GAPDH is tightly bound to the outside surface of the cell. Layers of peptidoglycan surround the plasma membrane and lie just below the outer hyaluronic acid capsule (see Figure 2). The surface-localized GAPDH was found in all of the serotypes that were tested and the protein appeared at similar levels. The authors[7] purified the protein and identified it as being 39kD by SDS-PAGE (i.e. denaturing gel electrophoresis). The protein eluted from a gel filtration column as a tetrameric 150kD protein that exhibited enzymatic activity.

The authors[7] designated the purified cell surface GAPDH as streptococcal SDH (for **S**urface **D**e**H**ydrogenase). Streptococcal SDH was observed to bind host fibronectin, which supports the hypothesis that GAPDH plays a role in the colonization of the pathogen. Fibronectin resides in the dermis and is an important adhesive protein. *Streptococcus pyogenes* would have to penetrate the skin epidermis in order to reach the dermal layer where it would be able to bind to fibronectin. The binding of surface-localized GAPDH to an adhesive host protein would secure the microorganism to the site of

infection, allowing colonization. Damaged skin becomes particularly susceptible to infection by *Streptococcus pyogenes* due to the ability of surface-localizing GAPDH to bind to the underlying dermal layer by adhering to fibronectin. Another complementary observation is that pathogenic GAPDH, which is surface localized, binds to host actin and myosin. These host proteins are major constituents of human cells, particularly myofibers that are found in both smooth and skeletal muscle. Hence, this property of streptococcal GAPDH binding to host cellular muscle proteins would enable the streptococcal microorganism to adhere to bruised or damaged tissue, enhancing streptococcal colonization particularly in damaged tissue, where the integrity of underlying myofibers is compromised. Therefore, these observations provide compelling evidence for GAPDH acting as a virulence factor.

Additionally, surface-localized GAPDH (or, so-called streptococcal SDH) binds to host lysozyme.[7] The host enzyme, lysozyme, provides innate immunity. The lysozyme is a protease that is abundant in human secretions, including tears, salvia, and mucus. The host lysozyme hydrolyzes 1,4-β glycosidic-linkages found in the peptidoglycan layer of the cell wall of invading microorganisms. Surface-localized GAPDH of *Streptococcus pyogenes* may act as a virulence factor by suppression of the innate immune system through the binding to and inhibition of the host lysozyme.

A plasmin(ogen)-binding protein was found on the surface of *Streptococcus pyogenes* in 1987 by Lottenberg and his coworkers,[16] well before it was identified as being GAPDH. Lottenberg and coworkers[17] later recognized that the surface protein was an ortholog of human GAPDH. The surface-localized GAPDH binds to both the host plasmin, as well as host plasminogen proteins. This interaction isolates the host fibrinolytic system at the surface of the microorganism. The bacterium-bound plasmin is still catalytically active and capable of proteolysis. It is conceivable that GAPDH-mediated binding to plasmin allows the bacterium to use the host's proteolytic action against the host, contributing to the pathogen's invasiveness. Streptococci that were designed to have less surface-localized GAPDH (i.e. five-fold less) exhibited substantially decreased plasminogen-binding properties.[18]

A high and low affinity plasmin-binding site exists on the surface-localized pathogenic GAPDH. The C-terminal end of the protein has an α-helix, which contains amino acid residues 306-336 (particularly important is the lysine residue at position 336), that is the high affinity site. A lower affinity site was identified in regions that flank the S-loop (i.e. located in the middle of the protein).[19] It is quite apparent that the GAS microorganism utilizes host plasmin-binding as a major strategy for virulence. The system for binding of the microorganisms to host plasmin is overbuilt in that it contains other plasmin-binding surface proteins besides the surface-localized GAPDH. This ensures that the mechanism of infection continues despite GAPDH interacting with other host proteins, as described above. Therefore, we see that GAPDH plays many roles as a bacterial surface protein, exhibiting numerous binding partners that contribute to diverse mechanisms of virulence.

Study Results

The study of the surface-localized GAPDH from *Streptococcus pyogenes* resulted in the breakthrough of still yet more potential mechanisms of virulence by this misconceived protein.[18-22] Nitric oxide (or, so-called endothelial-derived relaxation factor) is important for human cardiovascular function. This compound acts on vascular smooth muscle resulting in vasodilation. Nitric oxide readily reacts with GAPDH. Nitric oxide-modified surface GAPDH is mono-ADP-ribosylated in the presence of the coenzyme, NAD^+.[20] A single ADP-ribose is auto-catalytically attached to the active site cysteine residue of GAPDH and then transferred to a target protein. This catalytic property is poorly understood, however, recent evidence suggests that it may inhibit macrophage activity,[23] providing a growth advantage for this streptococcal microorganism.

The C-terminal α-helix and the flanking regions of the S-loop of GAPDH, binds to host pharyngeals cells via the host urokinase plasminogen activator receptor, mediating adhesion to human pharyngeal cells. The cell bound bacterium via interaction between surface GAPDH and the urokinase plasminogen activator receptor, enhances the genetic expression of more urokinase plasminogen activator receptor, populating the pharyngeal surface. This mechanism would increase the binding of the host urokinase to pharyngeal cells, promoting localized invasion to the infected tissue.

An additional mechanism involves bypassing the host immune surveillance due to the strong homology of

pathogenic GAPDH to human GAPDH, host immune cells may not identify it as foreign.

Streptococcal surface GAPDH may also have anti-phagocytic activity as evidence by engineered bacteria that show diminished levels of surface GAPDH also exhibit decreased anti-phagocytosis.[18] Interestingly, the re-distribution of GAPDH in these mutants results in the simultaneous loss of the surface M protein, which has known anti-phagocytic activity. The M-protein is found on pili (see Figure 2). It is thought that surface GAPDH may be attached via its association with the M protein. D'Costa and coworkers[24] provide evidence that *Streptococcus pyogenes* GAPDH is anchored to the cell surface by means of the M-protein.

Summary

In summary, *Streptococcus pyogenes* GAPDH not only acts as an important cytoplasmic, glycolytic energy generating enzyme, this misconceived protein is an important virulence factor. It becomes surface-localized by a currently unknown mechanism and on the surface of the pathogen it can wreak havoc. By binding host plasmin(ogen) it contributes to the microorganisms invasive properties. Pathogenic GAPDH can bind to intact host pharyngeal cells as well as to damaged host tissues via fibronectin, actin, and myosin. Additionally, GAPDH can affect the host immune system by directly inhibiting phagocytosis, as well as escaping the immune-surveillance. Despite the strong homology between pathogenic and human GAPDH there still exists differences in the protein sequence, which may allow for production of specific small molecular weight compounds as selective antibiotics. The fact that pathogenic GAPDH is so close in structure to the human GAPDH may provide insight into molecular mechanisms of autoimmune diseases.

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Disclosure

None reported.

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OFFICIAL MINUTES & REPORTS

April 5-7, 2013
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Meet MSMA's 2013-2014 President

James B. Wolfe, MD

Springfield, MO

Contact: jbwolfemd@hotmail.com

James. B. Wolfe, Jr., MD, a board-certified Otolaryngologist from Springfield, Missouri, will serve as President of the Missouri State Medical Association in 2013-2014. He was formally installed in Kansas City April 6, 2013, during the MSMA's 155th Annual Convention.

Dr. Wolfe was born in Hampton, Iowa, and grew up in Clear Lake and Des Moines, Iowa. He received his medical degree from the University of Iowa College of Medicine in 1970. He completed his post-graduate internship at the William Beaumont General Hospital at Fort Bliss in El Paso, Texas.

His Otolaryngology, Head and Neck Surgery residency at the Walter Reed Medical Center in Washington D.C included a year of general surgery at the Silas B. Hayes Army Hospital at Fort Ord, California.

His military experience after his surgical training was completed in 1977 as Otolaryngology Department Head at the Letterman Medical Center in San Francisco, California.

Dr. Wolfe has practiced in Springfield, Missouri, for thirty-three years, and is on the medical staff of Cox Hospital there.

In addition to his clinical practice, Dr. Wolfe has been long active in organized medicine. He is a Fellow of the American College of Surgeons, a member of the Missouri Ear, Nose and Throat Association, and has been a member of the Missouri State Medical Association since 1977. Dr. Wolfe has remained very active in the Greene County Medical Society as well.

For much of this time he has served in numerous positions for his local and specialty societies, including serving on the MSMA Council since 1995, as well as President of the Greene County Medical Society. He has served on the Board of Governors, and as a Legislative Liaison to the American Academy of Otolaryngology/ Head and Neck Surgery.

Dr. Wolfe and his wife, Jana, have been married 17 years, and have six children between them.

An aviator by hobby, he has had his private pilot's license since 1985.

Goals for MSMA during his tenure as President are:

- Identifying and pursuing policies to attract young physicians.
- Exploring policies to address the present and future challenges that the House of Medicine is facing.
- Ensuring that the quality of medical care to our Missouri patients continues to remain the highest quality.

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Barbara Hover to Lead Medical Alliance

Barbara Hover
Springfield, Missouri

Contact: arhover2@aol.com



Barbara Hover, Springfield, was installed as the 89th President of the Missouri State Medical Association Alliance (MSMA) during the Annual Meeting on April 6, 2013, in Kansas City at the Westin Crown Center.

A Springfield native, Hover received her B.S. in Chemistry from Missouri State University. Following that, she worked as a medical research assistant in the Pharmacology Department at the Washington University School of Medicine. She is a published co-author of numerous papers on Diabetes and Endocrinology. She is the mother of five and married forty-one years to Alexander Hover, MD, a gastroenterologist and a Senior Vice-President of Clinical Excellence with Mercy Springfield. They have eight grandchildren.



She currently sits on the board of Ozarks Fighting Back, an Advisory Board of Community Partnership of the Ozarks, the Greene County Medical Society Alliance (GCMSA) of which she is also a past president, and the Community Health Advisory Committee. Hover has previously been honored as the Missouri State Medical Association Alliance Sandra Mitchell Member of the Year, the Alliance Jean Duensing Literary Award, and GCMSA Pat Ash Member of the Year.

Having devoted over 30 years to issues affecting children, she served on the Springfield DWI Task Force and co-authored a paper measuring the effectiveness of a Community sponsored DWI Intervention for Teens. She also directed the GCMSA's first educational DVD Smoking Makes Me Ugly.

Her theme for this year is "Today's Alliance –The Power to Make a Difference." In her acceptance speech she noted that the Alliance has a unique opportunity because the Medical Alliance's name on a project or endorsement establishes credibility in communities. She plans to focus her year on health issues affecting communities and the promotion of a new animated DVD Pills are NOT a Party, a comprehensive youth prevention program targeting prescription drugs and over-the-counter medication abuse and addiction. It was created by the Greene County Medical Society Alliance.

She is a sustaining member of Junior League of Springfield and was City Coordinator for the Reading is Fundamental RIF project. She has served two terms on the Board of Directors of the Child Advocacy Center and served on the Board of Springfield Regional Opera. She has served as President of the Springfield Council of PTAs as well as PTA President for Kickapoo High school and Disney Elementary. Other volunteer activities include the American Heart Association, Springfield Symphony, Kitchen Clinic, Boy Scouts, Girl Scouts, and Messiah Lutheran Church.

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State of the Association: Presidential Address

by Stephen Slocum, MD, 2012-2013 MSMA President

It has been my pleasure to have served as your president for the past year. My duties have been extremely gratifying and rewarding, especially my travels to the various component organizations around the state.

It would be appropriate, at this time, to review the status of our organization in 2013, and reflect on the prospects for the future.

I would first point out that the status of the Missouri State Medical Association is solid, healthy and relevant. I couldn't be more proud of the organization.

I am proud of the organization's history, advocating for Missouri physicians since 1850.

I am proud of our leadership, composed of individuals who spend selfless hours working for the betterment of physicians and patients.

I am proud of our Alliance, an organization which supports our efforts and pursues many of their own, also for the betterment of our patients and our profession.

I am proud of our Foundation and its support of medical education.

I am proud of the Physicians Health Program, helping physicians through difficult personal circumstances.

I am proud of the MSMA Insurance Agency, helping physicians find liability insurance at a reasonable price, even when the tort system does not work in our favor.

I am probably most proud of our MSMA staff, individuals who work very effectively as a team to support all of the efforts of our organization.

The primary function of the MSMA is advocacy. This year, as usual, we have been working in the state legislature to help physicians better take care of their patients.

The number one item on our agenda has been tort reform. As you know, we have been working feverishly to restore the cap on noneconomic damage taken away by an unfortunate and curiously handled Missouri Supreme Court decision last summer.

Our 2005 legislation, which established a single $350,000 cap on noneconomic damages in malpractice suits, was extremely successful.

We saw a 58% reduction in suits against physicians, 27million dollars less spent by physicians on liability insurance (money better spent on patient care) and 1000 more physicians practicing in our state.

Unless we are successful at restoring the cap, we face a repeat of doctors leaving the state, doctors retiring early and doctors giving up high risk activities such as delivering babies and back surgery.

The good news is that things look hopeful in the Missouri capitol. We have bills circulating in both chambers which have received favorable committee hearings, with the house bill voted out of committee. We believe we have the votes to pass our legislation, but we still need your help in getting to the finish line. Even legislators considered our allies need to be contacted regularly to keep them in our camp.

We have been working on other issues as well. Advanced-practice nurses are once again attempting to establish their autonomy and practice freely and unsupervised. This applies primarily to nurse practitioners, nurse anesthetists and nurse midwives. Our legislative team is aggressively fighting to defeat this dangerous legislation.

Our efforts have been tremendously supported by our membership. Many physicians have given up time from their practices to serve as Physician of the Day in the Capitol.

Many have contributed generously to our Missouri Medical Political Action Committee, helping us keep open the lines of communication with our elected state legislators.

The MSMA has also had a presence in Washington, D.C., being regularly in contact with the offices of our federal Missouri Congressional Delegation. We have been actively pursuing a fix to the sustainable growth rate formula, the elimination of the Independent Payment Advisory Board and help for the threatened elimination of more graduate medical education positions, which limits medical care access to patients and puts a hold on careers of medical school graduates who cannot further their education.

I should mention membership in the MSMA. Our membership position remains strong, but could be considerably better. Our organization numbers 5000 physicians out the 14,000 physicians in the state.

The advocacy issues we have already mentioned should motivate all physicians to be part of our organization, but we still have problems with motivating younger physicians and employed physicians to join. With virtually all young physicians now in the employed category, the challenge is much more significant.

The MSMA has added several membership benefits

this year, which by themselves may not register high on the motivation meter, but should have a positive effect with nonmembers, especially those young and/or employed.

DocBook MD is a free smartphone app which can be downloaded to your mobile device. It allows form HIPAA compliant communication with your colleagues. Patient information including X-rays, EKGs and photos can be sent to facilitate patient care. This is an exclusive MSMA membership benefit.



Dr. Slocum addresses the House of the Delegates covering the current state of affairs of MSMA.

Resolve Physician Agency is also a new MSMA membership benefit. Resolve is an experienced firm which offers a wide range of physician services. These include employment contract review and negotiation, job placement, benefits analysis, practice evaluation and more. Resolve offers its services to MSMA members for a significant discount.

Oakstone Online CME offers online CME for a multitude of medical specialties. This is especially helpful at year's end when CME requirements for licensure are needed. Oakstone's products and services are available as an MSMA membership benefit for a significantly reduced cost.

MSMA has become known lately for its excellent communications efforts. Missouri Medicine is an award winning publication, thanks to its editor Dr. John Hagan and our Director of Communications Liz Fleenor. Progress Notes is an effective newsletter, keeping membership informed on significant current events. Our weekly legislative report from the state capitol during session keeps us aware of vitally important news concerning healthcare legislation. This information is timely, sent promptly at the end of each week by our lobbying team of Jeff Howell and Kenny Jackson.

MSMA's education efforts continue to expand. Hours of CME are available at this, our annual convention, much of which is available on Saturday, when our specialty societies meet. Outside of our convention, live CME conferences are sometimes offered, most recently on Accountable Care Organizations and Patient Centered Medical Homes. In addition, live webinars are increasingly being offered on a variety of topics, including information technology and most recently DocBook MD.

MSMA also offers a variety of resources on practice management, including those on heathcare finance, insurance companies, Medicare, PQRS, EMRs, ACOs, and ICD-10. These resources are useful to any physician concerned about the business aspects of practice, whether or not employed.

Many of these resources are available online on our website, as are numerous resources on public health issues such as immunizations, emergency response and disease control.

I would like to turn our attention at this time to what I believe is our largest and most significant resource. That is our wonderful staff. Nothing we do at MSMA is possible without our capable, talented and dedicated staff.

(I will at this point make some personal remarks about our entire staff, hopefully embarrassing them to no end.)

As to the future, what needs be said? There will be challenges to the practice of medicine from all sides. We are already seeing fallout from the Affordable Care Act. We always have state legislative issues, some very repetitive issues. Changes in payment modalities will be challenging. Information technology will continue to evolve, making more difficult changes to our lives.

But as you've just heard, the state of the MSMA is strong, and will continue to be the voice for Missouri physicians and a resource to help us deal with change. It is a strong voice, and extremely capable of dealing with challenging issues. We all are in good hands.

Once again, it has been my distinct pleasure to have served as president this past year. It is an honor I will always remember and cherish. Thank you very much for your support. MM

Presidential Inaugural Address

Making Hippocrates Proud

by Jame B. Wolfe, MD
2013-2014 MSMA President



Newly installed MSMA President James Wolfe, MD, grins as he gets ready to receive the sacred skull gavel from outgoing President Stephen Slocum, MD, that is passed from president to president.

I would like to thank all of you for being here this evening. I intend to keep my remarks as brief as possible. Prior to starting, however, I have some introductions that I would like to make.

I would like to introduce my wife, Jana. She has been my lighthouse for all our many years of marriage. Also attending are our children; Brad and his friend Barb; John, his wife Carla and their six children; Zachary, Brie, Rain, Sky, Trinity, and Aspen; Jennifer Henderson and her husband Steve; our special child, Heather; and Chad.

There are also some special guests that I want to acknowledge:

I want to thank Dr. Norm Knowlton for reciting the latest version of the Geneva revision of the Hippocratic Oath. I asked him to assist me since the majority of physicians in this room have sworn some form of this oath at their graduation from medical school and it is the foundation of medicine's credo even today. I wanted the oath fresh in everyone's mind since it forms the basis for my thoughts tonight.

Hippocrates lived in Greece around 400 BC and was known as a great physician and teacher. Although the Oath has changed over time, the principles forming the Hippocratic oath has have served physicians as a guiding light through the centuries. During this time one could say that Medicine has been afflicted by the old Chinese curse: May you live in interesting times. Consider the progress and pitfalls that Medicine has seen since the Greeks. Although archeologists archaeologists have evidence that Romans performed cataract surgeries and trephinations prior to the 1st Century BC, bloodletting was still performed in the 18th Century, hastening the death of our first President. Yet the last 60 years have probably been the most challenging when one considers how the creation of Medicare and Medicaid in 1965 transformed our medical delivery system. It has been asserted by several sources that presently over more than 60% of our health care costs in the U.S. are born by governmental entities. This will only increase dramatically in 2014 when Obama Care completely kicks in. At the same time we have seen the emergence of insurance companies dominating the private payment process with the creation of HMOs, medical home models, pre-authorization requirements, economic credentialing, and profiling.

The changes we see occurring today in medicine are also being facilitated by social factors such as the transition from primary care to specialization and sub-specialization; the migration from independent practice models to employed physician models; and the lack of past physician involvement in the political process. We have allowed others to define the practice of medicine, preferring to focus on the care of our patients as directed by the Hippocratic Oath. To this end we permitted insurance companies and governmental agencies to initiate the process of commodizing commoditizing medical care. We physicians also need to look in the mirror, since our own actions, such as using physician extenders, engaging in entrepreneurial behaviors such as the ownership of treatment facilities, and telemedicine have contributed to accelerating these changes.

In the past as presently, MSMA has been the premier state organization representing Missouri physicians. Our strengths and accomplishments are well known; from starting a successful malpractice insurance company when other insurers were leaving Missouri in droves; starting the

Left:
Barbara Hover, newly installed Alliance President, gets pinned from outgoing President Sandra Murdock.



Right:
Alliance members Allene Wright and Kathy Weigand donned their Derby hats and raised funds at the Alliance Foundation Fundraiser Derby Party.



Right:
MSMA's special guest from the AMA was Board of Trustee Joe Annis, MD (right), and he stands with AMA VP of Legislative Affairs Cynthia Brown (center), and MSMA member/AMA Board of Trustee Chair-Elect David Barbe, MD.



nation's premier physician rehabilitation program; and pushing through Tort Reform in 2005 and now again fighting to re-establish noneconomic damage award limits. MSMA has been, and remains active in, providing timely CME and topical continuing education to physicians—just look at the scientific program that was available all day long. Missouri Medicine has won several awards over the last 50 years for its excellent journalism. All of these strengths have been accomplished with the help of the loyal staff that has been the engine of MSMA. At this time I would ask that all MSMA staff stand so that we could recognize you.

To remain a vital and vibrant organization MSMA must recognize and deal with the future trends that I mentioned earlier. If we are to avoid the fate of Kodak we must embrace the future. (How many of you here know that Kodak invented digital photography but didn't pursue it because they felt it would destroy their primary business of selling film?) MSMA must be willing to venture outside of our "comfort zone." We need to identify successful techniques developed by other organizations so that we remain relevant to tomorrow's physicians. We may want to consider joining with neighboring state organizations to produce programs that provide membership value. We may even wish to initiate partnerships with large physician groups and healthcare organizations to facilitate recruiting and other meaningful activities.

However, MSMA will always be committed to Missouri physicians and their patients. Just as the "health of the patient" is the physicians' first consideration, MSMA's guiding principle is the welfare of Missouri physicians and citizens. During my Presidency I hope that all of you will join me in insuring ensuring that MSMA remains a vibrant force championing Missouri Medicine by responding to all of Medicine's challenges in a manner that would make Hippocrates proud.

MM

Recipients of the 50-Year Physician Pin

Forty career physicians earned their 50-Year Physician Pin during the MSMA Presidential Inauguration from MSMA President Stephen Slocum. After the Installation, many celebrated at the reception. Below is the listing of all pin recipients.





50-Year Physicians earned their pin and were honored by Dr. Slocum, top, with Nathaniel Murdock, MD, St. Louis, and bottom, Clarence Martin, MD, Neosho.

- George A. Aldridge, MD, Poplar Bluff, MO
- Martin J. Bell, MD, St. Louis, MO
- John P. Christy, MD, Poplar Bluff, MO
- John E. Codd, MD, St. Louis, MO
- David H. Cope, MD, Cape Girardeau, MO
- Robert E. Cuddihee, MD, Glencoe, MO
- Edwin J. Cunningham, MD, St. Louis, MO
- Rengasamy Gowdamarajan, MD, Kansas City, MO
- Hugh G. Harris, MD, Lebanon, MO
- Ira G. Hubbell, MD, Columbia, MO
- William J. Huse II, MD, Overland Park, KS
- Robert L. Kaufman, MD, St. Louis, MO
- John J. Kelly, MD, St. Louis, MO
- Cecile S. Khoury, MD, Prairie Village, KS
- Richard H. Loeb, MD, Springfield, MO
- Curtis W. Long, MD, Butler, MO
- Clarence A. Martin, MD, Neosho, MO
- Jerry N. Middleton, MD, St. Louis, MO
- H. Yale Muhm, MD, Marthasville, MO
- Nathaniel Murdock, MD, St. Louis, MO
- Karl D. Nolph, MD, Columbia, MO
- Paul Packman, MD, St. Louis, MO
- Robert J. Pelegrin, MD, Osage Beach, MO
- William J. Phillips, MD, Chesterfield, MO
- Richard C. Raynor, MD, Marshall, MO
- Glen H. Reed, MD, Appleton City, MO
- Thomas F. Richardson, MD, St. Louis, MO
- C. E. Gene Ridenhour, MD, Columbia, MO
- Jay I. Rozen, MD, Shawnee Mission, KS
- Barry D. Rutherford, MD, Kansas City, MO
- Carol A. Ryser, MD, Kansas City, MO
- Marcel T. Saghir, MD, St. Louis, MO
- Elson F. Seitz, MD, Grain Valley, MO
- Charles J. Sigmund, Jr, MD, Fort Myers, FL
- Jess S. Simmons, MD, Joplin, MO
- John A. Sopuch, MD, St. Louis, MO
- Mark M. Tendai, MD, Springfield, MO
- Hermanito R. Trinidad, MD, Chillicothe, MO
- Joseph A. Werth, MD, Jefferson City, MO
- Raymond H. Wilbers, MD, Mexico, MO

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House of Delegates Votes on Resolutions

Resolution #1 - MSMA Neutrality on Medicaid Expansion

Resolution Not Adopted

Resolved, that the position of the MSMA shall be to remain neutral on expansion of Medicaid in Missouri.



Members of Reference Committee A, from left to right: Nathan Granger, MD, Brad Harr, MD, William Reynolds, MD, Chair, Andy Wright, MD, and Robert Brennan, MD.

Resolution #2 - Prescription Drug Monitoring Program
Resolution #7 - Prescription Drug Monitoring Program

Adopted Substitute Resolution

That MSMA reaffirms its support for a Prescription Drug Monitoring Program and continues to work for its passage by the Missouri General Assembly.

Resolution #3 - Support for Ethics Ruling on Markups for Pathology Services

Referred to MSMA Council

Resolved, the MSMA will direct the Council on Ethical and Judicial Affairs to definitively rule, within the calendar year 2013, whether MSMA physicians who mark up and client bill for pathology services are behaving unethically.

Resolution #4 - Support for Direct Billing Legislation for Pathology Services

Referred to MSMA Council

Resolved, the MSMA will support with full force and vigor any and all efforts to pass direct billing legislation for pathology services in the State of Missouri.

Resolution #5 - Peer-to-Peer Appeals Process in Missouri

Adopted Amended Resolution

Resolved, that the MSMA actively work with the Missouri Department of Insurance to gather data regarding the training and background of physicians providing peer-to-peer review, and be it further

Resolved, that the MSMA actively work with the Missouri Department of Insurance to compel all health insurers in Missouri and their contractors to always provide physicians who are clinical peers to appropriately address peer-to-peer appeals, and to identify their background credentials if requested, and be it further

Resolved, that the MSMA actively work with the Missouri Department of Insurance to require more oversight of the peer-to-peer appeals process, and to study its effectiveness in optimizing patient care; and be it further

Resolved, that the MSMA work with the AMA to study and promote these objectives at a national level.

Resolution #6 - Sale of Pseudoephedrine to Prescription Only

Referred to MSMA Council

Resolved, the MSMA support legislation to limit the sale of pseudoephedrine to prescription only.

Resolution #8 - Support for Increase Funding for Prevention of Firearm Injuries and Deaths

Adopted

Resolved, that MSMA send a letter of support to the AMA to continue to urge Congress to provide the CDC with sufficient resources to study firearm related injury data and, be it further

Resolved, the AMA encourages the development and presentation of gun safety programs that educate the public on the responsible use and storage of firearms.



Members of Reference Committee B, from left to right: James DiRenna, DO, David Kuhlmann, MD, Chair, Elie Azrak, MD, William Turner, MD, and Jeffrey Thomasson, MD.

Resolution #9 - Support of Senator Feinstein's Bill for Stricter Control of Assault Weapons

Withdrawn by Resolution Sponsor

Resolved, that MSMA will draft a letter of support for the AMA's position on Sen. Feinstein's bill.

Resolution #10 – Medical Ethics

Referred to MSMA Council

Resolved, to help minimize lawsuits and practice the best medicine we should each seriously recognize and conscientiously follow good traditional ethical standards of beneficence, nonmaleficence, justice, and autonomy, then in addition appropriately the Judeo-Christian virtues of truth, honesty, compassion, charity, wisdom, responsibility, perseverance, courage, work, and faith. The right of physicians to practice according to their conscience must be protected by law.

Resolution #11 – Electronic Medical Records/Prior Authorization of Procedures

Referred to MSMA Council

Therefore be it resolved, that St. Charles – Lincoln County Medical Society supports legislation to ensure that, as electronic medical records are adopted broadly, such systems should adhere to the following principles;

Physicians must retain responsibility for treatment decisions for patients regarding prescriptions and procedures;

Electronic medical record systems should be provided through a neutral and open platform that does not advance the commercial interests of any particular participant (e.g., health insurers, hospitals, pharmacy benefit managers, pharmaceutical companies, etc.) to the potential detriment of the patient;

Electronic medical record systems must allow for submission and approval of prior authorization requests electronically, offering real-time feedback on such requests within hours;

(In the event an electronic prior authorization system is not readily available, a universal One-page prior authorization form for all payers must be used)

Messages transmitted to physicians and their staff through electronic medical record systems must be sourced from evidence-based third-party or academically published research;

Electronic medical record systems must support greater access to data for better clinical decision-making, including alerts to potential adverse events;

Information communicated via electronic medical record systems should not be selectively or competitively pushed to the physician and such distribution must not diminish a patient's right to appeal decisions;

Electronic medical record systems must conform to prevailing quality, transparency and technical standards established for such systems; and

Patient privacy must be protected; and be it further

Resolved, that St. Charles – Lincoln County Medical Society resolution be that prior authorization systems be transparent, with criteria for approval for a treatment readily available to the health care provider.

Resolution #12 – Conversion of Local City Hospital to a Nonprofit Organization

Adopted

Resolved, that MSMA support SB443 which will allow the conversion of a local city hospital to a nonprofit organization governed by Missouri's nonprofit corporation law. MM

Awards: Distinguished Service Award

Arthur Gale, MD, St. Louis, received the 2013 Distinguished Service Award during MSMA's 155th Annual Convention in Kansas City. The Distinguished Service Award is presented to recognize a career of extraordinary service to our profession, our colleagues, and our patients.

Dr. Gale is a highly respected physician in St. Louis, widely known for providing compassionate care to his patients, and his passion for individual rights and responsibilities. He did his undergraduate work at the University of Chicago and Washington University in St. Louis, and earned his medical degree at the University of Missouri School of Medicine. He did his internship and residency training at the Jewish Hospital in St. Louis, and a research fellowship in the Department of Allergy, Immunology and Arthritis at the renown Scripps Clinic and Research Foundation in California.



Arthur Gale, MD, (center), receives the Distinguished Service Award during a meeting of the St. Louis Metropolitan Medical Society, as he was unable to attend MSMA's Convention. Presenting the award was Stephen Slocum, MD, (right), MSMA Immediate Past President and David Pohl, MD, (left).

Dr. Gale is Board Certified in Internal Medicine, and is an Associate professor of clinical medicine at the Washington University School of Medicine.

He served on the organized medical staffs of Barnes-Jewish Hospital, where he was staff president, and at the Missouri Baptist Medical Center.

And for many years he played an active role in organized medical staff evening education programs.

Dr. Gale contributions to organized medicine are many. He is a Past President and member in good standing of the St. Louis Metropolitan Medical Society, and he established the Society's highly effective Physician Grievance Committee. He also organized the Round Table on Peer Review there, and made countless other contributions as a zealous advocate for physician rights.

In addition to that, Dr. Gale has been an active and loyal member of MSMA for 37 years, and for many years has been a dedicated member of the MSMA Publications Committee and a contributing editor for our award-winning journal, Missouri Medicine. He is also a member of the American Medical Association, and for 15 years served as an MSMA Delegates to the AMA House of Delegates.

Dr. Gale is a gifted and prolific writer who has contributed countless scholarly articles for St. Louis Metropolitan Medicine, Missouri Medicine, and other peer-reviewed journals. In fact, his dedication to Missouri Medicine is now immortalized by the Arthur Gale Freedom of Expression Award that goes annually to the physician who contributes the best commentary article to the MSMA journal. And on top of that, he has authored two extraordinary books on topics of medical economics.

And on several occasions, Dr. Gale he has served admirably as medicine's voice, advocating passionately for physicians and patients in the halls of the Missouri Capitol, testifying before legislative committees, and appearing before such governmental and regulatory bodies as the Board of Healing Arts, the Bureau of Narcotics and Dangerous Drugs, and others.

For his lifetime of extraordinary service to his patients and his profession, his dedication to organized medicine, we are proud to honor Dr. Art Gale with the MSMA Distinguished Service Award.

Editor's Note: Dr. Gale was not able to be at the Annual Convention, but his award was presented to him in May in St. Louis. See above photo. MM

Awards: Legislative Service



Dr. Keith Frederick receives the Legislative Award from President Jim Wolfe, MD.

Missouri Representative Keith Frederick, DO, an orthopedic surgeon from Rolla, received the 2013 Legislative Award during MSMA's 155th Annual Convention in Kansas City. The award reflects the close relationship MSMA has with state senators and representatives throughout the year to formulate policy and regulations that govern the practice of medicine in Missouri.

Rep. Frederick, represents the 121st House district, which encompasses portions of Phelps and Pulaski counties. He was elected to the House of Representatives in November 2010, and quickly earned the respect and admiration of his colleagues on both sides of the aisle. This year, Representative Frederick was appointed Chair of the important House Health Care Policy Committee. In this position, he controls the speed of any legislation in his committee which impacts physicians and the practice of medicine.

Representative Frederick has come to medicine's aid countless times during his service in the General Assembly. He has been a staunch supporter of our efforts to ensure prompt credentialing of physicians. He has also been a tireless advocate for patient safety.

And, he has been an important voice in our battle to restore the noneconomic damage caps through commonsense tort reform measures. Most importantly, he is a consistent protector of the practice of medicine when other health care professional groups attempt to expand their scope of practice. For example, this year she has led the charge in the House of Representatives to extinguish HB 314, which would allow nurses to practice without physician oversight. He also sponsored HB 387, an MSMA-backed bill which amends the physician assistant supervision rules.

Representative Frederick consistently seeks the advice of organized medicine on important healthcare issues at the Capitol, and shares that information with the members of his committee and colleagues.

Whether it is big issues, like Medicaid reform and nursing scope of practice, or the less visible ones, like tanning beds and medical records fees, Representative Fredrick has been a habitual supporter of Missouri physicians and their patients. MM



Medical students mingle in the MSMA Exhibit Hall with Ted Groshong, MD, (far right).

Sponsors & Exhibit Partners

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

- AEGIS® SCIENCES CORPORATION
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- MISSOURI BOARD OF HEALING ARTS
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Credentials & Appointments

The 155th Annual Convention of the Missouri State Medical Association was held at the Westin Crown Center in Kansas City, Missouri, April 5-7, 2013. Marsha Taylor, MD, Nixa, Missouri, presided as Speaker of the House of Delegates. Parliamentarian was Jo-Ellyn M. Ryall, MD, St. Louis.

The Committee on Credentials announced there were six Officers, 16 Councilors, and 62 Delegates in attendance for the Opening Session of the House of Delegates.

This report and the minutes of the 154th Annual Convention as published in the May/June 2012 issue of *Missouri Medicine* were approved.

At the Second Session of the MSMA House of Delegates, the Committee on Credentials reported there were six Officers, 19 Councilors, and 110 Delegates in attendance.

Reference Committee A members included Nathan Granger, MD, Brad Harr, MD, William Reynolds, MD, Chair, Andy Wright, MD, and Robert Brennan, MD. Reference Committee B members included James DiRenna, DO, David Kuhlmann, MD, Chair, Elie Azrak, MD, William Turner, MD, and Jeffrey Thomasson, MD.

The MSMA Nominating Committee members were: 1st District - Robert Corder, MD, St. Joseph; 2nd District - John Memken, MD, Hannibal; 3rd District - Edmond Cabbabe, MD, St. Louis; 4th District - Carson Agee, MD, O'Fallon; 5th District - Lisa Thomas, MD, Columbia; 6th District - David Kuhlmann, MD, Sedalia; 7th District - James DiRenna, DO, Glastone; 8th District - Alex Hover, MD, Springfield; 9th District - David Barbe, MD, Mountain Grove; 10th District - Clifford Talbert, MD, Cape Girardeau; and Organized Medical Staff Section & Chair - James Conant, MD, St. Joseph.

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Summary of Council Actions: 2012-2013

Meeting of April 1, 2012 - St. Louis

Stephen Slocum, MD, St. Louis, President, presided. Jeff Copeland, MD, St. Peters, was elected Chair, and Ann Romaker, MD, Kansas City, was elected Vice-Chair. David Redfern, MD, Springfield, was reelected Secretary. George Hruza, MD, St. Louis, was reelected Treasurer.

Meeting of July 15, 2012 - Jefferson City

Your MSMA strongly condemned the Missouri Supreme Court ruling that eviscerates one of the nation's most successful tort reform laws. In Watts v. Cox Medical Center, the Court ignored more than 25 years of precedent by striking down the state's cap on non-economic damages in medical liability lawsuits.

The caps were part of a sweeping tort reform package that passed the General Assembly with bi-partisan support in 2005.

"The ruling is an immeasurable disappointment," said MSMA President Stephen Slocum, M.D. "It turns back the clock to a time when a medical lawsuit crisis had pushed Missouri doctors to the breaking point. Scores of physicians moved away, and access to health care was threatened in every corner of the state."

Prior to the legal system reforms in 2005, Missouri physicians had seen their medical lawsuit insurance premiums skyrocket. Some lost their coverage altogether. As a result, many physicians left their practice, retired early, or abandoned high-risk services such as surgery and delivering babies.

But since the cap on non-economic damages went into effect, the number of lawsuits filed against physicians has fallen almost 58%, the state has added nearly 1,000 physicians, and Missouri has seen a $27 million decrease in lawsuit insurance premiums. This is money that did not go to fight lawsuits, but rather remained in the Missouri health care system, providing better services and better access to care.

MSMA is calling on the General Assembly and the Governor to make restoration of the cap their highest legislative priority in 2013.

"This is an issue that impacts every Missourian," said Dr. Slocum. "Who will tend to the sick? Who will deliver the babies? Who will staff the emergency rooms? For the sake of their constituents, our elected officials in Jefferson City must repair what the Supreme Court has done."

The Council voted to raise dues to $395 for active members, the first dues increase in seven years. Dues amounts for other categories of membership will remain unchanged.

MSMA is addressing the following issues gleaned from the non-member survey: that non-members consider MSMA as an arm of the AMA; their specialty societies provide many services they need; and MSMA does not provide them with all the services they desire.

CME

Based on the evaluation summaries from the 2012 Annual Convention, the CME Committee recommended the following general session topics for the 2013 Convention:

- The Supreme Court's Ruling on the Affordable Care Act
- Ramifications for Missouri Physicians/Quality Measurement
- Patient Centered Medical Home
- Accountable Care Organizations
- Importance of a Missouri State Plan for Alzheimer's Disease

The following organizations were reaccredited as providers of CME: Hannibal Regional, Mercy Springfield, St. Louis STD/HIV Prevention Training Center, Missouri Baptist Medical Center, Cox Health, Institute for International Medicine, Ozark Medical, and St. Anthony's Medical Center.

MSMA Insurance Agency

The MSMA Insurance Agency now as an agreement with Missouri Physicians Mutual, and reported that the Doctors Company had recently acquired Intermed Insurance.

Physicians Health Program

The MPH Program physician participants currently break down as follows: 30% from St. Louis, 32% from Kansas City, 18% from Columbia, 8%

from Springfield, with the remainder being outstate Missouri.

District Reports (Selected)

MSMA President, Stephen Slocum, MD, welcomed Margaret Wilson, DO, Dean of the A.T. Still University/Kirksville College of Osteopathic Medicine to the Council Meeting. He reported he's visited other state medical societies with major topics being membership and the Affordable Care Act. Attending several component medical societies in Southeast Missouri, Dr. Slocum has encouraged them to work with their hospital medical staffs to get physicians more active in organized medicine.

Rob Schaaf, MD, is serving on a special state committee to study cost saving measures for Medicaid. The Annual Meeting of the Metropolitan Medical Society of Greater Kansas City will be October 3.

In Greene County, Brian Biggers, MD, reported CoxHealth has entered into an agreement with Skaggs Health System, Branson, where all of the Skaggs holdings will be brought into the CoxHealth system. The University of Missouri School of Medicine has announced a joint effort with CoxHealth and Mercy Springfield to develop a satellite campus for the medical school in Springfield, with third and fourth year students going through rotation at Cox and Mercy. Greene County is also planning a joint Greene County Medical Society/Alliance picnic in September, and an annual CME activity and golf tournament in October.

The Medical Student Section will again sponsor the April 2013 "Dash for Diabetes" in conjunction with MSMA's Annual Convention in Kansas City.

AMA Report

David Barbe, MD, was elected Chair Elect of the AMA Board of Trustees at the recent AMA Annual Meeting. Sara Drystad, MD, was elected to the Governing Council of the Resident/Fellow Section. William Huffaker, MD, served as Chair of Reference Committee B, and Charles Van Way, MD, and Rebecca Hierholzer, MD, served on Reference Committee C.

The significant issues at the AMA meeting were Medicaid financing reform, ambulatory service payment discrepancies, patient expense transparency, and a proposal to transition Medicare from a "defined benefit" program to a "defined contribution" program in which Medicare-eligible Americans could choose between traditional Medicare and competitive Commercial Insurance programs, with the Federal government contributing a set amount to the program chosen. And, MSMA is supporting the AMA's Guidelines for Reporting Physician Data.

Appointments

Naveed Razzaque, MD, has been appointed to the Primaris Board. Councilor advisor appointments for 2012 are: Commission on Medical Economics-Ann Romaker, MD; Commission on Continuing Education-Peggy Barjenbruch, MD; Commission on Public Affairs-Joseph Corrado, MD; Commission on Interspecialty Medicine-Kirby Turner, MD; Physicians Health Committee-Ravi Johar, MD.

Alliance

Sandra Murdock, Alliance President, reported seven MSMA Alliance members attended the AMA Alliance Annual Meeting in June held in Chicago. She recently installed officers at the following local Alliances: St. Louis Metropolitan Medical Society, Cape Girardeau County Area Medical Society, and the Greene County Medical Society Alliance. The Alliance Leadership Conference was held July in St. Louis. Speakers covered the topics of Managing your Online Presence, Managing a Free Clinic, and HIV/AIDS research in Uganda, Africa. The Alliance Fall Conference will be held October 23-24 in Columbia.

Meeting of October 14, 2012 - Jefferson City

New membership benefits, legislation to fix the recent adverse tort reform ruling, and a great General Session speaker line-up for the Annual Convention gave 411 new physicians reasons to join the MSMA, according to the several reports from the Association's Council Meeting held last month in Jefferson City.

MSMA and other allied groups will be working with the General Assembly in 2013 to reinstate the cap on non-economic damages. Nationally, MSMA co-signed an AMA letter to Congress regarding a fix for the SGR.

The ASsociation is proud to announce it will offer:

- Discounts on online CME with Oakstone Publishing, providing web-based CME with content for more than 40 specialties, including board certifications.

- DocbookMD, a smartphone/tablet application that allows you to bypass the paging process entirely by sending and receiving critical patient information such as X-rays, EKGs, or images from your mobile device and message between your colleagues in a safe, secure, HIPAA-compliant interface.
- A partnership with the Resolve Physician Agency, which can help you with tailored job searches, contract reviews and a wide range of career services.

MSMA is expanding the number of General Sessions for the 2013 Annual Meeting to two days, both Friday and Saturday. Topics are: "What Missouri Physicians Need to Know: The Supreme Court Decision an Beyond," "The Future of Medicine: Accountable, Transparent, an Focused on Quality," "The Realities of the Patient-Centered Medical Home," "Why We Need an Alzheimer's Plan for Missouri," and "Hospital and Physician Alignment Post-ACA."

Advocacy

Missouri, along with 36 other states, has yet to establish a Health Insurance Exchange mandated by the ACA. The deadline is November 16.

The Council also heard reports on such legislative issues such as Medicaid expansion under the ACA, prompt credentialing, tanning bed regulation, and prescription drug monitoring.

The Legislative Committee was directed to research two issues:

Rural health clinics (RHC): current law requires the collaborating physician to maintain a geographic proximity and some type of coverage in case of the absence of the physician. The Missouri Association of Rural Health Clinics would like a time-limited waiver to allow the RHC to remain fully operational when the collaborating physician is outside the proximity limit.

Physician Assistant supervision: possible legislation that would remove the sixty-six and two-thirds percent supervision requirement in favor of a requirement Physician Assistants practice where the physician "routinely" practices.

Missouri psychiatrists have discussed mandating three hours of mental health CME as a requirement for licensure. MSMA will send a letter indicating we support the intent but do believe it should be mandated.

The Council tabled a resolution from the 2012 Annual Meeting regarding Mobile Screening Programs. MSMA is researching the extent of oversight, quality control, how many screening exams are performed, patient charges, and what kind of follow-up is provided. MSMA staff will continue to monitor this issue.

In Missouri, MSMA sent a letter of support to the Board of Healing Arts regarding a proposed rule on a mandatory informed consent form for the prescribing of HCG for weight loss.

The Council approved this position statement on early elective deliveries: Be it resolved that, MSMA supports efforts to reduce the rate of early elective delivery and to support educational efforts to reduce the rates of early elective delivery.

MSMA President Stephen Slocum, MD, stated he attended meetings of several component medical societies since the July Council meeting, and also the Annual Meeting of the Kentucky Medical Association.

Membership

The 2012 one-half year dues rate mailing was successful, and MSMA has 411 new members. 2013 Membership renewal is currently underway. MSMA also will assist with student and resident recruitment.

CME

Progress Reports were approved for the following: Lake Regional Health System and St. John's Mercy Medical Center. All 2012 CME activities are being reported by accredited providers via the ACCME's Program Activity Reporting System, including MSMA. The Association's accredited providers have been provided training resources, as well as an in-house training/workshop in October.

AMA Report

James Conant, MD, reported that in addition to the Missouri Delegates and Alternates that will attend the AMA Interim Meeting in November, MSMA is also represented by David Barbe, MD, Chair-Elect of the AMA Board of Trustees; Jerry Kennett, MD, AMA Council on Legislative Affairs; and Ed Cabbabe, President-Elect of the Board of the AMA Foundation.

Insurance Agency

Professional liability insurance is the number one insurance product for the Agency, with health insurance being number two.

Medical Student Section

The Dash for Diabetes will be in Kansas City the weekend following the MSMA Annual Meeting in April. Planning is underway for MSS participation at the upcoming AMA Student Section meeting.

Alliance

MSMA Alliance President-Elect, Barbara Hover, reported on programs in several county Alliances, such nursing student scholarships, the Hands are Not for Hitting program, and the Smoking Makes Me Ugly DVD. The Alliance Fall Conference was October 23-24 in Columbia.

Meeting of January 20, 2013 - Jefferson City

MSMA's top legislative priority in 2013 is tort reform, and was discussed at length during MSMA's Council Meeting in January in Jefferson City. A toolkit is available at www.msma.org/tortreform complete with letters to the editor, talking points, the proposed legislation, and the history of the issue.

Additional legislative efforts include prompt credentialing, drug monitoring, midwifery, tanning salons, and more. Legislation has again been introduced to grant independent practice to APRNs, and MSMA will oppose this effort.

Advocacy

In other Advocacy efforts, the Association will work on legislation to allow APRNs in a rural health practice to continue to see patients when the collaborating physician is absent. Present rules require rural health clinics to stop seeing patients whenever the physician is outside the 50-mile proximity limit. Under the new language, there is a 28-day per year limit and a restriction that it would only apply to collaborative agreements in a rural health clinic.

MSMA will work on legislation from the physician assistants (PA) that would change their practice act, including changes in the amount of time practicing together, and removal of the geographic proximity waiver process. It would prohibit the PA from practicing outside the specialty of the supervising physician. The Association will also work on the expansion of the Medicaid program under the Affordable Care Act.

The Legislative Committee was directed to study aspects of a possible program to provide a new category of physicians for graduating medical students who do not match for a residency program. Under this suggestion, the "physician extenders" would practice medicine under the supervision of a licensed physician. This possible new program could orient the students to practice in primary care rather than in a specialty area. MSMA is working with the Board of Healing Arts on this issue.

MSMA co-signed two American Medical Association (AMA) letters aimed at the looming sequestration and other "fiscal Cliff" discomforts, and eliminating the ICD-10.

MSMA President Stephen Slocum, MD, has participated in meetings with the Medical Group Managers Association, and the medical societies in Pettis County, Audrain County, Cape Girardeau and Boone County. He also represented MSMA at the officer installations for St. Louis Metropolitan Medical Society and Greene County Medical Society.

In other news, representatives from Anthem Blue Cross in St. Louis have changed the Physicians Consultative to a Physicians Advisory Council. MSMA will present the 2013 Legislative Award to Representative to Representative Keith Frederick, DO, Rolla.

Membership

MSMA's annual Advocacy Training Conference, which was held in conjunction with the Council meeting, was well attended, and participants received valuable advocacy tips and information from five excellent speakers. The Association has also provided educational conferences on Medicare RACs, PQRS, 2013 Medicare updates, and the Insurance Conference will be held in June. Dr. Slocum reported three new membership benefits: DocBookMD, a mobile device app that allows secure communication between physicians; Oakstone Publishing to provide online CME, Resolve Physician Agency to provide employment contract review, job placement services, compensation analysis and other career services.

MSMA announced it is now on Twitter. Members can follow at #momedicalassn.

CME

The preliminary program for the 2013 Annual Convention was reviewed. Activity reviews were approved for St. Francis and Southeast Health in Cape Girardeau. The Commission recommended to not

adopt Resolution #3 "Crendentialing CME" from the 2012 Annual Convention. The CME Commission urges the MSMA to continue to collaborate with the ACCME, PhRMA, and the AMA to review, revise and update procedures and forms as they relate to simplifying the planning process and cost associated with CME.

Medical Economics

The Commission considered Resolution #7-"Facilities Fees Charge to Patients" from the 2012 Annual Convention which asks MSMA to oppose the imposition of facility fees on outpatient E/M visit codes. This is already MSMA policy. The second resolve calls for the AMA to eliminate the CPT code for facility fees. This is a federal issue and is being addressed on the national level. The Council agreed to not approve the second resolve.

Publications

St. Louis physician Arthur Gale, MD, proposed that MSMA create a "Freedom of Expression" annual award and a monetary prize for the physician who writes the best commentary article published in Missouri Medicine. Dr. Gale will donate funds to help fund with the award and prize.

Members of the Editorial Board for Missouri Medicine were approved for 2013.

Physicians Health Program

The program is following 130 physicians who are either in treatment or are being monitored. Some program participants agree to a lifetime commitment of monitoring.

MSMA Insurance Agency

Celebrating its ten-year anniversary this year, the majority of the Agency's business in 2012 was in the professional liability area, and the Agency continues to assist physicians with other insurance needs.

Appointments

Jim Rogers, MD, Springfield will be re-appointed to the Primaris Board, and Steve Smith, MD, St. Louis, has been appointed to the Center for Patient Safety Board.

AMA

A summary of the actions at the AMA Interim Meeting in November was published in Missouri Medicine. Several physicians and residents will attend the AMA Advocacy Conference in Washington in February. MSMA's guest from the AMA during its Annual Convention will be Joe Annis, MD. Several MSMA members hold AMA leadership positions: David Barbe, MD, is the Chair Elect of the AMA Board of Trustees; Jerry Kennett, MD, serves on the Council on Legislation; and Ed Cabbabe is seeking a term on the Council on Long Range Planning and Development, and is currently the President of AMA Foundation.

Councilor District Reports (Selected)

Councilors from the St. Louis Metropolitan Medical Society recognized Executive Vice President, Tom Watters, who is retiring.

Audrain Medical Center will soon become affiliated with the SSM system.

Greene County reported that Mercy System has opened an orthopedic facility in the Springfield area. In March, the Society will hear a health care presentation from the Missouri Hospital Association. Construction is underway on the Mercy Hospital in Joplin to replace the St. John's Hospital destroyed in the 2011 tornado. The new hospital is scheduled to open in 2016.

In the Bootheel area, small hospitals are becoming affiliated with other hospital systems.

Alliance

The Alliance is implementing the Smoking Is Not For Me contest for middle school youth statewide. During its Fall Conference in October, the Alliance heard programs on where medicine is going in relation to the Affordable Care Act; the Missouri Arthritis Program spoke on "Self-Management of the Chronic Disease;" and there was a presentation on "What Doctors Cannot Tell You."

The annual Alliance Advocates for Health Care Day at the Legislature is scheduled for February 19-20. Alliance members will visit their state legislators to discuss political topics that affect physicians. The Foundation Fundraiser will be held Friday, April 5, in conjunction with MSMA's Annual Convention, and information can be found at www.msma.org/annualconvention. MM

Reports of the Delegate Handbook: 2012-2013

Secretary

The Missouri State Medical Association had 5,021 members as of the December 2012 audit. This was a net loss of 318 members from our membership of 5,339 as of the December 2011 audit. Following is a breakdown according to classification.

Year	Students	Residents	Active	Honor	Total
2011	1,033	269	3,540	497	5,339
2012	-57	-190	-52	-19	-259

Number of member deaths reported during 2012 totaled 25.

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

President Elect to fill the expired term of James Wolfe, MD, Battlefield

Three Vice Presidents to fill the expired terms of Robert A. Brennan, Jr., MD, St. Louis; Thomas Macdonnell, MD, Marshfield; and Arthur Freeland, MD, Kirksville.

A Speaker and Vice Speaker to fill the expired terms of Marsha Taylor, MD, Springfield, Speaker and David Chalk, MD, Washington, Vice Speaker. Both are ineligible for re-election to their current position.

Three Delegates and Four Alternate Delegates to the AMA to fill the vacancies created by the expiration at the conclusion of the 2013 Annual Convention of the terms of Delegates James Conant, MD, St. Joseph; Rebecca Hierholzer, MD, Leawood, KS; William Huffaker, MD, Chesterfield; and Alternate Delegates Warren Lovinger, Jr., MD, Nevada; Mr. Cory Offutt, Columbia.The new two year-terms will begin at the conclusion of the 2012 MSMA Annual Convention and end at the conclusion of the 2014 MSMA Annual Convention.

The terms of the following Councilors will expire in 2013: 2nd District - Sandra Ahlum, MD, Hannibal; 3rd District - Elie Azrak, MD, St. Louis; Joseph A. Craft, III, St. Louis; Ravi Johar, MD, Chestefield; Laurence Levine, MD, Creve Coeur; 4th District - Jeffrey Copeland, MD, St. Peters; 6th District - Warren Lovinger, Jr., MD, Nevada; 7th District - John Stanley, MD, Kansas City; 8th District -Duane Sherrod, MD, Joplin; 10th District - Kirby Turner, MD, Poplar Blufff; Organized Medical Staff Section - Peggy Barjenbruch, MD, Mexico; Young Physician Section - Ibrahim M. Saeed, MD, Kansas City; Resident Fellow Section - Sara Dyrstad, MD, St. Louis; Medical Student Section - Mrs. Caroline Doo, Kansas City.

The terms of the following Vice Councilors will expire in 2013: 2nd District - Phillip Tweedy, MD, Hannibal; 4th District - Kevin Weikart, MD, Lake Saint Louis; 6th District - David Kuhlmann, MD, Kansas City; 8th District - Alexander Hover, MD, Springfield; 10th District - Mark Hahn, DO, Cape Girardeau; Organized Medical Staff Section - James Conant, MD, St. Joseph; Young Physician Section - Nicholas Golda, MD, Columbia; Resident Fellow Section - Jacob Becker, MD, Columbia; Medical Student Section - Mr. Kyle Riggs, Lee's Summit.

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

The entire session will be held at the Westin Crown Center in Kansas City. The House of Delegates will hold its First Session on Friday, April 5, 2013, 8:00 am and the Second Session is on Sunday, April 7.

Registration facilities will be open on Thursday, April 4, at 3:30pm; Friday, April 5 at 6:30 am and Saturday, April 6 at 6:30 am. Registration will be in the Concourse Foyer.

Treasurer

The report of the Treasurer is covered in the Financial Statement which is published in the March/April issue of *Missouri Medicine*.

Executive Vice President

The report of the Executive Vice President is covered in President's State of the MSMA speech on page 244.

Alliance

Your Missouri State Medical Association Alliance had a bountiful year filled with projects affecting small and large communities and the entire state of Missouri.

Projects around the state included St. Louis' Voices of Excellences - teaching speaking and presentation skills to underprivileged youth; Greene County's Doctors' Day Charity Outreach program and Smoking Makes Me Ugly DVD; Cape Girardeau's Meals on Wheels program and nursing scholarship program; Buchanan County's SAVE program; and Kansas City's educational monthly workshops.

After the Alliance held its Executive Board Meeting in May, President Sandra Murdock traveled to the Alliances of St. Louis, Cape Girardeau and Springfield to install those

county Alliance's officers. She also traveled extensively around the state representing the MSMA Alliance, especially at the AMA Alliance's 90th meeting in Chicago in June.

Workshop educational sessions from our Summer Leadership Meeting held in St. Louis and from our Fall Conference held in Columbia included topics on managing free health clinics, monitoring your online presence, HIV-AIDS, the Affordable Care Act, chronic disease, and communication in medicine.

The Alliance Advocates for Health Care Annual Day at the Legislature was held in February along with the Winter Board Meeting, where we had members visiting lawmakers and passing out helpful information on bills MSMA supported and opposed, as well as health information on how to identify a stroke.

We are looking forward to our Annual Meeting held in conjunction with MSMA's Annual Convention in April, and hope that everyone can attend the Foundation Fundraiser on Friday, April 5.

The MSMA Alliance continues to make a difference in your community. Thank you for your support.

Commission on Continuing Education

The Commission reviewed and approved the following accreditation actions:

Reaccreditations for Organization: Ozarks Medical Center-West Plains, and St. Anthony's Medical Center-St. Louis.

Initial Accreditations for Organizations: Southeast Health-Cape Girardeau.

The Commission conducted an audit and approved the activity reviews of live programs for the following facilities as part of the process for initial accreditation:International Institute for Medicine-Kansas City; Saint Francis Medical Center Cape Girardeau; Southeast Health-Cape Girardeau.

The following facility's progress reports were accepted: Hannibal Regional Medical Center-Hannibal, Mercy Hospital-Springfield, St. Louis STD/HIV Prevention Training Center - St. Louis, Missouri Baptist Medical Center - St. Louis, Cox Health - Springfield, Lake Regional Health System - Lake of the Ozarks, Mercy Hospital - St. Louis.

The following facility was asked to submit a second progress report: Chritian Hospital - St. Louis.

The Commission planned and approved the 2012 Annual Convention CME Program approved for 17.75 hours of AMA PRA Category 1 creditsTM.

In 2012 none of the Missouri State Medical Association accredited providers relinquished accreditation. Currently, there are 35 MSMA accredited providers.

Benita Stennis, MSMA staff, participated in the ACCME's monthly noon conference calls and reported back to the Commission on issues and trends relevant to CME.

MSMA staff conducted two new staff trainings for accredited providers at MSMA headquarters.

Membership Committee

The MSMA Membership Committee wishes to recognize and give thanks to retired physicians, Douglas Bogart, MD, and Gary Pettett, MD, for their past service on the membership committee, as well as MSMA Past Resident Councilor Ren Vitkovitsky, MD.

The Committee was given results from our non-member survey, and a good deal of discussion on this subject led to greater concentration on recruitment, and prospect activities to target specific groups by utilizing theme issues of *Missouri Medicine* in our mailings to non-members. We've also secured a stronger presence at specialty conferences around the state. The Board of Healing Arts recently incorporated a field for searching and filtering physician listings by specialty, and that has helped in streamlining efforts to reach specific new members.

Also in response to feedback received from the non-member survey, MSMA staff has signed a contract to begin offering online CME through Oakstone Publishing, with video and audio targeting more than 40 medical specialties.

Another new feature MSMA is happy to bring to our members this year is DocBookMD, an exciting new member benefit that costs MSMA and our members nothing, while allowing members to communicate with one another securely over their mobile devices via a downloadable app, which is HIPAA-compliant.

And, in effort to better attract our younger physician population, MSMA has partnered with Resolve Physician Agency to provide a wide range of career services, including employment contract review and negotiation, tailor-made job placement, benefits analysis, practice evaluation, compensation analysis, etc. Resolve is offering their services to MSMA members at a significant discount. The Agency has been conducting free seminars to inform residency programs of this benefit around the state.

Online dues payments are steadily increasing since this feature was implemented on our secure website in 2010. Look for MSMA's social media presence to increase this year as well.

Missouri Physicians Health Program

This has been a busy year as indicated by the number of referrals and the 113 Missouri physicians that were

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

In 2013, MPH will be iniatiting its "500 Doctors: $500" Campaign to elicit individual donations from physicians.

Missouri State Medical Association Insurance Agency

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

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

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

Missouri State Medical Foundation

Your Missouri State Medical Foundation loaned $321,500 to Missouri medical school students in 2012. The Foundation has loaned more than $11 million to Missouri medical students over the last fifty years.

In addition to continuing to make student loans, the Foundation is funding the annual MSMA scholarships and assisting local medical societies initiating their own scholarship funds by providing matching grants to:

- St Charles / Lincoln County Medical Society
- Boone County Medical Society
- Northeast Missouri Medical Society
- Northwest Missouri Medical Society
- Cole County Medical Society
- Quad County Medical Society
- Metropolitan Medical Society of Greater Kansas City
- MSMA Alliance

The annual financial statement audit received an unqualified (clean) opinion from the auditor. The current financial strength of the Foundation is due to the strong support received from the MSMA and the MSMA Alliance.

Public Affairs Commission

MSMA mounted a media campaign on vaccinations based on a *Missouri Medicine* article, "Are Parents Avoiding Vaccinations Because of Safety Fears? *Missouri Medicine* Addresses a Growing Concern," in its January/February 2012 issue. MSMA coordinated statewide media activity, as well as brought aboard 15 partners and collaborators to speak to their own local media, staff and patients to assuage parental fear of vaccinations.

MSMA held its annual Advocacy Training at the January Council Meeting. More than 45 participants from component and medical specialty societies completed leadership and grassroots advocacy training.

MSMA also launched a media campaign supporting Proposition B, which was the initiative to raise the Missouri state Tobacco Tax. Physicians from all over the state wrote letters to the editor to encourage passage.

Publications Committee

Volume 1, Number 1 of our forebear The Journal of the Missouri State Medical Association was published July 1904 with C.M. Nicholson, MD, as the first Editor. The May/June 2004 *Missouri Medicine* reproduced that 1904 original cover. As further celebration of its Centennial during 2004 we reproduced excerpts, reprints, and reflections from this 100-year period. July 2013 we shall celebrate 110 years of publication excellence. For Volume 109, *Missouri Medicine* produced 496 pages.

Your current *Missouri Medicine* is peer-reviewed, indexed by MEDLINE, The National Library of Medicine, and PubMed Central. By the end of the first quarter of 2013, we should have our most current content linked to PubMed Central. We are included in EBSCOhost databases, the largest premium online information resource for researchers.

Every year over the past dozen years the number of non-solicited articles to *Missouri Medicine* has increased. As with any first class journal, papers are not published without critical peer-review. A

minimum of two, and often three, highly qualified physicians vet each paper to determine suitability for publication; if the paper is to be published reviewers also submit recommendations to improve the manuscript construct, presentation, and content. Acceptance standards equal or exceed many national journals and free circulation newspapers/magazines. For example in 2012, there were 38 non-request manuscripts submitted for peer-review, only 44.7% were accepted for publication.

Missouri Medicine gives acceptance and publication preference to MSMA members in good standing. If at all possible, the editorial staff will extend themselves to help with re-drafting a MSMA member's paper to publication standards.

May/June issue is for open papers and November/December is the legislative preview and also open papers. For the other four issues we turn to Missouri's six medical schools to produce a "theme issue" of high clinical relevance. We are proud to regularly partner with these medical schools: University of Missouri, University of Missouri-Kansas City, Kansas City University of Medicine & Biosciences, Saint Louis University, Washington University, and Kirksville College of Osteopathic Medicine-A.T. Still University. An alternative form of contribution ("mini-series") is sequential preparation and publication of one paper every two months for up to a year.

Visual presentation of *Missouri Medicine* has modernized with improvements and redesigns to: covers, the masthead, font and page layout, QR bar codes. A completely electronic version of each issue is created for the website; to save postage costs the e-issue goes to students, residents, and fellows with free membership, as well as regular members that wish to opt out of the mailed paper issue. The e-issue is posted to a "members only" section of the MSMA website (www.msma.org). In the fourth quarter, all issues from the previous year are moved to full public access.

Being on the *Missouri Medicine* editorial board is a great honor and recognition of high regard by physician peers and the leadership of MSMA. All members are asked to participate in peer-review, contribute articles, and solicitation of highly qualified authors on issues we wish to publish. Special thanks for their good work year after year: Drs. Milamari Cunningham, David Fleming, Art Gale, William Reynolds, and Charles Van Way, III. On behalf of *Missouri Medicine* we wish to thank Douglas B. Bogart, MD, a longtime friend and colleague for his exemplary service to our Editorial Board in Cardiology. Jerry Kennett, MD, a former MSMA President, has joined *Missouri Medicine* as our new cardiology editor. We also welcome Eric Lederman, MD, who is the Conlon and Rectal Surgery editor and Brian L. Mahaffey, MD, as the Sports Medicine editor.

Kenneth Haller, MD, and Anthony Slocum, MD, of SLUSM/Cardinal Glennon Children's Medical Center (January/February 2012) comprehensively addressed the problem of children not being vaccinated due to fears such as inducing autism. MSMA and Missouri state health organizations conducted a very effective immunization education program based on this stellar publication.

In the nation's most authoritative review to date, "Legalization, Decriminalization & Medical Use of Cannabis: A Scientific and Public Health Perspective." (March/April 2012) Dragan M. Svrakic, MD, and co-authors disabused any valid reason to make 'Mary Jane' an honest woman.

A totally new paradigm that is shaking the core of cardiology and exercise physiology while upsetting ultra-exercise addicts and the various fitness industries they support, was reported in July/August 2012. The authors, many runners themselves, are Drs. Harshal Patil, James O'Keefe, Carl Lavie, Anthony Magalski, Robert Vogel, and Peter McCullough. Their first report was in the Mayo Clinic Proceedings, second world publication - featuring elaboration and detailed exercise guidelines - was in *Missouri Medicine* and recently editorialized in the international journal Heart. The authors have had over 100 media interviews.

MedHelp.org (www.medhelp.org) is a top world health internet site with over 12 million unique visitors per month and likely 150 million visits in 2012. *Missouri Medicine* became the first medical journal in the United States to enter into an agreement to provide content to a top internet health destination. *Missouri Medicine* and MedHelp review our upcoming articles, and we mutually pick the two with the widest public interest. A 400-word "patient language" summary precedes the full text article. They are posted to the appropriate forums and communities from among the more than 350 forums and communities they have. *Missouri Medicine* papers

are consistently highly ranked by MedHelp viewers. An active link at the end of the article connects with the MSMA website. MedHelp has an electronic health newsletter with a subscription of over a quarter of a million readers. Our articles are included in the e-newsletter also. Because of this growth, *Missouri Medicine* authors and staff regularly receive reprint requests from across the United States and as far away as China, South America, and the Middle East.

Missouri Medicine has an informal agreement to provide reprinted papers selected by the Editors of General Surgery News, Anesthesia News, Clinical Oncology News, and Pain Management News. Articles based on *Missouri Medicine* content have appeared in the St. Louis Post-Dispatch, the Kansas City Star, the Wall Street Journal, Runner's World, NBC, Outside Magazine, EyeNet, the Journal of the American Medical Athletic Association, the Journal of Cataract & Refractive Surgery Today, Ophthalmology Times, and Ocular Surgical News, to name a few. *Missouri Medicine* selectively reprints articles from St. Louis Metropolitan Medicine, the Journal of the Greene County Medical Society and the Medical Bulletin of the Metropolitan Medical Society of Greater Kansas City. Select national articles appropriate to Medicine in Missouri are also occasionally reprinted.

Our new goals for 2013 are to construct on the MSMA website in the public section a virtual textbook on keeping the heart healthy. Chapters will be those papers we've published in our two-year Preventive Cardiology mini-series and other germane papers. We also plan to create a place on the MSMA website to advertise books by members and link to sources for purchase. Through the generosity of a Contributing Editor Arthur H. Gale, MD, we are pleased to announce the Freedom of Expression Award selected from our published authors by a special MSMA committee.

The Publication Committee, Editor, John C. Hagan, III, MD, and Managing Editor, Lizabeth Fleenor, appreciate the many contributions of the MSMA, Alliance members, and others who have contributed to *Missouri Medicine*. The Committee appreciates the Association's continued support of the Journal.

Resident Fellow Section

The Resident and Fellow Section of the MSMA has had a dynamic year. Advocating for increased GME funding is a top priority in the RFS at both the state and national levels. We are excited that membership has increased during this year, and continue to be successful in representing Missouri as part of the AMA-RFS Region 2, which includes the states of Illinois, Iowa, Minnesota, Nebraska, North Dakota, South Dakota and Missouri. In this way, we work in conjunction with residents from our region on issues related to us on a broad scale, such as addressing GME funding, duty hour regulations, and student loan debt. In September, the GMEC at Washington University School of medicine held their first New House Staff Social which had informational booths that both MSMA and AMA membership participated in and the event was successful with more than 80 new house staff in attendance. The MSMA-RFS continues to spark interest in organized medicine amongst new residents and fellows in the state. We had two new MSMA members attend the AMA Interim 2013 meeting with MSMA delegates winning third place in the MSS-RFS Research Poster Symposium. During the MSMA Annual Convention on Saturday, April 6, the MSMA-RFS will participate in a panel for the MSMA Medical Student Section (MSS) over the noon hour at KCUMB to help address any MSS questions regarding residency training and match process. Additionally, on Saturday afternoon, there will be a Clinical Skills Workshop held for the MSS with RFS members. The RFS business meeting will take place following the Workshop. All residents of Missouri are welcome to attend the RFS business meeting and education session during MSMA Annual Convention in Kansas City.

Medical Student Sections

A.T. Still University – KCOM

This year ATSU-KCOM MSMA-MSS is happy to welcome 17 new members to our organization from the first and second year class. So far this year we have put on the Succeeding in Medical School (SIMS) event. We partnered with The Red Cross to raise donations for blood products and collected over 60 pints, 26 of which came from our members! Our project last year working with the National Disaster Life Support Foundation helped train and achieve certification for an entire class of medical students in Basic and Advanced Disaster Life Support! This training also benefits our surrounding community by giving Emergency Medical Services personnel,

Firefighters, and local public health, access to these classes. We have continued working with the Disaster Awareness and Response Training committee this year to further this educational endeavor for future classes. For the upcoming year, we have many exciting programs coming up for our members. The first of these will be with different physicians at our school, advising us on how to decide on future career paths in medicine, by telling us their stories. We will also be having a rotation and residency meeting with residents from our local hospital, where they will advise us on how to best succeed in preceptorships/rotations, crucial stages in our career. We will also be having a lecture by our Neurology professor about neurolinguistic behavior, or as we like to call it, how to tell if someone is telling you the truth!

All of us are looking forward to White Coat Day and the Annual MSMA Convention, as well as upcoming elections for the students that will continue our success and productivity into the next year.

Kansas City University of Medicine and Biosciences

The KCUMB MSMA-MSS chapter has capitalized on a membership resurgence occurring a year ago to become one of the largest, most active organizations on our campus. After earning recognition as one of the nation's Top 10 AMA chapters in the area of recruitment last year, we were able to increase membership by over 100 students this year. By continuing to inform our peers of the importance and benefits of joining the MSMA and AMA, our chapter membership is now over 215 students.

Our chapter began the school year with a focus on welcoming first-year students and building relationships with them during their orientation week. We interacted with many students through our informational booth during the KCUMB Student Organization Fair that was attended by MSMA's Director of Membership Haley Wansing. To conclude orientation week, our chapter organized an overwhelmingly popular meet-and-greet that brought together more than half of the University student body.

In late August, the chapter hosted a recruitment event that featured guest speaker and MSMA Councilor Lancer Gates, DO. The event focused on the benefits of being involved with state and national medical societies. Dr. Gates urged us all to become informed and engaged in promoting legislation and clinical standards that ensure the best for physicians, patients and the public health.

As has been tradition, our chapter's executive board strives to not only help educate students professionally, but also in the classroom. As winter break neared, so did the first-year final exams that included the hardest pharmacology section of the year. The executive board held a pharmacology review for all first-year students. This event was successful and very popular as more than 100 students attended.

As we embark on the second semester of this school year, the chapter will focus on fundraising, academic and professional enrichment, and community service. In February, we will host a 3-on-3 basketball tournament as a chapter fundraiser. In March, we will conduct a microbiology review for the first-year class before their final exams. On April 5-6, KCUMB will host the AMA-MSS Region 2 Meeting with the theme of Reaching Beyond Medical School. AMA-MSS representatives from six states will congregate on KCUMB's campus to hear presentations centered on thinking past graduation, attend a clinical skills workshop and participate in a community service event at Hope Faith Ministries. To cap off an exciting school year, on April 13, our chapter will partner with UMKC's MSS to organize and host Dash for Diabetes, a 5K run/walk event with all proceeds going to the American Diabetes Association. Last year, this event raised over $5,000 and we expect an even greater turnout this year.

We look forward to finishing the school year strong as a chapter and electing new officers who will continue to pass along the importance and traditions of MSMA.

Saint Louis University School of Medicine

We are having an exciting school year. One of our primary goals this year was to increase awareness and student memberships for AMA and MSMA. Our heavy recruiting strategies have resulted in more than a 20 percent increase in first year membership from the previous year. Also in the fall we hosted a "Success in Medical School" event which had a significant turnout. Our panel for this event helped answer questions about not only AMA and MSMA, but also how to succeed and plan throughout all four years of medical school.

In the spring we have planned several events which will feature guest speakers who will discuss

topics covering the current state of health care and health care advocacy. In addition, in collaboration with Washington University School of Medicine, we will be once again organizing a 5K "Dash for Diabetes" with all proceeds donated to the Saint Louis Chapter of the American Diabetes Association. The event will take place April 14 on the St. Louis Arch Grounds. We will be having several socials and fundraisers to help raise money and awareness for the event. We are thrilled with the progress made in our Chapter and hope to establish a strong foundation for SLU's MSMA-MSS for coming years.

University of Missouri – Columbia

Our MSMA/AMA-MSS at University of Missouri – Columbia started off the year with a successful recruitment event sponsored by our Boone County Medical Society (BCMS). We had approximately 40 percent of our incoming first-year medical students join MSMA with a few upperclassmen joining as well. Our BCMS graciously supplied membership incentives, including Maxwell Medical Reference Guides, reflex hammers and a Littmann Cardiology III stethoscope that was raffled off to new members. This supplemented those incentives provided by our MSMA, which was also a huge draw to new members and included MSMA bags and stationary supplies. Also, our AMA provided strong incentives in the form of a choice between Netter Anatomy Flashcards or a Rapid Review: Pathology book by Goljan (a key resource for any first or second year medical student). We had more than 75 students in attendance at our first meeting. David Barbe, MD, our esteemed AMA Board of Trustees Chair-Elect gave a talk on organized medicine and the importance of student involvement within organized medicine.

We also had a very successful fundraiser organized by our Chapter's vice-president, Doug Crase, which raised money for MedZou, our local free clinic run entirely by medical students with support from our medical school and attending physicians who volunteer their time for our patients. We were able to raise more than $800 by putting on our annual Halloween party, Terrortoma.

This year our chapter also added the position of Community Service Chair, which was held by Blake Bodendorfer. He worked closely with Boys and Girls Town of Missouri to coordinate a health and wellness event last fall and organized a supply drive for them last spring. He also worked with the Lion's Club to put together an eyeglass drive, which was extremely successful.

We were able to send a delegate, Lauren Stephenson, and alternate delegate, Nathan Nolan, to represent Mizzou and Missouri at the AMA-MSS Interim meeting in Honolulu in November. We also sent Inna Hadass to the AMA-HOD meeting as Alternate Regional Delegate and Cory Offutt as State Alternate Delegate.

Mizzou had a very successful year in the form of representation at the MSMA-MSS. Inna Hadass served as our MSMA-MSS State Chair, Lauren Stephenson served as Vice-Chair, Kyle Riggs served as Vice-Councilor, Rachel Waller served as our State Secretary and as aforementioned Cory Offutt served as State Alternate Delegate. This made Mizzou hold five of the seven elected positions for our MSMA-MSS Governing Council, being the most representation Mizzou has had at the state level to date.

University of Missouri – Kansas City

The UMKC Chapter of the MSMA-MSS has had an amazing year thus far. We started the year with our recruitment event, where we were able to welcome over 20 new members from the incoming first year class alone. We appreciate the physician viewpoint provided by Dr. Charles Van Way, a significant contributor to MSMA and AMA. It was a two-day event and the second day included a panel of older medical students who gave advice and answered questions on how to succeed in medical school. The event won 2012 September "Event of the Month" from AMA's Section Involvement Grant (SIG) program.

In November, we sent 5 students to 2012 AMA Interim meeting in Honolulu, Hawaii. Our attendees learned about the AMA on a national and regional level. The students brought back their experience and presented to the UMKC Medical School Advisory Council.

Our top priority this year is to increase activity from all of our members and improve participation at our monthly meetings. Our first chapter meeting had over 60 members in attendance, the highest number in more than two years, as well as 10 new members.

In addition, we are planning to educate our members with a resolution-writing workshop in February and teaching leadership skills in the

upcoming months. We look forward to helping with Dash for Diabetes, participating in MSMA-MSS White Coat Day and 2013 AMA-MSS Region 2 meeting. It has been a great year thus far, and we are excited for better things to come.

Washington University

Our chapter has had another great year, building off the foundation set by previous years and forging new traditions to improve the Washington University Chapter of the MSMA-MSS. Since the last MSMA Annual Convention, we have had great successes infusing energy and excitement into younger members of our chapter.

This year, our new chapter Board focused on building an institutional memory at our school in the AMA by promoting participation across classes, as well as maintaining strong recruitment. This year we recruited 55 new four-year members of MSMA, an increase of 16 percent over last year. In order to build such a memory, we created several subcommittees within the organization similar to those at the State, Regional and National levels. In doing so, participation has vastly improved across events with each subgroup of our chapter, legislative, community service, and recruitment having a core 10-15 students who regularly meet or volunteer. The committees have been structured such that maintenance of involvement is encouraged even as our members enter their clinical years.

Our school's corollary committee to the Regional and National Committee on Legislation and Advocacy (COLA) was founded and has been particularly active this year, with multiple group discussion activities regarding resolution writing, as well as discussing various hot topics debated in the news and at the AMA Interim conference. In October, we sent two members from the committee, one first year and one second year, as delegates to the Interim AMA Convention in Honolulu, HA. Since one member had attended the previous convention, they were able to use their experience to help guide the first-year student toward taking advantage of the opportunities that were presented and gain valuable insight in developing the chapter.

Each attendee returned emboldened and inspired. For instance, at the Interim conference, with our fellow other Missouri Chapters, we tackled the question of how to boost cooperation among Missouri's medical schools and provide training for first year students prior to the first interim national conference.

As a result, Washington University has been planning a State Interim Medical Conference to be held in the fall of 2013. For AMA Advocacy day, we are sending 3 first year medical students who have been active in the committee to Washington, DC. Finally, one exciting avenue that our school's COLA is attempting to take, is to become an advocacy avenue for researchers at Washington University in order to make their latest findings heard, particularly when the scientific findings have implications on health care policy and medical care.

For service, our chapter currently fields two community service committees. The blood drive committee has since August organized and held multiple blood drives in conjunction with the American Red Cross on campus with great success. Before the end of the year, we plan on having more and continuing that momentum. Our second community service committee is beginning to ramp up work for our marquee event, Dash for Diabetes, which is hosted, in collaboration with Saint Louis University School of Medicine, and in previous years has helped to raise over $2,000 for the American Diabetes Association. As part of the AMA Wellness initiative, in conjunction with the Washington University in St. Louis SOM Yoga Club, we are hosting more than 15 free Yoga classes for students throughout this semester taught by professional yoga masters. The classes are provided in order to allow relief from stress, as well as provide an opportunity for exercise during the school year.

Our board, in conjunction with our recruitment committee, has throughout the year hosted lunch and dinner talks with members of the Washington University and Private practice community in order to educate the entire student body over the basics of health policy, and the matching process. Finally, this year, our chapter was awarded a community service grant in order to continue to host a first-fourth year dinner, which has been very well received and attended in past years. We look forward to continuing to be active and increasing our activity within our state, regional and national MSMA/AMA.

MM

MSMA Elects Leadership

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Secretary
David Redfern, MD, Springfield
Treasurer
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Honorary Vice President
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Honorary Vice President
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Immediate Past President
Stephen Slocum, MD, Chesterfield
Speaker
David Chalk, MD, Washington
Vice Speaker
Lancer Gates, DO, Kansas City

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Sri Devi Kolli, MD, St. Louis
Young Physician Section
Ramona Behshad, MD, Chesterfield
Resident Fellow Section
Jane Jones, MD, Mission Hills
Medical Student Section
Caroline Doo, Kansas City

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David Barbe, MD, Mountain Grove
10th District
Clifford Talbert, MD, Cape Girardeau
Organized Medical Staff Section
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International Medical Graduate
Ramona Aitken, MD, St. Louis
Young Physician Section
Sarah Florio, MD, Lee's Summit
Resident Fellow Section
Brad Harr, MD, Kansas City
Medical Student Section
Avik Som, St. Louis



Joe Craft, MD, St. Louis, testifies on a resolution during the MSMA Reference Committee hearings.

AMA Delegates & *Alternate Delgates

Edmond Cabbabe, MD, St. Louis
James Conant, MD, St. Joseph
Ted Groshong, MD, Columbia
Rebecca Hierholzer, MD, Leawood, KS
William Huffaker, MD, St. Louis
Lent Johnson, MD, Hannibal

*Elie Azrak, MD, Chesterfield
*Charles Van Way, MD, Kansas City
*Warren Lovinger, MD, Nevada
*Nathaniel Murdock, MD, St. Louis
*Inna Hadass, Columbia, Student

AMA Board of Trustees, Chair-Elect
David Barbe, MD, Mountain Grove

AMA Resident Fellow Section Delegate
Sara Dyrstad, MD, St. Louis

AMA Regional Student Section Delegate
Lauren Stephenson, Columbia

Alliance

President Barbara Hover, Springfield
President-Elect Kathy Weigand, St. Joseph

2013 Annual Convention Attendance

Delegates	115
Members	153
Exhibitors	62
Staff	23
Guests	182
Officers	7
Councilors/Vice	25
Alliance	49
Total	616

(Actual numbers will not balance due to overlaps in positions served.)

OFFICERS
Brennan, Jr., Robert, MD
Chalk, David, MD
Redfern, David, MD
Slocum, Stephen, MD
Sparkman, Thomas, MD
Taylor, Marsha, MD
Wolfe, James, MD

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Ahlum, Sandra, MD
Azrak, Elie, MD
Barjenbruch, Peggy, MD
Copeland, Jeffrey, MD
Corrado, Joseph, MD
Craft, Joseph, MD
Doo, Caroline
Dyrstad, Sara Woodward, MD
Gates, Lancer, DO
Hubbell, George, MD
Johar, Ravi, MD
Lovinger, Jr., Warren, MD
Romaker, Ann, MD
Schaaf, Rob, MD
Stanley, John, MD
Turner, Kirby, MD

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DiRenna, Jr., James, DO
Kuhlmann, David, MD
Riggs, Kyle
Thomas, Lisa, MD
Tweedy, Philip, MD
Weikart, Kevin, MD

DELEGATES

First District

Buchanan County Medical Society
Conant, James F., MD

Second District

Northeast Missouri Medical Society
Bukstein, Michael J., MD
Halpin, Stephen E., MD
Johnson, Lent, MD
McHardy, Bryson R., MD
Memken, John A., MD
Tweedy, Philip D., MD

Third District

St. Louis Metropolitan Medical Society
Arnold, Donald, MD
Bohigian, George, MD
Brennan, Jr., Robert A., MD
Butler, David F., MD
Cabbabe, Edmond, MD
Craver, Jeff, MD
Eggleston, Harry C., MD
Goodhope, Karen, MD
Greco, Thomas J., MD
Horenstein, Simon, MD
Huffaker, William H., MD
Laird, John M., MD
Meyer, Jay, MD
Murdock, Nathaniel H., MD
Page, Sam, MD
Payne, Meredith J., MD
Pohl, David, MD
Rollo, John, MD
Ryall, Jo-Ellyn M., MD
Slocum, Stephen, MD
Stadnyk, Michael, MD
Thomasson, Jeffrey L., MD
Vickar, Garry M., MD
Wild, Alan P.K., MD

Fourth District

St. Charles-Lincoln Medical Society
Agee, Carson K., MD
Glaser, Jeffrey S., MD
Meier, Matthew W., DO
Sill, William, DO
Willman, Martin L., MD

Tri-County Medical Society
Chalk, David, MD
Moore, John D., MD

Fifth District

Audrain County Medical Society
Andelin, Clark O., MD

Boone County Medical Society
Clapper, Adam T., MD
Cunningham, Milamari, MD
Early, Bridget, MD
Groshong, Ted, MD
Heimburger, Richard A., MD
Kennett, Jerry, MD
Murrell, H. Jerry, MD
Rieger, III, Frank G., MD
Thomas, Lisa A., MD

Cole County Medical Society
Wankum, Robert, MD

Lake of the Ozarks Medical Society
Buchanan, Sarah M., MD

Sixth District

Pettis County Medical Society
Kuhlmann, David, MD

West Central Medical Society
Haynie, William, MD
Long, Curtis, MD
Thompson, Frederick L., MD
Torontow, John, MD
Turner, William A., MD

Seventh District

Metropolitan Medical of Greater Kansas City
Allen, Thomas, MD
Buchanan McCanse, Barbara, MD
Butin, Richard, MD
Caughron, Michael, MD
Caughron, Samuel, MD
Delaney, III, Adrian J., MD
DiRenna, Jr., James A., DO
Dorzab, William, MD
Drees, Betty, MD
Farnham, Milo M., MD
Gibbons, Robert, MD
Granger, Nathan, MD
Hagan, III, John C., MD
Hahn, Jr., Frederick, MD
Hierholzer, Rebecca, MD
Kuennen, Scott, MD
Laughlin, Thomas, MD
McGuire, Stephanie, MD
Millspaugh, Dan, MD
Montello, Sam, MD
Munro, Stuart, MD
O'Dell, Michael, MD
Perryman, Kathy, MD
Potts, Donald, MD
Reintjes, Steve, MD
Rues, Larry, MD
Striker, Adam, MD
Thomas, James J., MD
VanWay, III, Charles W., MD
Youmans, Ronald, MD

Eighth District

Greene County Medical Society
Ashley, Michael E., MD
Blaine, James R., MD
Clarke, Michael S., MD
Hover, Alex R., MD
Knowlton, III, Norman, MD
Lilly, John, DO
Lurie, Harold H., MD
Redfern, David, MD
Reynolds, William R., MD
Taylor, Marsha, MD
Wolfe, James B., MD
Wright, Andy J., MD

Ozarks Medical Society
Betz, Robert F., MD
Hamilton, William P., MD

Ninth District

South Central Counties Medical Society
Barbe, David, MD

Tenth District

Cape Girardeau County Area Medical Society
Jung, John Marshall, MD
Sparkman, Thomas C., MD
Talbert, Clilfford R., MD

Jefferson County Medical Society
Shaplin, Alfred D., MD

STUDENT SECTION

St. Louis University
Lee, Daniel S.
Zheng, Albert Y.

University of Missouri-Columbia
Blount, Lucas R.
Nolan, Nathan

University of Missouri-Kansas City
Bader, Hasan H.
Monfared, Sara H.

Washington University
Benzoni, Nicole
Oetjen, Kyle

Kansas City University of Medicine
Randall, Gabriel
Traum, Daniel J.

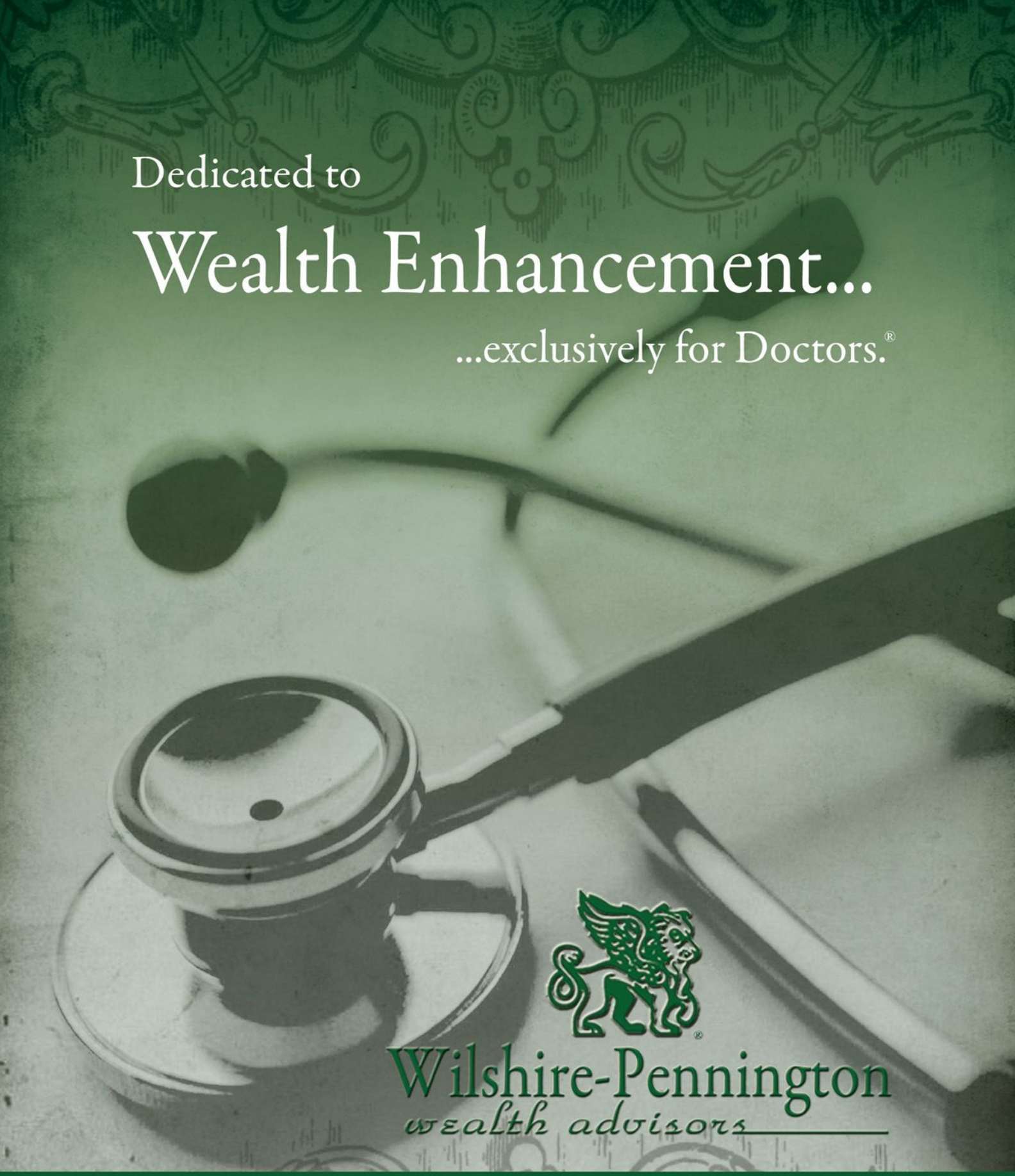
DELEGATES-AT-LARGE

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Hahn, Jr., Frederick, MD
Johnson, Lent, MD
Kennett, Jerry, MD
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Murrell, H. Jerry, MD
Slocum, Stephen, MD
Sparkman, Thomas, C., MD
Thomasson, Jeffrey, L., MD
VanWay, III, Charles, W., MD
Youmans, Ronald, MD

Speaker
Taylor, Marsha, MD

Vice Speaker
Chalk, David, MD

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Ajans, Zaki, MD
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Azrak, Elie, MD
Bandara, Rohan
Barjenbruch, Peggy, MD
Barth, Bradley, MD
Batterson, James, MD
Belshe, Sidney, MD
Char, Douglas, MD
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Chow, Kevin
Colbert, Stephen, MD
Cole, Donald, MD
Cole, Sherman, MD
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Conway, Robert, MD
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Corrado, Joseph, MD
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Craft, Joseph, MD
Craig, Stefan, MD
Crase, Douglas
Curti, Steven
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Daus, Arthur, MD
Dawson, Patrick, DO
Dean, Greg, MD
DeBoard, James, MD
DeMelo, Ryan, MD
Devineni, V. Rao, MD
Dixon, G. David, MD
Doo, Caroline
Doo, Josephine
Dyrstad, Sara Woodward, MD
Easterwood, Jonathan, DO
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Fischer, Keith, MD
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Gardner, Laura, MD
Gates, Lancer, DO
Gooden, Christie, MD
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Hagen, Douglas, MD
Hagen, John, MD
Harr, Brad
Hassien, Joel, MD
Heidt, Jonathan, MD
Higginson, Sean, MD
Hoeman, Michael, MD
Hoffarth, Sharon, MD
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Hubbell, George, MD
Husain, Neha
Husain, Syed Arshad, MD
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Jung, Christopher, MD
Junker, James, MD
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Kim, Michael
King, III, Dana, MD
Koboldt, Timothy, MD
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Landrum, Alice, MD
Lange, Emily, MD
Lewis, Noel, MD
Littlejohn, Robert, MD
Lombardo, Joseph, MD
Lovinger, Daniel
Lovinger, Jr., Warren, MD
Maitz, Carlos, MD
Manalaysay, Alvin, MD
Manning, Zachary
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Martin, Clarence, MD
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McMurry, Ted, MD
Mecham, Jesse, MD
Messmore-Arn, V. Paula, MD
Metlis, Schuyler, MD
Meyer, Thomas, DO
Middleton, Jerry, MD
Miller, Ramona, DO
Mills, Paul, MD
Mishra, Shruti
Montes, Arturo, MD
Moon, Joseph, MD
Morris, John, MD
Myers, Carl
Nguyen, Helen, MD
O'Brien, Edward, MD
Offutt, Cory
Oliver, Malcolm, MD
Ott, Kate
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Petersen, Larry, MD
Petit, Carl, MD
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Scheu, James, MD
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Sheeran, Paul, MD
Shukla, Monica
Slaughter, Larry, MD
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Stamos, Thomas, MD
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Stewart, Larry, MD
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Threlkeld, Kevin, MD
Turner, Kirby, MD
Ulloa, Eduardo, MD
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Weigand, Tom, MD
Weikart, Kevin, MD
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Winn, Hung, MD
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Zanaboni, Paul, MD
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