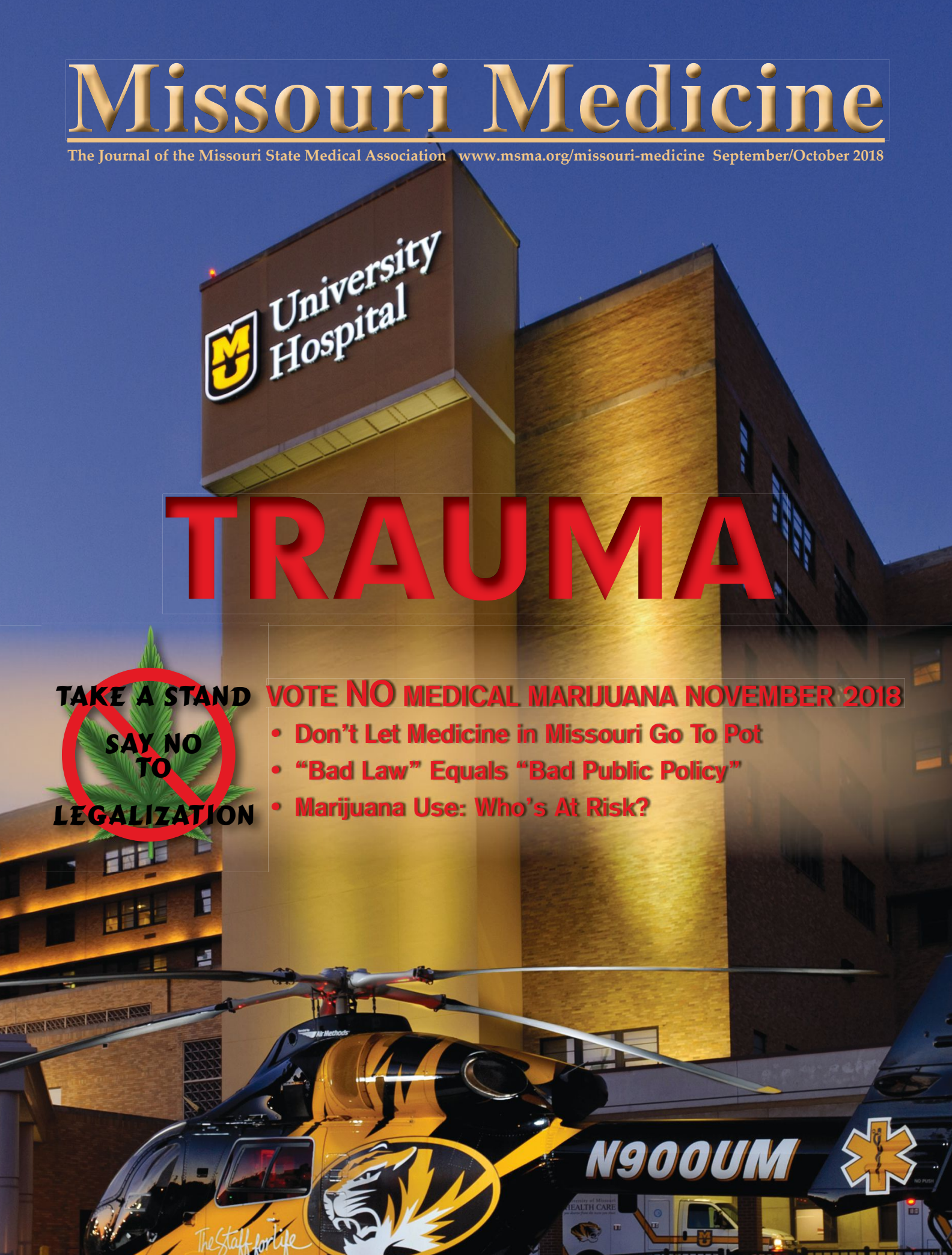
Missouri Medicine

The Journal of the Missouri State Medical Association www.msma.org/missouri-medicine September/October 2018



Give them focus.

Give to the Missouri State Medical Foundation.



Helping students focus on their medical education for over 50 years, the Missouri State Medical Foundation has benefitted thousands of medical students statewide. We thank the many donors who have committed their energy and resources to fulfilling the Foundation's mission, and we are grateful for their generosity.

For over 15 years, MSMA Scholarships have been funded by the Foundation for students at each of Missouri's medical schools.

The Foundation has also facilitated the creation of scholarship funds through a matching grant program. Our scholarship partners include:

- Boone County Medical Society
- Cole County Medical Society
- Kansas City Medical Society
- Northeast Missouri Medical Society
- Quad Counties Medical Society
- Saint Charles-Lincoln County Medical Society
- MSMA Alliance

Donations may be sent to:
Missouri State Medical Foundation | P.O. Box 1028 | Jefferson City, MO 65102
Contact Patrick Mills at 800-869-6762 | Email pmills@msma.org

The Missouri State Medical Foundation is a 501(c)3 organization.

Missouri Medicine

The Journal of the Missouri State Medical Association - Since 1904

Volume 115 | Number 5 | September/October 2018 www.msma.org/missouri-medicine

EDITORIAL



Don't Let Medicine in Missouri Go to Pot: Oppose Sham Medical Marijuana Referenda on November 2018 Ballot
by **John C. Hagan, III, MD** 392

GUEST EDITORIAL

"Bad Law" equals "Bad Public Policy": Why Three Missouri Medical
Marijuana Ballots Issues Need to Be Voted Down
by Cynthia A. Walsh, JD 394

PERSPECTIVE

Marijuana Use in the Era of Changing Cannabis Laws: What Are the Risks? Who is Most at Risk?
by **William V. Stoecker, MD**, Emily E. Rapp & Joseph M. Malters, MD 398

Artificial Intelligence and the Softer Side of Medicine
by **Joseph A. Craft III, MD** 406

Leading the Way: Women in Missouri Medicine
by **Joanne Loethen, MD** & **Lauren Umstattd, MD** 410

AS I SEE IT

What We Owe To Each Other
by **Frances Mei Hardin, MD** 416

PRESIDENT'S FORUM

Sulla Strada di Nuovo... "On the Road Again"
by **Joseph A. Corrado, MD** 418

MEDICAL SCHOOL PERSPECTIVE

A Triplicate Mission to Improve Lives
by **Patrick Delafontaine, MD** & Jerry C. Parker, PhD 425

SCIENCE OF MEDICINE | FEATURE SERIES

School of Medicine

Presented by the University of Missouri School of Medicine Acute Care Surgery Division

Overview: Management of the Injured Patient
by Salman Ahmad, MD 428

Initial Evaluation and Management of the Injured Patient
by Jeffrey Coughenour, MD 429

New Advances in the Care of the Hemorrhaging Patient
by Tessa N. Woods, DO, Keela R. Scott, MS3 & Jacob A. Quick, MD 434

Pediatric Trauma Update
by Dane C. Paneitz, MS3 & Salman Ahmad, MD 438

Evaluation and Management of the Burn Patient: A Case Study and Review
by Jeffrey S. Litt, DO 443

Simulation Training in Trauma
by Jacob A. Quick, MD 447

Mass Casualty Incident Management
by Salman Ahmad, MD 451

SCIENCE OF MEDICINE

A Cross-Sectional Study of Firearm Injuries in Emergency Department Patients
by Heather de Anda, MD, Taylor Dibble, Charles Schlaepfer, Randi Foraker, PhD & Kristen Mueller, MD 456

The Potential of Quantum Computing and Machine Learning to Advance Clinical Research and Change the Practice of Medicine
by Dmitry Solenov, PhD, Jay Brieler, MD & Jeffrey F. Scherrer, PhD 463

Giant Cell Arteritis: 2018 Review
by **Anne Winkler MD** & David True, DO 468

FROM YOUR ASSOCIATION

Medical Society Spotlight 422
Missouri Medicine In the News 420
Member Services Directory 472

On the Cover: Justin Kelley/MU Health Care

www.msma.org/engage

momedical @momedicalassn mostatemedicalassociation momedical momedical

MSMA member names in bold

Missouri Medicine

Missouri Medicine, a peer-reviewed, award-winning medical journal printed on acid-free paper, has been in continuous publication since 1904. All scientific articles are peer-reviewed. Original articles are accepted for publication on the condition that they have not been published or submitted to other medical journals for consideration. *Missouri Medicine* does not accept single or small series case reports with a literature review unless it is a first or second world literature report or there is some unique unreported aspect of the case. Notification of receipt of your manuscript is within 10 days. Peer review is completed within 30-45 days of receipt. Refer to the American Medical Association Manual of Style, 10th Ed., AMA, Chicago, 2007, for style or visit www.msma.org/missouri-medicine for Instructions for Authors. MSMA members are given publishing preference and priority. Material appearing in *Missouri Medicine* is protected by copyright. Reprints of articles may be purchased. Single, entire issues may be purchased, if available. Previous issues are archived and available at www.msma.org/missouri-medicine-library.

ADVERTISING

For reader and demographic profiles, statistics, and advertising rate sheet and contract, visit www.msma.org/missouri-medicine or email lfleenor@msma.org.

COPYRIGHT & POSTAL ENTRY

Owned and published since 1904 by the Missouri State Medical Association. *Missouri Medicine*, the Journal of the Missouri State Medical Association [ISSN 0026-6620], is published bi-monthly at 113 Madison Street, Jefferson City, Missouri 65102. Periodicals postage paid at Jefferson City, Missouri and at additional mailing offices. Postmaster: Send address changes to Missouri State Medical Association, c/o Membership Dept., P.O. Box 1028, Jefferson City, MO 65102. Copyright 2018 by the Missouri State Medical Association. Printed by the Ovid Bell Press, Inc., Fulton, Missouri. The subscription price per year for non-members is $75.00. Annual subscription for members is included in the annual membership dues. Single copies are $15.00, if available.

DISCLAIMER

All articles, editorials, and letters published represent the opinions of the authors and do not reflect the official policy of the MSMA or the institution with which the author is affiliated unless clearly specified.

CONTACT

Editor John C. Hagan, III, MD at jhagan@bizkc.rr.com
Managing Editor Lizabeth Fleenor at lfleenor@msma.org

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

Executive Vice President: Patrick Mills	Tel Ext - 123	pmills@msma.org
Governmental Relations/Legal: Jeff Howell	Tel Ext - 126	jhowell@msma.org
Legislative Affairs: Heidi Geisbuhler	Tel Ext - 122	heidi@msma.org
Communications: Lizabeth Fleenor	Tel Ext - 134	lfleenor@msma.org
Scientific Affairs: Benita Stennis	Tel Ext - 138	bstennis@msma.org
Membership: Haley Wansing	Tel Ext - 135	hwansing@msma.org
Marketing: Stephen Foutes	Tel Ext - 130	stephen@msma.org
Medical Specialties: Sarah Luebbert	Tel Ext - 128	sarah@msma.org
Finance: Lisa Cassmeyer	Tel Ext - 133	lisa@msma.org
Membership Database: Cassie Williams	Tel Ext - 127	cwilliams@msma.org
Office: Cheri Martin	Tel Ext - 121	cmartin@msma.org
Reception: Fran Draper	Tel Ext - 120	fran@msma.org
Administrative: Carol Meyer	Tel Ext - 132	cmeyer@msma.org

Editorial Board

OWNER & PUBLISHER
Missouri State Medical Association

MISSOURI MEDICINE EDITOR
John C. Hagan, III, MD
Tel: 816-478-1230 / 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 & PUBLICATIONS COMMITTEE
John C. Hagan, III, MD
Justin M. Albani, MD
Jeffrey G. Copeland, MD
Betty M. Drees, MD
David A. Fleming, MD
Arthur H. Gale, MD
William R. Reynolds, DDS, MD
Charles W. Van Way, III, MD
Jessica D. Bauerle, MD, Young Physician Contributing Editor

EDITORIAL BOARD
Susan S. Berdy, MD, Allergy/Immunology
Mitchell D. Botney MD, Pulmonary Medicine
Nancy J. Bunge, MD, Pediatrics
Edmond B. Cabbabe, MD, Plastic Surgery
Christopher R. Carpenter, MD, Statistics/Methodology
Octavio R. Chirino, MD, OB/Gyn
Joseph A. Corrado, MD, General Surgery
David H. Cort, MD, Gastroenterology
Juan C. Corvalan, MD, Psychiatry
John S. Daniels, MD, Internal Medicine
Louis P. Dehner, MD, Pathology
Jose M. Dominguez, MD, Colon/Rectal Surgery
Jon A. Dyer, MD, Dermatology
John F. Eisenbeis, MD, Otolaryngology
Eden M. Esguerra, MD, Infectious Disease
Gregory R. Galakatos, MD, Orthopaedics
Lancer G. Gates, DO, Hospital Medicine
Gary S. Gottesman, MD, Medical Genetics
John B. Holds, MD, Ophthalmology
Albert Hsu, MD, Chair, MSMA Young Physician Section
Kan N. Huang, MD, Hematology/Oncology
Jerry D. Kennett, MD, Cardiology
Katherine R. Lichtenberg, DO, Public Health
Joanne Loethen, MD, Chair, MSMA Resident and Fellow Section
Brian L. Mahaffey, MD, Sports Medicine
Callie Morris, Chair, MSMA Medical Student Section
Michael C. Murphy, MD, Cardiac Surgery
W. Kirt Nichols, MD, Vascular Surgery
John H. Niemeyer, MD, Radiology
Michael L. O'Dell, MD, Family Practice
James H. O'Keefe, MD, Preventive Medicine
Kathy M. Perryman, MD, Anesthesiology
Joshua E. Petrikin, MD, Neonatology
Elizabeth A. Piontek, MD, Urology
Keith M. Rich, MD, Neurosurgery
Howard M. Rosen, MD, Endocrinology
Pradeep K. Sahota, MD, Neurology
Gary G. Singer, MD, Nephrology
Mark T. Steele, MD, Emergency Medicine
Anne E. Winkler, MD, Rheumatology
Gregory M. Worsowicz, MD, Physical Med/Rehab

EDITOR EMERITUS
Donald G. Sessions, MD, 1988-1992
J. Regan Thomas, MD, 1992-2000

FIGHT THE FLU

Help your patients save money with the Missouri Drug Card. Call MSMA for a supply of cards at: 1-800-869-6762

Pharmacy Coupon | Prescription

Coupon MBR ID: Enter Year & Time (Example: Year 2017; Time 9:14; Enter ID 2017914)

RxGRP: MORX

RxBIN: 610709

This coupon has no expiration date and is reusable on Brand and Generic Rx's. Savings can be as high as 75%.

PATIENT INSTRUCTIONS: This card/coupon is pre-activated and can be used immediately. Present this card/coupon to any participating pharmacy to receive a discount on prescription medications.

PHARMACIST INSTRUCTIONS: Submit as a primary claim (cannot be processed as secondary) using the following pharmacy processing information. For processing questions and comments please call the Pharmacy Helpline below.

MISSOURI DRUG CARD
WWW.MISSOURIDRUGCARD.COM

Customer Service: 877-321-6755 Pharmacy Helpline: 800-223-2146 This is a point-of-sale discount program. This program is not insurance.

-Plus-

YOU COULD **SAVE UP TO 75%** ON YOUR PRESCRIPTION MEDICATIONS.



DRUG NAME	QTY	RETAIL	DISCOUNT PRICE	SAVINGS
Azithromycin 500mg	6	$60.23	$53.40	11%
Fluticasone Prop 50 MCG Spray	16GM	$70.99	$34.76	51%
Guaifenesin-Codeine Syrup 100MG/5ML	120ML	$15.99	$9.88	38%
Levofloxacin (Levaquin) 500mg	30	$343.47	$43.69	87%
Promethazine-Codeine Syrup 6.25-10/5	240ML	$49.99	$21.38	57%

*Discounted prices were obtained from participating pharmacies. Prices vary by pharmacy and region and are subject to change.

MISSOURI DRUG CARD
WWW.MISSOURIDRUGCARD.COM

For more information please contact:
Nataile Meyer
Email: modrugcard.com
Phone: 314.919.2032

Google Play App Store
SCAN FOR FREE APP OR VISIT FREERXCARD.COM TO DOWNLOAD

Compliments of: MSMA Missouri State Medical Association



Don't Let Medicine in Missouri Go to Pot: Oppose Sham Medical Marijuana Referenda on November 2018 Ballot

by John C. Hagan, III, MD

Learn more about the ballot issues at www.msma.org/medical-marijuana

Docs, listen up. Keep Missouri voters from passing legal but 'sham' non-needed, medical marijuana laws. Vigorously oppose all three referenda[1] on the Missouri November general election ballot that would legalize medical marijuana ('pot, weed, cannabis') in the Show Me state.

We don't need more social/medical nightmares like tobacco and opioids, both of which physicians initially aided and abetted. (Figure 1) Physician colleagues and medical professionals, "Show Me' some responsibility this time! Commit to educating your patients, contributing your time, your money, and your vote to defeating sham medical pot. Every state, notably well documented in Colorado,[2] that has enacted medical cannabis has created a tsunami of medical, social, educational, judicial, law enforcement, and business crises. Medical marijuana cards are available to practically anyone and diversion to recreational use and under-aged youth is the inevitable default setting. We don't need these problems in Missouri.

"Big Weed" is the termed coined for the coalition of businesses, corporations, individuals that is profiting enormously from state by state passing 'medical' and/or 'recreational' marijuana into law by referenda. Millions of Big Weed dollars are flowing into Missouri to open a new market of cannabis dependent customers, much the same as Big Tobacco abetted habituating millions to their nicotine laced, health destroying products. Big Weed is contemptuously, but effectively, emulating the marketing plan of "Big Tobacco."



Vote NO on All Three Medical Marijuana Referenda November Missouri Elections!

Big Weed's resources far surpass the responsible 'weed-killing' opposition. Big Weed's high-power advocates have cleverly 'sweetened' their noxious products by allocating a tiny 2-15% tax to be used for the likes of military veterans, cancer research, childhood education, and drug addiction. What, not widows, orphans, and homeless animals? Clever? Yes. But this is the equivalent of 'hiding behind hostages." There are no limits on the greed, duplicity and 'total war' tactics of Big Tobacco, Big Opioids and now Big Weed, the latest member of the Health Apocalypse Henchmen.

In Canada, which has virtually anything goes cannabis, several large brewing companies are spooling up to sell cannabis infused drinks[3] to offset the fall in beer sales. Idiotically, their industry refers to this as "the logical fourth leg" of commercialization: beer, wine, liquor and cannabis. Obviously, they imbibe a lot of their own products. I have unsolicited received about a half dozen offers to invest in limited partnerships that will profit from distributing sham medical marijuana of unknown composition. Medical weed is not even remotely a proper medicine of known composition, known quantity, and approved by FDA testing/approval process. Substantial monies are promised to investors and a growing, eventually nation-wide pot market. Medical marijuana laws are Big Weed's Trojan Horse to create astronomical profit from dependent non-medical customers and pave the way for eventual recreational 'anything goes' cannabis.

Much to their regret and shame, Colorado physicians and medical groups did not actively oppose medical and later recreational cannabis. The Colorado Medical Society[4] is urging other state medical organizations not to make the same mistake: "Other states facing legislative efforts to legalize marijuana should consider Colorado's experience as a cautionary tale. ***Approving medical treatments by ballot initiatives sets a dangerous precedent for public health***. This will be one of the great social experiments of the century." (emphasis added)

John C. Hagan, III, MD, FACS, FAAO, MSMA member since 1975, is a Kansas City, Missouri, ophthalmologist and *Missouri Medicine* Editor since 2000. He is a multi-year Super Diamond Contributor to MMPAC.
Contact: jhagan@bizkc.rr.com

Responsible Missouri physician organizations are officially on board opposing the three sham medical marijuana referenda include: Missouri State Medical Association, AMA, Kansas City Medical Society, Greene County Medical Society, St. Louis Metropolitan Medical Society, Missouri Society of Eye Physicians & Surgeons (we ophthalmologists don't need marijuana to treat glaucoma, makes treatment worse). *Missouri Medicine* regular readers will note many articles outlining scientifically the case against using true medical problems of patients as a straw man/woman for passing medical marijuana.[5] Many of these cannabis articles are from a writing group from Colorado coordinated by Ken P. Finn, MD, a widely known and respected pain-management specialist. This issue of *Missouri Medicine* presents other vital information for physicians beginning on the next page.

Many patients, and some physicians, believe that legitimate FDA approved medical research is not being done and would be facilitated by passing these sham medical marijuana referenda. Not so! The FDA has approved cannabis-based medicines via legitimate pure drug pathway: canabidiol (Epidolex) for the treatment for certain rare seizure disorders but with potential to help other more common types of childhood seizures; dronabinol (Marinol) for nausea and vomiting of chemotherapy and weight loss/poor appetite in HIV patients; and nabilone (Cesamet) for nausea and vomiting of chemotherapy when other drugs fail. Some restrictions on legitimate research on pure cannabis chemicals as real drugs might certainly be considered at the FDA level. Nor should we confuse this vote with the issue of decriminalization of small amounts of pot for personal use. Twenty-four states and over 50 large municipalities have passed decriminalization law more are in the process. This is not the issue we are voting on, nor is alcohol caused social/medical/judicial problems. Conflating tobacco, alcohol, and opioid problems to make cannabis appear a minor vice is a debating trope used by Big Weed to misdirect and misinform voters. This issue is sham medical marijuana.

It is worth stating again that all state legalization of cannabis for sham medical and recreational use is in violation of Federal Law, a fact all Presidents to date have chosen not to enforce and whom two, Clinton and Obama, have admitted to recreational pot use.

Most physicians look back with incredulity and disgust on some of our forebears: physicians, dentists, nurses in the 1940s and 50s who recommended and were used in commercial advertisements (Figure 1) for tobacco products; late 1990s to mid 2000s opioid industry compensated physicians like Russell Portenoy, MD,[6] and the Kansas City Center for Practical Bioethics/Myra Christopher, RN, who shilled for the pain pill industry[7] We must not make the same mistakes. We physicians, and hopefully a broad coalition of healthcare professionals, institutions, educators, law enforcement, children and public welfare advocates and all informed citizens must band together and defeat the three harmful sham medical marijuana referenda on the Missouri November General Election Ballot (Figure 2).

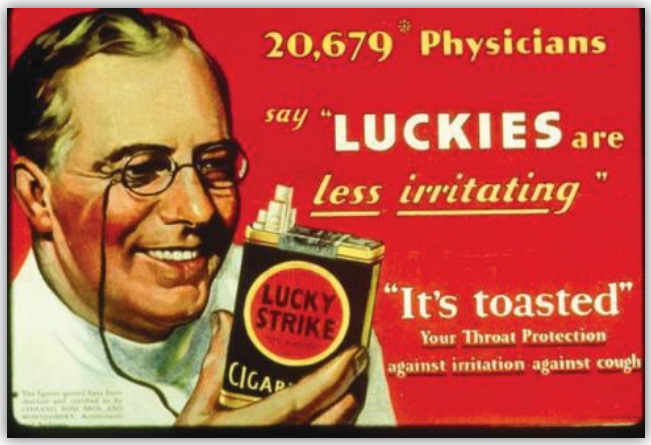


Figure 1. Physicians, dentists and nurses were used to promote and sell cigarettes. Many prescribed smoking for throat irritation, nervousness and anxiety. Physician and medical professionals must avoid these mistakes and oppose sham medical marijuana in Missouri.



Figure 2. Medical marijuana quickly degenerates to anyone/any indication as long as they have cash to purchase. Diversion to recreational use is routine. Under the influence of cannabis in Colorado schools increased 44%.
Source: https://www.flickr.com/photos/adam_jones/6933957739 courtesy Adam Jones

Don't let Medicine in Missouri go to pot!

References

1. https://www.sos.mo.gov/default.aspx?PageID=9456
2. https://drive.google.com/file/d/0B0tmPQ67k3NVQlFnY3VzZGVmdFk/view
3. https://www.wsj.com/articles/constellation-brands-expands-investment-in-cannabis-company-canopy-growth-1534332997
4. http://www.cms.org/articles/marijuana-legalization
5. Svrakic DM, Lustman PJ, Mallya A, Lynn TA, Finny R, Svrakic NM. Legalization, Decriminalization & Medical Use of Cannabis: A Scientific and Public Health Perspective. Missouri Medicine 2012;109(2):90-95
6. Gale AH. Drug Company Compensated Physicians Role in Causing American's Deadly Opioid Epidemic: When Will We Learn? Missouri Medicine 2016;113(4):
7. Hagan JC III. Kansas City Center for Practical Bioethics at Epicenter of Congressional Concerns about Conflicts of Interest with Pain Pill Industry. Missouri Medicine 2016;113(4):247

MM



"Bad Law" equals "Bad Public Policy": Why Three Missouri Medical Marijuana Ballots Issues Need to Be Voted Down

by Cynthia A. Walsh, JD

Introduction and Defining Bad Law

Due to limited space, this article highlights just a few of the plethora of problems identified in the Missouri medical marijuana amendments that are of blatant legal concerns. These amendments have been set for the November 2018 ballot. However, I will discuss why, even just the issues I have brought to the reader's attention, makes the amendments bad law and should not be approved by the electors. Bad law is a legal term of art which is applied to a law, or proposed law, that is harmful, vague, lacks enforceability, or is in conflict with other well accepted public policies. In reviewing the Missouri medical marijuana amendments, I find that each qualifies as bad law. The only way to cure or fix bad law is to repeal it or never adopt it in the first place. Readers should decide for themselves if each of these amendments meets the definition of bad law. And, bad law results in bad public policy.

Purpose of a Constitution vs. Statutes

A constitution is a document that provides the framework under which a state or federal government functions. In changing a constitution, one is changing the core framework by which the government pegs the development of future laws and public policies. Therefore, modifying constitutions is designed to be a slow and burdensome process so that this framework is not changed without a great deal of contemplation and purpose. Modifying a constitution should never be used in situations where issues can be handled through statutory law. Based on this fundamental understanding of the purpose of a constitution vs. laws, two of the three pro-medical marijuana proposed amendments should be defeated as they are not a proper topic to be enshrined in a constitution.



Cynthia A. Walsh, MA, JD, is certified in Health Care Ethics by the University of New Mexico Health Sciences Department and is an accredited veteran's attorney through the Veterans Administration. Since 2014 she has been working to address the growing crisis of state legalization of marijuana.
redtick@sleepingtortoise.com

Highlights of the Three Ballot Issues

There are three ballot issues in Missouri that will in one way or another be promoting the consumption of marijuana:

- Amendment 2: Medical Marijuana and Veterans Healthcare Services Initiative (4% tax on medical marijuana sales);
- Amendment 3: Bradshaw Amendment (would create two new entities — Biomedical Research and Drug Development Institute, and the Land Acquisition Board; 15% tax on medical marijuana sales); and
- Proposition C: Missourians for Patient Care Act (statutory amendment with a 2% tax on medical marijuana).

The focus on all three amendments is to use as sources for medical marijuana, plants that contain high levels of THC (tetrahydrocannabinol) as these amendments are not focusing on growing hemp-marijuana with its low .3% THC level and high CBD (cannabidiol). The Bradshaw Amendment specifically states that its definition of marijuana does not include hemp. None of the three proposed amendments limit the amount of THC in the

Learn more about the ballot issues at www.msma.org/medical-marijuana

plants grown nor in any of the end products which will be consumed as 'medicine.'

All three amendments legalize taking medical marijuana by any method currently known or that any physician recommends, which includes but is not limited to vaping, edibles, lotions, smoked, suppositories, and derma patches in order to get the marijuana into one's body or on it. The boiler plate language found in all three amendments provides an extensive list of health conditions for which medical marijuana can be recommended, including but not limited to glaucoma, seizures, cancers, intractable migraines, multiple sclerosis, Parkinson's disease, etc. Additionally, if any illness has been overlooked there is a catchall phrase for those as well — "… any other debilitating medical condition as determined in the professional judgment of a physician." There is no mechanism in place to remove an illness from the list of legally approved medical conditions for the use of medical marijuana. Both the open-ended list (vagueness) and the lack of ability to remove any medical condition (in ability to enforce or apply sound public policy) makes these amendments bad law.

Government entities will issue licenses for the medical marijuana cultivation sites (grows), manufacturing of medical marijuana, and/or medical marijuana dispensaries. Will local communities (counties or cities) be able to prohibit these medical marijuana operations in their jurisdiction? Answer: maybe and, then again, maybe (probably) not. For example, in one of the proposed amendments, the citizens would have to hold a special election in which "… two-thirds majority of the registered voters vote to prohibit medical marijuana operations" in order to stop the marijuana operations in a community. Such an election result would be nearly impossible to achieve since the standard is not two-thirds of those who vote in that election but it is two-thirds of the actual registered voters who must vote against marijuana operations in their community. Again, this appears to meet the standard of bad law as this option for the citizenry would simply be unrealistic.

The Bradshaw Amendment requires that if a local government wants to opt out for the first five years and then a citizenry vote for the next five years, it must submit this in writing to a government oversight board. This would typically be normal procedural law but the oversight board does not have to honor the opt out requests because the language is merely permissive, i.e. the board 'may' (or might not) accept the opt out requests but does not have to. Again, another example of bad law in which the public has no recourse to preserve their quality of life.

Ranking the Amendments — Is Lesser of Evils Possible?

In my opinion, the worst amendment is the Bradshaw Amendment, the second worst is the Medical Marijuana and Veterans Healthcare Services, and the lesser of the evils is the Missourians for Patient Care Act. The only reason the statutory one is the least of the evils is because it is in the form of a statute and can be more easily corrected in the future. All three of these ballot amendments are, however, bad law and should each receive a 'no' vote in November.

Why is the Bradshaw Amendment the Worst?

In addition to its being an amendment to the state constitution, it creates a massive new governmental institution which would be known as the Biomedical Research and Drug Development Institute with a very powerful board of directors. The powers given to this constitutionally enshrined body are breathtaking and there appears to be no means of real oversight. Reading how this institute and its governing board would be established and run raises tremendous concerns of the amount of power concentrated into one governmental body. The concerns are too numerous to address in this brief article, so I would urge the reader to read the extensive powers that would be held by this board and ask yourself: (1) what controls are in place to avoid conflict of interests in research? (2) what controls are established for assuring research meets medical research ethical standards? (3) what mechanism is there for the reporting of ethical or legal breaches? (4) what mode of oversight and accountability is there over the proposed institution and its board of directors? (5) since the purpose of the research is to find cures using marijuana, what happens if the research shows that marijuana as a medicine either is ineffective or is actually dangerous? The answers that I arrived at leads me to conclude that the Bradshaw Amendment is bad law.

Hope for Your Future

Whether or not you like politics or legal questions,

the topic is being foisted upon the public this fall by those who advocate for marijuana. Remember that the vast majority of Americans do not consume marijuana. In Colorado 73% of its jurisdictions have banned marijuana grows, marijuana manufacturing, and dispensaries. There is public guilt being pushed by those advocating for these amendments that to vote "no" is denying people essential medicine. This argument ignores the fact that the FDA has approved several medicines that are marijuana based and available by prescription so there is no need to grow one's own marijuana medication. Where is the compassion by those advocating for medical marijuana for those who have been harmed by medical marijuana from suicides, murders, and rising crime rates in general where marijuana has been legalized?

Disclosure

This is not intended as legal advice. If you need legal advice contact an attorney who is licensed in the state of Missouri.

Resource Links

Drug Free Idaho funded a documentary, Chronic State: How Marijuana Normalization Impacts Communities, it was mostly filmed in Pueblo, Colorado about the impact of marijuana in Colorado.

- http://www.DrugFreeIdaho.org
- https://vimeo.com/280127474

When the topic of compassionate use of medical marijuana comes up, let the public know about the victims of marijuana consumption. One source is an electronic memory quilt of loved ones whose deaths are linked to marijuana produced by MomsStrong.org

- http://momsstrong.org/2018/05/12/memorial-quilt-the-many-ways-marijuana-kills/

"It's High Time We Took A Breath From Marijuana Commercialization" By Bob Troyer, US Attorney For District of Colorado, Denver Post, September 28, 2018. Troyer highlights the failed promises of the marijuana industry and that Colorado's children now consume marijuana at a rate 85% higher than the national average.

- https://www.denverpost.com/2018/09/28/colorado-marijuana-commercialization/

MM



Today – Do more of what you love

At Mercy Clinic, we span across four states with a team of more than 2,100 Mercy primary care and specialty care physicians, 600 advanced practitioners. Mercy was named one of the top five largest U.S. Health Systems in 2017 by Truven, an IBM Watson Health Company and we serve millions annually. Mercy includes 44 acute care and specialty (heart, children's, orthopedic and rehab) hospitals, more than 700 physician practices and outpatient facilities, more than 40,000 co-workers and more than 2,000 Mercy Clinic physician in Arkansas, Kansas, Missouri and Oklahoma. Mercy also has outreach ministries in Arkansas, Louisiana, Mississippi, and Texas.

To find out about Physician and Advanced Practitioners openings across the Mercy System please contact:

Tammy D. Hager, Director of Physician Recruitment
Tammy.Hager@mercy.net | 417-820-6650

Or go to **http://www.mercy.net/careers** to search for your specialty opportunities.

Mercy

List of Specialties:

- Anesthesiology
- Cardiology - Electrophysiology
- Cardiology - Interventional
- Cardiology - Non-Invasive
- Critical Care - Intensivist
- Dermatology
- Emergency Medicine
- Endocrinology
- Family Medicine
- Family Medicine - OB
- Gastroenterology
- General Surgery
- General Surgery - Breast Surgery
- Geriatric Medicine
- Gynecology - Urogynecology
- Hematology and Oncology
- Hospitalist
- Infectious Disease
- Internal Medicine
- Maternal-Fetal Medicine
- Med-Peds
- Neonatology
- Nephrology
- Neurological Surgery
- Neurology
- Neurology - Neuroimaging
- Obstetrics and Gynecology
- Obstetrics and Gynecology - OB Hospitalist
- Occupational Medicine
- Oncology - Gynecological
- Oncology - Surgical
- Ophthalmology
- Oral and Maxillofacial Surgery
- Orthopaedic Surgery
- Orthopaedic Surgery - Adult Reconstructive Surgery
- Orthopaedic Surgery - Hand Surgery
- Orthopaedic Surgery - Trauma
- Otolaryngology
- Pain Medicine
- Palliative Care
- Pediatrics
- Pediatrics - Emergency Medicine
- Pediatrics - Hospitalist
- Pediatrics - Ophthalmology
- Pediatrics - Surgery
- Pediatrics - Urgent Care
- Physical Medicine and Rehab
- Plastic Surgery
- Psychiatry
- Psychiatry - Child
- Pulmonary Disease
- Pulmonary Disease - Critical Care
- Radiation Oncology
- Radiology
- Rheumatology
- Sleep Medicine
- Telemedicine
- Trauma Surgery
- Urgent Care
- Urology
- Vascular Surgery



There are opportunities for physicians to gain extraordinary experience serving part-time in America's Navy Reserve. And all while maintaining a civilian practice. You can work in any of more than 30 specialty/subspecialty areas – from General Practice to Neurosurgery. Enjoy excellent pay and benefits – including the potential for additional specialty pay of up to $75,000.* And be part of a network that's both patient-focused and world-class.

WANT TO LEARN MORE? CONTACT YOUR NAVY RESERVE MEDICAL RECRUITER TODAY.

800-777-6289 | jobs_stlouis@navy.mil

*Contact a Navy Reserve Medical Recruiter for details. ©2015. Paid for by the U.S. Navy. All rights reserved.

1003DADRM011

AMERICA'S NAVY RESERVE



Marijuana Use in the Era of Changing Cannabis Laws: What Are the Risks? Who is Most at Risk?

by William V. Stoecker, MD, Emily E. Rapp & Joseph M. Malters, MD

Abstract

We review recent findings on medical aspects of marijuana use in order to identify those who are at greatest risk of marijuana-related medical problems. We analyze the impact of medical marijuana laws on health, in particular the disproportionate effects on adolescents and children. Chronic marijuana use predominantly affects certain areas of the brain that overlap the default mode network, linked hubs in the brain that play a supervisory role in critical thought processes such as attention, memory, and social interactions. Disruption of the default mode network areas has been documented in schizophrenia and Alzheimer's disease, illnesses with symptoms and brain changes that parallel findings in marijuana abusers. These findings counter the claim that marijuana is a harmless drug and are a cause for alarm in persons with cannabis dependence.

Introduction

As the November general election nears with three ill-conceived referenda which would legalize 'medical' marijuana, physicians should carefully consider the many medical, social, educational and law enforcement problems that other states, notably Colorado, have encountered after enacting similar legislation. If legalization occurs, physicians should think how they will respond to demands for marijuana prescriptions and the potential liability for adverse marijuana caused side effects, illnesses or accidents.

Consider this statement from the Colorado Medical Association: "Other states facing legislative efforts to legalize marijuana should consider Colorado's experience as a cautionary tale. Approving medical treatments by ballot initiatives sets a dangerous precedent for public health. This will be one of the great social experiments of the century." Source: http://www.cms.org/articles/marijuana-legalization.

In this article, we review properties of marijuana, to identify who may be at increased risk of problems if marijuana becomes widely available. We review the general impact of putative medical marijuana laws, including changes in marijuana use and diversion to non-medical and under-age users. Finally, we identify adverse changes in the brain that can occur in chronic marijuana users. Here marijuana or equivalently "cannabis" refers to all parts of the plant in the genus *Cannibis*, including stems seeds, stalks, and any extracts derived from the plant. We consider all forms of administration including ingestion by vaporization or smoking, ingestion by eating or drinking or by contact with the skin of any cannabis products or chemicals, whether natural or synthesized, collectively referred to as "cannabinoids." The cannabinoids we discuss include 'high/mood-altering' delta-9-tetrahydrocannabinol, commonly referred to as THC, which is used in the recreational use products and the 'non-high/mood-altering' cannabidiol, or CBD, which is the form in which medicinal properties reside.

Medical Marijuana Laws and Marijuana Use after Legislation

Thirty-one states and the District of Columbia have passed medical marijuana laws (MML) as of September 2018. Few of these states maintain medical marijuana registries, so the National Academy of Sciences report on therapeutic marijuana relied on patients reporting qualifying illness(es) in Oregon and Colorado to obtain information



William V. Stoecker, MD, MS, MSMA member since 1984, is with S&A Technologies and The Dermatology Center, Rolla, Missouri, and the Department of Dermatology, University of Missouri Health Sciences Center, Columbia, Missouri. Emily E. Rapp is a student in Chemical Engineering, Missouri University of Science and Technology, Rolla, Missouri. Joseph M. Malters, MD, is with The Dermatology Center, Rolla, Missouri.
Contact: wvs@mst.edu

Table 1. Medical indications for marijuana and level of evidence[1]

Indication	Level of Evidence
Anxiety (individuals with social anxiety disorders)	Limited
Chemotherapy-induced nausea, vomiting	Substantial
Chronic pain	Substantial
Glaucoma	Limited
Improving clinician-measured multiple sclerosis spasticity symptoms	Limited
Improving clinician-measured multiple sclerosis spasticity symptoms	Limited
Improving symptoms of Tourette syndrome	Limited
Increasing appetite/decreasing weight loss with HIV/AIDS	Limited
Insomnia (improving short-term sleep outcomes)	Moderate
PTSD	Limited

on the proportion of patients reporting qualifying illnesses of medical marijuana users.[1] By far the largest proportion of these users (90-93%) reported severe pain. Other conditions reported by 2% or more of medical marijuana users are muscle spasms and multiple sclerosis (25-29%), nausea (12-13%), PTSD (8%), cancer (4-6%) and seizures (3%).[1] (More than one condition may be reported). Only 1% of medical marijuana users listed glaucoma as the medical qualifying condition.

The level of evidence (quality of studies available) for marijuana therapy for these indications is moderate or substantial for only three indications: chronic pain, chemotherapy-induced nausea and vomiting and insomnia (improving short-term sleep outcomes) (Table 1).[1] For these conditions, alternate therapies are either more effective or have fewer adverse effects. For example, marijuana alleviates chemotherapy-induced nausea, yet it can induce the cannabis hyperemesis syndrome.[2-5]

Marijuana Laws, Marijuana Use and Adolescents

A large proportion of youth in the US are exposed to marijuana. For US youth 15 to 16 years old, 35.8% are said to have used marijuana.[6,7] One critical question is whether adolescent use of marijuana increases after marijuana laws are passed. Here we consider both medical marijuana laws as well as recreational marijuana laws.

Keyes et al. and Sarvet et al. found no overall increase in adolescent use of marijuana after the passage of MMLs.[8,9] Chu commented on the Sarvet study, "MMLs could encourage existing casual users to become regular or heavy users. As the majority of social costs are incurred by a small number of heavy users, the effects of MMLs on the intensive margin [heavy users of marijuana] must be evaluated carefully, as this is a significant policy implication.[10] Chu further cited five studies that all showed an increase in adult use of marijuana after passage of MMLs. Chu asked, "Why do MMLs affect adolescents differently from adults? For example, could MMLs reduce the black-market supply and so limit adolescents' access to marijuana? Or could making a substance legal or semi-legal reduce teenagers' preference for it?"

In another study, Chu analyzed marijuana arrests among adult males following the passage of MMLs and found an increase in marijuana arrests among adult males by about 15-20%.[11] Admissions to rehabilitation facilities for marijuana treatments similarly increased after the passage of MMLs. There is some concern that the perception of harmfulness of marijuana, possibly a key factor in lowering rates of adolescent marijuana use, may fall after MML passage. A fall in perceived harmfulness of marijuana in the general population has been noted[8] and confirmed by Cerdá et al. in Washington but not Colorado.[12]

Hasin et al. analyzed US national survey data collected in three periods from 1991 to 2013 from 118,497 participants. They determined that the risk for cannabis use and cannabis use disorders increased at a significantly greater rate in states that passed MMLs than in states that did not.[13]

After recreational marijuana use was legalized in the state of Washington, both eighth and tenth graders in that state perceived marijuana use as more harmless.[12] Marijuana use increased in both grades following the passage of recreational marijuana laws. In Oregon, following similar legislation, rates of undergraduate marijuana use increased from pre- to post-2015, at a rate that was similar to the increase that was also observed at other universities in states where marijuana was still illegal.[14] Increases in rates of undergraduate marijuana use were significantly greater in Oregon than in comparison institutions, but only among students reporting recent heavy alcohol use, an indication of co-morbidities in students with substance abuse.

In contrast, Colorado did not exhibit any differential change in perceived harmfulness or past-month adolescent marijuana use following legalization. Yet Jones et al. found the frequency of marijuana use in Colorado college students

is much higher than the national average, especially the percentage of daily or almost daily users.[15] The same study found significant differences between the marijuana non-users and the once a week or more marijuana users in grade point average.[15] Cerdá suggests investment in evidence-based adolescent substance use prevention programs in any additional states that may legalize recreational marijuana use.[12]

Marijuana Laws, Children, Emergency Rooms, and Schools

Calls to Poison Control Centers have reported an increase in marijuana exposure among younger children.[1] Accidental ingestion of marijuana edibles has resulted in respiratory failure and coma.[16,17] An increase in overall pediatric exposures has followed MML enactment. From 2000 to 2013, the annual rate of Poison Control Center calls for marijuana exposure for children younger than six was 2.82 times higher in states that had MMLs prior to 2000, than in states where marijuana remained illegal as of 2013.[18] Sergeant P. Bret Hinkle of the Marijuana Unit of the Denver Police Department cited instances of parents that grow marijuana and make it available to children.[19]

Emergency rooms are seeing a relatively new syndrome, the marijuana hyperemesis syndrome.[2,5] Persistent vomiting is observed in cannabis users, at a rate that has increased significantly in states where marijuana has been legalized.[2] The number of emergency room visits for cyclic vomiting, including cannabis-induced vomiting, doubled since legalization in Colorado.[3] Although hot showers are often recommended for cannabis hyperemesis, these are of variable effectiveness, as marijuana cessation appears to be the best remedy.[4] Phelps County Regional Medical Center ER physician Dr. Francina Hoffman has seen her first cases in recent years. She said, "They [marijuana users] come in because they can't stop vomiting. We prescribe Phenergan or Zofran, but they are often noncompliant. On the third ER visit, they get admitted."[5]

Overall, the yearly rate of emergency department visits related to marijuana increased 35 percent after the legalization of recreational marijuana in Colorado.[20] The number of hospitalizations related to marijuana also increased steadily during this period, nearly doubling from 2011 to 2014.[20]

The superintendent of Rolla schools, Dr. Aaron Zalis, said that medical marijuana laws add work for school administrators.[21] "There is more to unwind," said Dr. Zalis. "Alcohol, opiates and marijuana, right now, all are illegal for juveniles ... The schools are required to check out all the drugs that students have ... The distinction of medical marijuana makes it a lot more complicated ... There will be more documentation and compliance with new regulations. Additionally, any legislation that makes marijuana available could lead to other substance abuse. I've always viewed marijuana as a gateway. Based on the counselors that we work with, over a 34-year period ... [marijuana] leads to other things.[21]

Groups at Increased Risk of Adverse Effects of Marijuana

Epidemiologic evidence shows strong correlation between heavy marijuana use during adolescence and schizophrenia.[22] Other evidence shows increased risk for schizophrenia with early use of marijuana in males. Onset of marijuana use in early adolescence (before age 16) has been associated with more severe psychosis.[7,23-26] Recent findings using a polygenic risk score for schizophrenia and cerebral cortical thickness obtained from MRI imaging showed progressive thinning of the cerebral cortex in males with a high genetic risk for schizophrenia and early marijuana use.[7] The researchers found no increased risk for females. Two factors may be responsible for increased vulnerability of males to schizophrenia with marijuana use: earlier onset of schizophrenia in males and sex differences in dynamics of brain development, with greater changes in male white and gray matter volumes in male adolescents compared to females.[27,28] The anatomic locations in the brain for both schizophrenia and brain alterations with chronic use of marijuana are similar, involving especially the hippocampus and pre-frontal cortex.[29]

Users of High-Potency Weed: "Skunk"

There has been a general increase in the potency of available marijuana, with available marijuana quadrupling in strength from the 1980s to 2012.[29,30] Sometimes called "skunk," a name apparently generated by users' comments about odor, the high-potency weed has higher levels of active cannabinoids. Marijuana potency is usually judged according to concentrations of THC, the primary psychoactive constituent in marijuana. Marijuana also contains other cannabinoids such as CBD, which has been thought to lack most of the psychoactive effects of THC and even to moderate the effect of THC.[31] Uncertainty about the ameliorative effect of CBD on THC was raised by recent animal studies showing an increased THC level mediated by cannabidiol and cannabidiol inhibits the metabolism of THC.[32,33] There is no limit on the potency of marijuana in the US, as there is for example in some nations, e.g. Uruguay.[31,34] Fifteen states do have limits on THC content for a different purpose—to allow access to what are considered "non-psychoactive" products such as cannabidiol oil.[1]

Volkow et al. noted in a review in the *New England Journal of Medicine* that higher marijuana potency raises concerns that the "consequences of marijuana use may be worse now than in the past," and "may account for the significant increases in emergency department visits by persons reporting marijuana use and the increases in fatal motor-vehicle accidents."[29,35,36] The Volkow group also said, "This increase in THC potency over time also raises questions about the current relevance of the findings in older studies on the effects of marijuana use, especially studies that assessed long-term outcomes."

Freeman and Winstock showed that high-potency skunk marijuana resulted in greater memory impairment and likelihood of paranoia.[31] Eighty-two percent of skunk users had memory impairment as opposed to 4% of users of "other types of grass." Skunk was also more likely to induce a feeling of paranoia than other types (78% vs. 7%), yet it remained by far the most preferred type of marijuana, giving the "best high" and was the most available type of marijuana.[31]

Adverse Effects of Marijuana on the Lungs: Chronic Bronchitis Symptoms

The organ with best evidence for adverse effects from chronic marijuana use, besides the brain, is the lower respiratory system. The National Academy of Sciences report[1] found association between smoking marijuana on a regular basis and an increase in chronic cough and phlegm production as well as more frequent chronic bronchitis episodes.[1] Quitting marijuana smoking reduces these adverse effects. Tetrault et al. found a lower FEV_1 in long-term marijuana exposure.[37] Hancox et al. found higher forced vital capacity (FVC), although other studies varied in their conclusions on objective measures such as FEV_1 and FVC.[1,38]

Brain Changes in Regular Users of Marijuana

Lorenzetti et al. reviewed anatomic brain changes in chronic marijuana users.[39] Chronic marijuana use was defined as exposure to marijuana on a daily or almost daily basis. Most users in the study started smoking marijuana between the ages of 15 to 17 and continued for a duration between two and 23 years. Lifetime episodes of marijuana use, typically referring to the number of joints smoked, ranged from 402 to 5,625. The brain abnormalities found were associated with higher levels of marijuana use, taking into consideration dosage, age of onset, and duration.

The review found substantial overlap between the location of the changes in the brains of marijuana users and the location of concentrated THC receptors.[39,40] The most consistent alterations, in comparison to control subjects, were found in the hippocampus and pre-frontal cortex. Yucel and Ashtari found a 12-13% volume reduction in the hippocampus.[41,42] Additional groups found other changes in the hippocampus such as shape and gray matter content.[43-46] Changes in amygdala were also well documented.[39] Figure 1 shows the three areas of the brain for which morphological and functional changes are best documented.

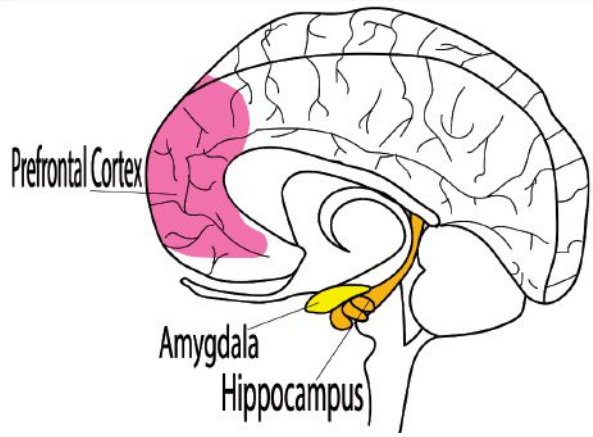


Figure 1. Three areas of the brain for which morphological and functional changes are best documented.

The brain regions most affected in regular users of marijuana, the hippocampus and regions of the cerebral cortex (parietal cortex, inferior frontal gyrus), are "integral components of the brain reward, memory, and executive-attention systems." This may explain the deficits that marijuana users show in these areas.[39,47-51] Rueda et al. cited work by Posner and Raichle showing that the regulatory effects of these executive areas "apply just as well to brain areas involved in processing the semantics of words, storing information in memory, and generating emotions such as fear and sadness.[52,53]

Risks for Psychoses

Alongside changes in major brain structures, marijuana has been repeatedly linked to an increased risk for psychosis. The review committee for the National Academy of Sciences found multiple high-quality studies that confirmed association between marijuana use and development of schizophrenia and other psychoses, including manic-depressive disorder, hypomania, depression, and suicide, as well as well as a marijuana and psychosis dose-response relationship.[1] In a recent review, Marconi et al. found substantial evidence for the ability of marijuana "to induce

long-lasting psychotic disorders."[54] Increased marijuana use was associated with a "higher risk of schizophrenia and other psychosis-related outcomes compared to nonusers." Marijuana use has been "widely reported to induce acute psychotic experiences,[55-57] to affect the severity of psychotic symptoms,[58-59] and previous meta-analyses have reported a two-fold increase in the risk to develop a psychotic disorder in [marijuana] users compared to nonusers."[54] Following this pattern, in another study where "the history of [marijuana] use and a spot urine test for cannabinoids were obtained" for 137 persons diagnosed with schizophrenia in treatment, the "subjects who were using cannabis during the six-month observation period presented with a significantly higher degree of delusional and hallucinatory activity than those who did not. Moreover, the group using cannabis made a higher average number of visits to the hospital during the same period."[61] Not only does marijuana work to induce and increase severity of psychotic episodes,[63] but marijuana use is also linked to "increased risk of relapse,[64] earlier relapse,[65] longer inpatient stay,[66] and an increased risk of violence and criminal activity[67] as well as being associated with higher rates of transition to psychosis.[68]"[69] Substance abuse (including marijuana, amphetamines, and cocaine) leads to increased mortality from overdoses.[70] Rosen et al. found that substance abuse-linked illness, including overdoses, accounted for 27.6% of deaths among 169,051 male Vietnam-era veteran psychiatric patients, vs. 8.8% among psychiatric patients in the same group of veterans without substance abuse.[70] In summarizing the link between chronic marijuana use and psychoses, the National Academy review stated: "The higher the use, the greater the risk."[1]

Persons with schizophrenia and substance abuse, including marijuana, amphetamines and cocaine, are at risk of increased risk of relapse of schizophrenia symptoms[71] as well as increased mortality from overdoses.[70] Rosen et al. found that substance abuse-linked illness, including overdoses, accounted for 27.6% of deaths among 169,051 male Vietnam-era veteran psychiatric patients, vs. 8.8% among psychiatric patients in the same group of veterans without substance abuse.[70]

Brain Regions Affected by Marijuana, Schizophrenia, and Earliest Areas of Alzheimer's Disease Overlap and Symptoms are Similar

Sheline, Raichle et al. studied a group of functionally normal persons with PET scans using Pittsburgh Compound B (PIB) imaging.[72] The PIB-positive PET scan patients were considered to have an early marker predictive of later-onset Alzheimer's disease.[73] Early changes were found in and around the hippocampus, anterior and dorsal cingulate area of the prefrontal cortex and precuneus; most of these areas are associated with abnormalities from chronic marijuana use.[39,74]

Further studies of preclinical Alzheimer's disease used functional MRI for imaging with similar findings.[75] Studies of schizophrenia have shown abnormalities in related brain regions.[76-78] The clinical similarity between schizophrenia and dementia was observed in early descriptions of schizophrenia, which was termed "dementia praecox," used to describe "a deteriorating process involving intellectual functions and behavior but no involvement of consciousness."[79] Clinical descriptions of schizophrenia, early dementia, and chronic marijuana use overlap.[79]

Importance of the Default Mode Network

The discovery of the default mode network by Raichle and other researchers at Washington University was widely cited and confirmed by other laboratories.[80,81] These linked hubs within the brain have been described as "orchestra conductors," directing other specialized parts of the brain that can be compared to orchestra sections. Raichle said, "The [default mode network] is thought to behave something like an orchestra conductor, issuing timing signals, much as a conductor waves a baton, to coordinate activity among different brain regions."[82]

The functioning of the default mode network, the orchestra director in the brain, was further described by Andrews-Hanna.[83] She surveyed new findings in psychology bolstered by imaging studies that showed the function of these midline core areas. The default mode network allows humans to "spontaneously and deliberately" engage in "introspective and adaptive mental activities," thinking about the past and planning the future, placing high value on "personally significant information," especially about 'friends, family members, and romantic partners." [83]

The areas of the brain[83] affected by chronic marijuana use are very closely associated with the default mode network defined originally by Raichle and colleagues. The results of chronic marijuana use are believed to negatively influence the ability to focus attention, to retain information, and to succeed in social roles.[84]

Conclusions

In this review, we discussed the general impact of medical marijuana laws, changes in marijuana use after medical marijuana laws are passed, and groups at increased risk when restrictions on the availability of marijuana are loosened. Changes that occur in the brain with chronic use of marijuana are of primary concern, especially for males. Earlier use of marijuana, stronger marijuana, and those with schizophrenia or polygenic risk for schizophrenia are at increased risk for adverse changes in the brain. Similar

areas in the brain are affected in schizophrenia, Alzheimer's disease, and chronic marijuana use. Research findings raise critical concerns for chronic marijuana users. Marijuana should not be considered a medicine or pure drug.

References

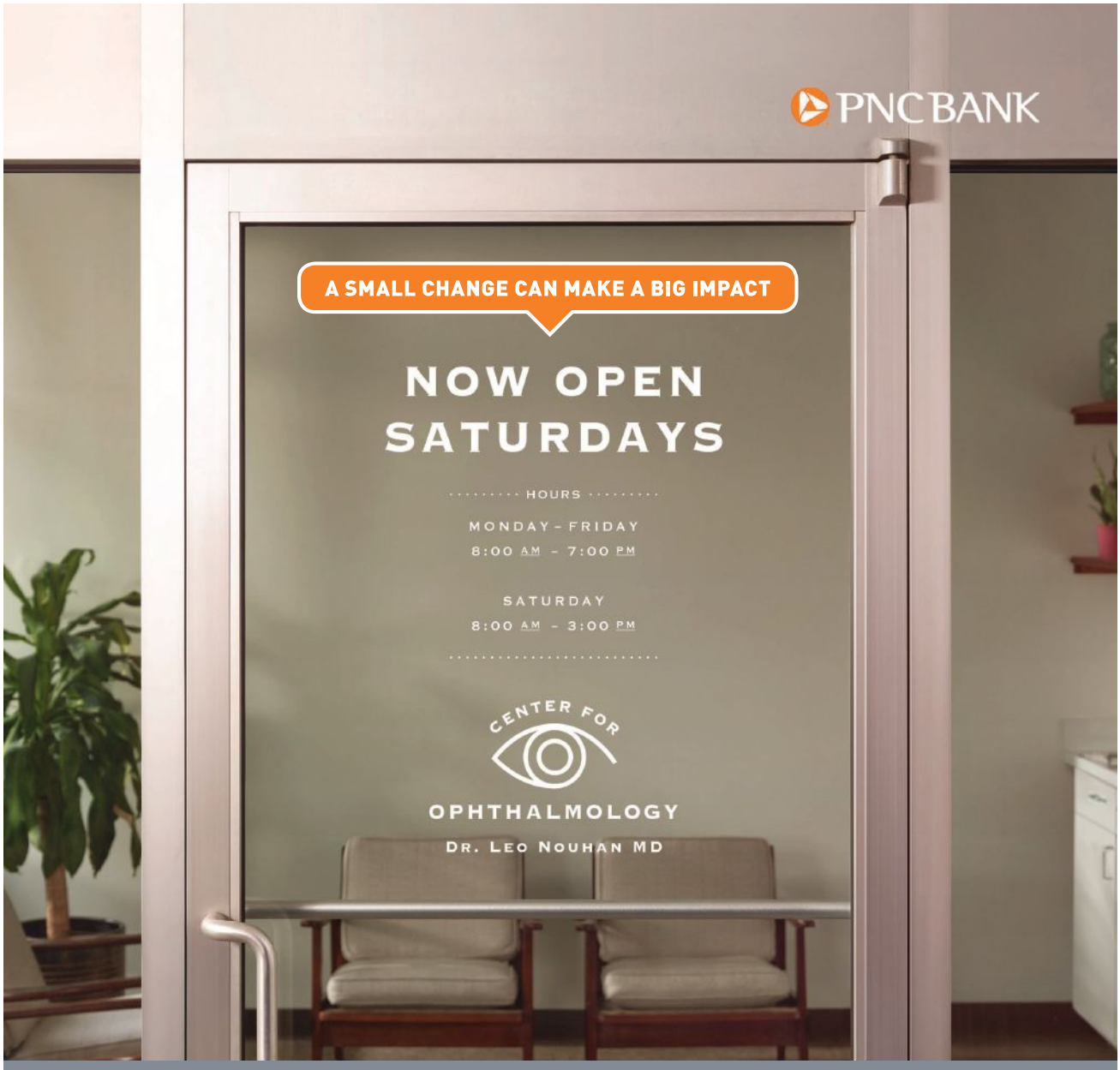
1. National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington (DC): National Academies Press (US); 2017 Jan 12. Book Available Online at https://www.ncbi.nlm.nih.gov/books/NBK423845/ Accessed September 8, 2018.
2. Kim HS, Monte AA. Colorado cannabis legalization and its effect on emergency care. Ann Emerg Med. 2016;68(1):71–5.
3. Kim HS, Anderson JD, Saghafi O, et al. Cyclic vomiting presentations following marijuana liberalization in Colorado. Acad Emerg Med. 2015;22(6):694–9.
4. Sorensen CJ, DeSanto K, Borgelt L, Phillips KT, Monte AA. Cannabinoid Hyperemesis Syndrome: Diagnosis, Pathophysiology, and Treatment-a Systematic Review. J Med Toxicol. 2017 Mar;13(1):71-87
5. Interview with Dr. Francina Hoffman, Phelps County Regional Medical Center Emergency Physician, September 16, 2018.
6. Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. Monitoring the Future: National Results on Drug Use: 1975–2013: Overview, Key Findings on Adolescent Drug Use. Ann Arbor: Institute for Social Research, The University of Michigan; 2014.
7. French L, Gray C, Leonard G, Perron M, Pike GB, Richer L, et al. Early cannabis use, polygenic risk score for schizophrenia and brain maturation in adolescence.JAMA Psychiatry. 2015 Oct;72(10):1002-11
8. Keyes KM, Wall M, Cerdá M, Schulenberg J, O'Malley PM, Galea S, Feng T, Hasin DS. How does state marijuana policy affect US youth? Medical marijuana laws, marijuana use and perceived harmfulness: 1991-2014. Addiction. 2016 Dec;111(12):2187-2195.
9. Sarvet AL, Wall MM, Fink DS, Greene E, Le A, Boustead AE, Pacula RL, et al. Medical marijuana laws and adolescent marijuana use in the United States: a systematic review and meta-analysis.Addiction. 2018 Jun;113(6):1003-1016.
10. Chu YL. Commentary on Sarvet et al. (2018): What do we still need to know about the impacts of medical marijuana laws in the United States? Addiction. 2018 Jun;113(6):1017-1018.
11. Chu YW. The effects of medical marijuana laws on illegal marijuana use. J Health Econ. 2014 Dec;38:43-61.
12. Cerdá M, Wall M, Feng T, et al. Association of State Recreational Marijuana Laws With Adolescent Marijuana Use. JAMA pediatrics. 2017;171(2):142-149. doi:10.1001/jamapediatrics.2016.3624.
13. Hasin D, Sarvet A. L., Cerda M., Keyes K. M., Stohl M. S., Galea S. et al U.S. adult illicit cannabis use, cannabis use disorder, and medical marijuana laws: 1991–1992 to 2012–2013. JAMA Psychiatry 2017; 74: 579–588. [PubMed]
14. Kerr DCR, Bae H, Phibbs S, Kern AC. Changes in undergraduates' marijuana, heavy alcohol and cigarette use following legalization of recreational marijuana use in Oregon. Addiction. 2017;112(11):1992-2001.
15. Jones J, Nicole Jones K, Peil J. The impact of the legalization of recreational marijuana on college students. Addict Behav. 2018 Feb;77:255-259.
16. Amirav I, Luder A, Viner Y, Finkel M. Decriminalization of cannabis--potential risks for children? Acta Paediatr. 2011 Apr;100(4):618-9
17. Appelboam A, Oades PJ. Coma due to cannabis toxicity in an infant. Eur J Emerg Med. 2006 Jun;13(3):177-9.
18. Onders B, Casavant MJ, Spiller HA, Chounthirath T, Smith GA.Marijuana Exposure Among Children Younger Than Six Years in the United States. Clin Pediatr (Phila). 2016 May;55(5):428-36
19. Interview with P. Bret Hinkle, Marijuana Unit, Denver Police Department, September 13, 2018.
20. https://www.rmhidta.org/html/FINAL%202017%20Legalization%20of%20Marijuana%0in%20Colorado%20The%20Impact.pdf accessed September 16, 2018
21. Interview with Dr. Aaron Zalis, Superintendent Rolla Public Schools, September 14, 2018.
22. Manrique-Garcia E, Zammit S, Dalman C, Hemmingsson T, Andreasson S, Allebeck P. Cannabis, schizophrenia and other non-affective psychoses: 35 years of follow-up of a population-based cohort. Psychol Med. 2012;42(6):1321–1328.
23. Pope HG, Jr, Gruber AJ, Hudson JI, Cohane G, Huestis MA, Yurgelun-Todd D. Early-onset cannabis use and cognitive deficits: what is the nature of the association? Drug Alcohol Depend. 2003;69(3):303–310.
24. Fontes MA, Bolla KI, Cunha PJ, et al. Cannabis use before age 15 and subsequent executive functioning. Br J Psychiatry. 2011;198(6):442–447.
25. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. Biol Psychiatry. 2005;57(10):1117–1127.
26. Wilson W, Mathew R, Turkington T, Hawk T, Coleman RE, Provenzale J. Brain morphological changes and early marijuana use: a magnetic resonance and positron emission tomography study. J Addict Dis. 2000;19(1):1–22.
27. Paus T, Nawaz-Khan I, Leonard G, et al. Sexual dimorphism in the adolescent brain: role of testosterone and androgen receptor in global and local volumes of grey and white matter. Horm Behav. 2010;57(1):63–75.
28. Lenroot RK, Gogtay N, Greenstein DK, et al. Sexual dimorphism of brain developmental trajectories during childhood and adolescence. Neuroimage. 2007;36(4):1065–1073.
29. Volkow ND, Baler RD, Compton WM, Weiss SRB. Adverse health effects of marijuana use. N Engl J Med. 2014 Jun 5; 370(23): 2219–2227.
30. ElSohly MA. Potency Monitoring Program quarterly report no 123 — reporting period: 09/16/2013-12/15/2013. Oxford: University of Mississippi, National Center for Natural Products Research; 2014.
31. Freeman TP, Winstock AR. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. Psychol Med. 2015 Nov;45(15):3181-9.
32. Klein C, Karanges E, Spiro A, Wong A, Spencer J, Huynh T, et al. Cannabidiol potentiates Δ9-tetrahydrocannabinol (THC) behavioural effects and alters THC pharmacokinetics during acute and chronic treatment in adolescent rats. Psychopharmacology. 2011;218 (2):443–457.
33. Nadulski T, Pragst F, Weinberg G, Roser P, Schnelle M, Fronk EM, Stadelmann AM. Randomized, double-blind, placebo-controlled study about the effects of cannabidiol (CBD) on the pharmacokinetics of Delta9-tetrahydrocannabinol (THC) after oral application of THC verses standardized cannabis extract. Ther Drug Monit. 2005;27 (6):799–810.
34. Coombes R. Cannabis regulation: high time for change? BMJ. 2014 May 21;348:g3382.
35. Drug Abuse Warning Network, 2011: national estimates of drug-related emergency department visits. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2011. http://www.samhsa.gov/data/2k13/DAWN2k11ED/DAWN2k11ED.htm. Accessed September 8, 2018.
36. Brady JE, Li G. Trends in alcohol and other drugs detected in fatally injured drivers in the United States, 1999–2010. Am J Epidemiol. 2014;179:692–9.
37. Tetrault JM, Crothers K, Moore BA, Mehra R, Concato J, Fiellin DA. Effects of marijuana smoking on pulmonary function and respiratory complications: a systematic review. Arch Intern Med. 2007;167(3):221-8.
38. Hancox RJ, Poulton R, Ely M, Welch D, Taylor DR, McLachlan CR, et al. Effects of cannabis on lung function: a population-based cohort study. Eur Respir J. 2010 Jan;35(1):42-7.
39. Lorenzetti V, Solowij N, Yücel M. The role of cannabinoids in neuroanatomic alterations in cannabis users. Biol Psychiatry. 2016;79:e17–e31
40. Glass M, Dragunow M, Faull RL. Cannabinoid receptors in the human brain: a detailed anatomical and quantitative autoradiographic study in the fetal, neonatal and adult human brain. Neuroscience. 1997 Mar;77(2):299-318.

41. Yücel M, Solowij N, Respondek C, Whittle S, Fornito A, Pantelis C, et al. Regional brain abnormalities associated with heavy long-term cannabis use. Arch Gen Psychiatry. 2008;65:1-8.
42. Ashtari M, Avants B, Cyckowski L, Cervellione KL, Roofeh D, Cook P, et al. Medial temporal structures and memory functions in adolescents with heavy cannabis use. J Psychiatr Res. 2011;45:1055-1066
43. Matochik JA, Eldreth DA, Cadet J, Bolla KI. Altered brain tissue composition in heavy marijuana users. Drug Alcohol Depend. (2005) 77:23–30.
44. Demirakca T, Sartorius A, Ende G, Meyer N, Welzel H, Skopp G, et al. Diminished gray matter in the hippocampus of cannabis users: Possible protective effects of cannabidiol. Drug Alcohol Depend. 2011;114:242-245.
45. Battistella G, Fornari E, Annoni J-M, Chtioui H, K. Dao K, Fabritius J, et al. Long-term effects of cannabis on brain structure. Neuropsychopharmacology. 2014;39:2041-2048
46. Solowij N, Walterfang M, Lubman DI, Whittle S, Lorenzetti V, Styner M, et al. Alteration to hippocampal shape in cannabis users with and without schizophrenia Schizophr Res. 2013;143:179-184
47. Rueda MR, Posner MI, Rothbart MK. The development of executive attention: Contributions to the emergence of self-regulation. Dev Neuropsychol. 2005;28:573-594
48. Hyman SE, Malenka RC, Nestler EJ. Neural mechanisms of addiction: the role of reward-related learning and memory. Annu Rev Neurosci. 2006;29:565-98.
49. Ramus SJ, Davis JB, Donahue RJ, Discenza CB, Waite AA. Interactions between the orbitofrontal cortex and the hippocampal memory system during the storage of long-term memory. Ann N Y Acad Sci. 2007 Dec;1121:216-31.
50. Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. J Neurophysiol. 2008 Dec;100(6):3328-42.
51. Takagi M, Yücel M, Cotton SM, Baliz Y, Tucker A, Elkins K, Lubman DI. Verbal memory, learning, and executive functioning among adolescent inhalant and cannabis users. J Stud Alcohol Drugs. 2011 Jan;72(1):96-105.
52. Posner, MI, Raichle, ME. Images of mind. New York: Scientific American Books, 1994.
53. Posner, MI, Raichle, ME. (Eds.). Overview: The neuroimaging of human brain function. Proceedings of the National Academy of Sciences, USA, 95, 763–764.
54. Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis. Schizophrenia Bulletin. 2016;42(5):1262-1269.
55. Moore THM, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet. 2007;370:319–328.
56. Henquet C0, Murray R, Linszen D, van Os J. The environment and schizophrenia: the role of cannabis use. Schizophr Bull. 2005;31:608–612.
57. Semple DM, McIntosh AM, Lawrie SM. Cannabis as a risk factor for psychosis: systematic review. J Psychopharmacol. 2005;19:187–194.
58. Tien AY, Anthony JC. Epidemiological analysis of alcohol and drug use as risk factors for psychotic experiences. J Nerv Ment Dis. 1990;178:473–480.
59. Hall W, Solowij N. Adverse effects of cannabis. Lancet. 1998;352:1611–1616.
60. Hall W, Degenhardt L. Adverse health effects of medical cannabis use. Lancet. 2009;374:8.
61. Negrete JC, Knapp WP, Douglas DE, Smi th WB. Cannabis affects the severity of schizophrenic symptoms: results of a clinical survey. Psychol Med. 1986;16:515–520.
62. Foti DJ, Kotov R, Guey LT, Bromet EJ. Cannabis use and the course of schizophrenia: 10-year follow-up after first hospitalization. Am J Psychiatry. 2010;167:987–993.
63. Henquet C, Krabbendam L, Spauwen J, Kaplan C, Lieb R, Witt- chen HU, et al. Prospective cohort study of cannabis use, predispo- sition for psychosis, and psychotic symptoms in young people. Bmj 2005; 330(7481): 11.
64. Linszen DH, Dingemans PM, Nugter MA, Van der Does AJ, Scholte WF, Lenior MA. Patient attributes and expressed emotion as risk factors for psychotic relapse. Schizophr Bull 1997; 23(1): 119-30.
65. Hides L, Dawe S, Kavanagh DJ, Young RM. Psychotic symptom and cannabis relapse in recent-onset psychosis. Prospective study. Br J Psychiatry 2006; 189: 137-43.
66. Isaac M, Isaac M, Holloway F. Is cannabis an anti-antipsychotic? The experience in psychiatric intensive care. Hum Psychopharma- col 2005; 20(3): 207-10.
67. Miles H, Johnson S, Amponsah-Afuwape S, Finch E, Leese M, Thornicroft G. Characteristics of subgroups of individuals with psychotic illness and a comorbid substance use disorder. Psychiatr Serv 2003; 54(4): 554-61.
68. Kristensen K, Cadenhead KS. Cannabis abuse and risk for psycho- sis in a prodromal sample. Psychiatry Res 30 2007; 151(1-2): 151- 4.
69. Bhattacharyya S, Fusar-Poli P, Borgwardt S, Martin-Santos R, Nosarti C, O'Carroll C, et al. Modulation of mediotemporal and ventrostriatal function in humans by Delta9- tetrahydrocannabinol: a neural basis for the effects of Cannabis sativa on learning and psychosis. Arch Gen Psychiatry. 2009;66 4: 442- 51.
70. Rosen CS, Kuhn E, Greenbaum MA, Drescher KD. Substance abuse-related mortality among middle-aged male VA psychiatric patients. Psychiatr Serv. 2008;59:290–296.
71. Swofford CD, Kasckow JW, Scheller-Gilkey G, Inderbitzin LB. Substance use: a powerful predictor of relapse in schizophrenia. Schizophr Res. 1996;20:145–151.
72. Sheline YI, Raichle ME, Snyder AZ, Morris JC, Head D, Wang S, Mintun MA. Amyloid plaques disrupt resting state default mode network connectivity in cognitively normal elderly. Biol Psychiatry. 2010 Mar 15;67(6):584-7.
73. Mintun MA, Larossa GN, Sheline YI, Dence CS, Lee SY, Mach RH, Klunk WE, Mathis CA, DeKosky ST, Morris JC. [11C]PIB in a nondemented population: potential antecedent marker of Alzheimer disease. Neurology. 2006;67:446–452.
74. Jacobus J, Goldenberg D, Wierenga CE, Tolentino NJ, Liu TT, Tapert SF. Altered cerebral blood flow and neurocognitive correlates in adolescent cannabis users. Psychopharmacology (Berl). 2012 Aug;222(4):675-84.
75. [Sheline13] Sheline YI, Raichle ME. Resting state functional connectivity in preclinical Alzheimer's disease. Biol Psychiatry. 2013 Sep 1;74(5):340-7.
76. [Hugdahl15] Hugdahl K, Raichle ME, Mitra A, Specht K. On the existence of a generalized non-specific task-dependent network. Front Hum Neurosci. 2015 Aug 6;9:430.
77. [Calhoun12] Calhoun VD, Adalı T. Multisubject independent component analysis of fMRI: a decade of intrinsic networks, default mode, and neurodiagnostic discovery. IEEE Rev Biomed Eng. 2012;5:60-73.
78. [Bluhm07] Bluhm RL, Miller J, Lanius RA, Osuch EA, Boksman K, Neufeld RW, et al. Spontaneous low-frequency fluctuations in the BOLD signal in schizophrenic patients: anomalies in the default network. Schizophr Bull. 2007 Jul;33(4):1004-12.
79. [Kraepelin96] Kraepelin, E. Psychiatrie, 5th ed., Leipzig, JA Barth. 1896.
80. [Raichle01] Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. Proc Natl Acad Sci U S A. 2001 Jan 16;98(2):676-82. Proc Natl Acad Sci U S A. 2001 Jan 16; 98(2): 676–682.
81. [Fox05] Fox MD1, Snyder AZ, Vincent JL, Corbetta M, Van Essen DC, Raichle ME. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proc Natl Acad Sci U S A. 2005 Jul 5;102(27):9673-8.
82. [Raichle18] Marcus E. Raichle, personal communicaton, August 31, 2018.
83. [Andrews-Hanna12] Andrews-Hanna JR. The brain's default network and its adaptive role in internal mentation. Neuroscientist. 2012 Jun;18(3):251-70.
84. Broyd SJ, van Hell HH, Beale C, Yücel M, Solowij N. Acute and chronic dffects of cannabinoids on human cognition-A systematic review.Biol Psychiatry. 2016 Apr 1;79(7):557-67.

Disclosure

None reported.

MM



WORK WITH A DEDICATED HEALTHCARE BANKER WHO UNDERSTANDS YOUR BUSINESS.

As a healthcare provider and business owner, you know it's often the little things that make the biggest difference. That's why you're always looking for ways to improve your practice. PNC's dedicated Healthcare Business Bankers can offer you guidance and cash flow tools to help you make your business better. Whether you're managing payables and receivables, purchasing new equipment or expanding your services, talking to a banker who knows your practice is another small change that can make a big impact.

CALL A HEALTHCARE BUSINESS BANKER AT 877-566-1355 • PNC.COM/HCPROFESSIONALS

Banking and Lending products and services, bank deposit products and treasury management services, including, but not limited to, services for healthcare providers and payers, are provided by PNC Bank, National Association, a wholly owned subsidiary of PNC and Member FDIC. Lending and leasing products and services, including card services and merchant services, as well as certain other banking products and services, requires credit approval. All loans and lines of credit are subject to credit approval and require automatic payment deduction from a PNC Bank business checking account. Origination and annual fees may apply. ©2017 The PNC Financial Services Group, Inc. All rights reserved. PNC Bank, National Association. **Member FDIC**

Artificial Intelligence and the Softer Side of Medicine

by Joseph A. Craft, III, MD

"Technology is unlocking the innate compassion we have for our fellow human beings."
– Bill Gates

Technology impacts nearly every facet of our daily lives. Yet, healthcare has adopted tech advances more slowly. A decade or two ago, electronic health record (EHR) champions promised a sea change in patient care efficiency. Although we can all now read each other's notes, EHRs work only slightly less clunky than a decade ago at a hefty price. Instead of speeding and enhancing care, many clinicians feel victimized by a "productivity paradox".[1] Physicians lament the constant data entry responsibilities and time away from direct patient care. EHRs and associated bureaucratic tasks have made arguably the largest contribution to the national epidemic of physician burnout.[2] [3]

Mobile health information resources have had a more resounding and welcome impact for most doctors. Indeed, point of care access to online medical journals, drug guidelines and clinical references like UpToDate threaten the obsolescence of medical libraries and textbooks. The explosion of young healthcare startup companies throughout the country has invigorated doctors and investors over what health care soon will be. With all this change, one cannot help wonder how to meld best of the old and the new.

We hear incessantly that payers and regulators seek "value" in health care. (What a curious repurposing of that word. Have patients never before found healthcare valuable?) Care has "value" when patients receive evidenced based evaluations and therapies at reasonable cost - e.g. venous thromboembolism prevention perioperatively. Quality metrics are considered proof of value and therefore viewed as precious commodities. With present EHR technology, reporting quality to payers and regulators has been laborious. Countless resources in physician practices, health systems, government and industry are employed to mine "discrete data elements" from EHRs, insurance claims data, and pharmacy information repositories. But like mining with a pick axe, finding high quality yield from EHRs has been a slow grind.

To simplify quality reporting, some groups even advocate changing all physician notes to an automaton's ledger of checkboxes. (Coronary artery disease? - Yes. Having angina? - No. Taking aspirin? - Yes…) Indeed, a national health tech "expert" with an elite governmental position once chided me for not wanting to distill my notes to accommodate our limited data analysis capabilities. He preached that a patient's story and social history could not easily be extracted and quantitated from the EHR, and therefore had become antiquated fluff. The message: physicians should serve the limited EHR, not the other way around. Sadly, this revered government tech expert was a physician.

It seems laudable to prove to ourselves and others that physicians practice evidence based, cost effective medicine according to clinical best practice. Strangely however, despite years of effort, our tactics above have yielded limited success. For example, adherence to hospital-level quality measures in obstetrics do not consistently predict maternal and neonatal morbidity.[4] In addition, publicly reported operative complications in Urology do not correlate well with adherence to perioperative quality metrics.[5] Even financially incentivizing hospitals to prioritize quality metrics through "pay for performance" programs and "value based purchasing", has not significantly impacted patient outcomes.[6]

To date, health information technology (IT) has not fulfilled the high expectations. To fix it, we must troubleshoot the disconnect. Despite an era of smartphones and smartwatches, are health analytics still not that smart? Or in our fascination with technology, have we left something out? The answers may be yes and yes.

Artificial intelligence (AI) may prove the next great tech revolution since the internet. AI might be defined as a computer performing tasks in a rational human-like manner. Machine learning comprises a subset of AI, in which software algorithms attempt to predict future events,



Joseph A. Craft, III, MD, FACC, MSMA member since 2004, is Past President, St. Louis Metropolitan Medical Society, and is a cardiologist at the Heart Health Center at St. Luke's Hospital, St. Louis, Missouri.
Contact: jcraft@hearthealthcenter.com



Image of IBM Watson assisting in Radiology diagnoses, on display at the Radiology Society of North America (RSNA) Conference in 2016 in Chicago, IL.
Source: https://rsna2016.rsna.org/dailybulletin/index.cfm?pg=16mon71

after being trained in rule-based logic, pattern recognition and reinforcement techniques. Deep learning, a sub-type of machine learning, utilizes artificial neural networks, loosely modeled after webs of neurons and synapses in the human brain. Artificial neural networks are constructed in interacting layers, in which each layer performs a slightly different job.

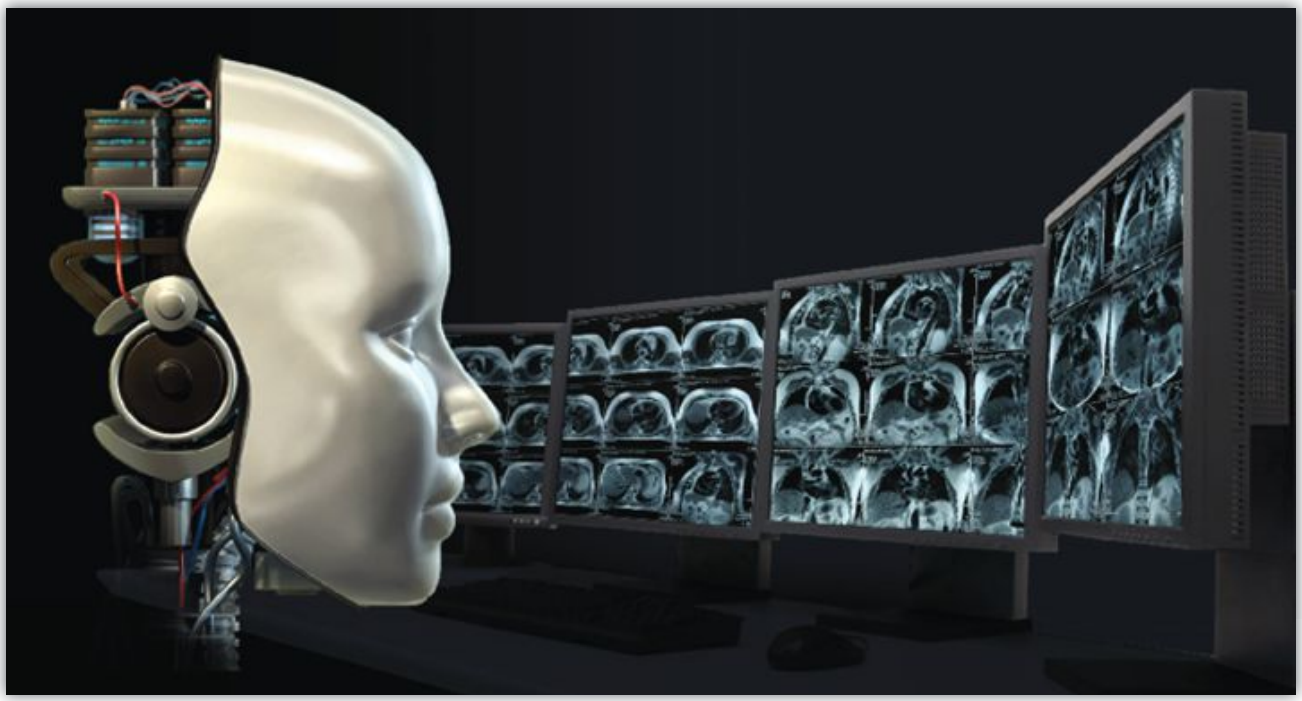
Myriad industries currently benefit from artificial intelligence. Machine learning techniques help computers translate acronyms or cursive writing into text based words. Google uses machine learning to improve online search quality. Deep learning techniques have led to natural language processing improvements in Dragon dictation software used in hospitals and clinics around the country, as well as commercial voice chatbots like Amazon's Alexa.

A gold rush of health related AI applications is expected soon, and the first pioneers have already arrived. IBM has poured billions of dollars and seemingly endless data into Watson, the company's artificial intelligence platform and global leader in AI applications. After reviewing charts from thousands of patients, IBM Watson's cancer therapy recommendations correlated with those of physician-led tumor boards in greater than 90% of patient cases at Memorial Sloan-Kettering and the University of North Carolina Chapel Hill.[7]

A slew of newer health related AI ventures are set to launch. In May 2018, the U.S. Food & Drug Administration (FDA) approved use of OsteoDetect, a machine learning based detection and diagnostic software. OsteoDetect can identify wrist fractures on plain film X-rays, and is designed as an adjunct to a Radiologist's read. According to the company's research, OsteoDetect improved Radiologists' sensitivity, specificity, positive and negative predictive values compared to readers' unaided performance.[8] In the same month, the FDA gave the go-ahead to the NeuralBot System by Neural Analytics for commercial marketing and patient use. Using machine learning, Neural Analytics has demonstrated that its robot can adjust transcranial doppler ultrasound to optimize imaging at the bedside for stroke patients, equivalent to a trained technologist.[9]

Recent publications suggest many routine clinical duties might become easier soon. Early in 2018, the FDA green-lighted a cloud-based AI software program called IDx-DR, developed by an Iowa company called IDx LLC. Using a retinal camera, a primary physician could obtain screening retinal pictures in his or her office, and upload the images for IDx-DR analysis. The primary physician would then receive prompt feedback about whether the pictures revealed more than mild diabetic retinopathy necessitating referral to an Ophthalmologist. In a similar vein, a German team showed that deep learning neural network could slightly out-perform Dermatologists in discriminating melanomas from benign nevi on dermascopic images.[10] Multiple labs have shown progress toward developing an AI-based model to automate Warfarin prescribing.[11] [12] By evaluating brain PET scan images, a novel machine learning algorithm can predict which patients with mild cognitive impairment will progress to Alzheimer's dementia in the following 24 months.[13]

The potential impact of AI on population health management appears massive. At the Clinical Machine Learning Lab of the Massachusetts Institute of Technology (MIT), researchers hone and apply probabilistic modeling and deep learning to EHRs.[14] Working with colleagues at New York University (NYU) School of Medicine, these powerful tools studied over 950 clinical and lab test variables per person, in a population of 790,000 patients. This population health based AI analysis predicted diabetes onset accurately, outstripping classical prediction models.[15]



Stanford University, Management Science and Engineering: AI Takes on Radiology.
Source: https://mse238blog.stanford.edu/2017/08/imunizr/ai-takes-on-radiology

AI should produce smoother, more realistic voice recognition, unprecedented diagnostic aids, and markedly decreased clerical duties. Some will say the sky is falling and fear that physicians would soon be replaced by machines. Physician leaders say no chance that happens anytime soon.[16] When I was a resident, on service at the VA, my colleagues and I routinely drew patients' blood and spun down urine samples ourselves in the middle of the night - all jobs now automated and delegated. I remain grateful for those formative late night experiences in my training years. Given the choice, I would do it all over again - during my training. But I prefer not to do them now. Physicians have since found other productive ways to stay occupied. Similarly, as artificial intelligence permeates clinical practice, physicians should simply have more time to practice high level care - more time at the bedside, learning, leading care teams, innovating and talking to one another. A premium would be placed on physician knowledge and judgement, compassion and understanding of the individual patient.[17] [18] Physicians should collectively insist that new tech moves us in this direction.

As artificial intelligence influences medicine in the coming decade, how will medical practice look? With the wind of inertia at their back, some health care influencers will predictably demand an even greater focus on status quo quality measurements. I believe we should do better. What if the tremendous power of AI were to reinvigorate the patient-doctor relationship?

What if we could do predictive modeling from both objective data sources and subjective patient feedback? Not surprisingly, evidence suggests that predictive analytics of patients' self-reported symptom changes can powerfully predict outcomes among dialysis patients.[19] Furthermore, deep learning tools can scan and accurately identify mental health conditions from individuals' subjective descriptions on social media posts.[20]

Intuitively, physicians know that patients' personal stories, their perceptions of symptom flux and their experience of illness have always been vital to high quality care. The personal interchange and bond between patient and physician have always been paramount to the humanity of high quality medicine. But in recent history, EHRs and other databases have had no way to evaluate this softer side of medicine.[21] As such, the obsession with current quality metrics may have led us to devalue the human connection in medicine. It would be no small irony if the era of artificial intelligence were to refocus our attention on the patient-doctor relationship. But what a bright future that would be.

References

1. Wachter, RM; Howell, MD. Resolving the Productivity Paradox of Health Information Technology: A Time for Optimism. JAMA. Published online May 29, 2018.
2. Peckham, C. Medscape National Physician Burnout & Depression Report 2018. https://www.medscape.com/slideshow/2018-lifestyle-burnout-depression-6009235#1
3. Shanafelt, T, et al. Relationship Between Clerical Burden and Characteristics of the Electronic Environment With Physician Burnout and Professional Satisfaction. Mayo Clinic Proceedings. July 2016 Volume 91, Issue 7, Pages 836–848.

4. Howell, E, et al. The Association between Hospital-level Obstetric Quality Indicators and Maternal and Neonatal Morbidity. JAMA. 2014 Oct 15; 312(15): 1531–1541.
5. Auffenberg, G., et al. Comparing Publicly Reported Surgical Outcomes With Quality Measures From a Statewide Improvement Collaborative. JAMA Surg. 2016;151(7):680-682.
6. Jha, A. JAMA Forum: Value-Based Purchasing: Time for Reboot or Time to Move on?. Feb 1, 2017. https://newsatjama.jama.com/2017/02/01/jama-forum-value-based-purchasing-time-for-reboot-or-time-to-move-on/
7. Cavallo, J. http://www.ascopost.com/issues/june-25-2017/how-watson-for-oncology-is-advancing-personalized-patient-care/
8. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm608833.htm
9. https://www.businesswire.com/news/home/20180530005536/en/Neural-Analytics-Receives-FDA-Clearance-Robotic-Ultrasound
10. Haenssle, HA, et al. Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparison to 58 dermatologists. Annals of Oncology, mdy166, May 28, 2018.
11. Martin, et al. Using Machine Learning to Prescribe Warfarin. University of Canterbury, New Zealand, AIMSA 2010, LNAI 6304, pp. 151–160, 2010.
12. Sharabiani, et al. Revisiting Warfarin Dosing Using Machine Learning Techniques. University of Illinois Chicago, Comput Math Methods Med. 2015; 2015: 560108.
13. Mathotaarachchi, S, et al. Identifying incipient dementia individuals using machine learning and amyloid imaging. Neurobiology of Aging. November 2017. Volume 59, Pages 80–90.
14. http://clinicalml.org/research.html
15. Narges, R, et al. Population-Level Prediction of Type 2 Diabetes From Claims Data and Analysis of Risk Factors. Big Data. Volume: 3 Issue 4: December 1, 2015.
16. Verghese, A, et al. What This Computer Needs Is a Physician - Humanism and Artificial Intelligence. JAMA. 2018;319(1):19-20.
17. Runge, M. Artificial intelligence will put a premium on physicians' knowledge and decision-making skills. https://www.statnews.com/2018/04/19/artificial-intelligence-physicians-knowledge-judgment/
18. Verghese, A, et al. Ibid.
19. Sharif, A. http://www.himss.org/news/building-better-predictive-models-subjective.
20. Gkotsis, G. Characterisation of mental health conditions in social media using Informed Deep Learning. Nature Scientific Reports volume 7, Article number: 45141 (2017).
21. Greenbaugh, T, et al. Evidence based medicine: a movement in crisis? BMJ 2014;348:g3725.

Disclosure

JC discloses St. Louis University MedLaunch Biomedical Incubator, Advisory Board; Epharmix, remote chronic care management system, Minority Investor, Clinical Advisor.

Editor's Note

See "Quantum Computing The Potential of Quantum Computing and Machine Learning to Advance Clinical Research and Change the Practice of Medicine," in this issue on page 463.

PHYSICIAN DRIVEN ♦ PATIENT FOCUSED

♦ Medical Professional Liability Insurance
♦ Superior Claims Protection
♦ Innovative Risk Management
♦ Cyber Security Insurance
♦ Advocacy



KAMMCO
Specializing in exemplary service and unwavering commitment to defend good medicine.

KAMMCO
800.232.2259
www.KAMMCO.com

Leading the Way: Women in Missouri Medicine

by Joanne Loethen, MD & Lauren Umstattd, MD

We reached out to five prominent female physicians who continue to pave the way for women in medicine and serve as inspiration for all physicians in Missouri. As leaders in their respective specialties, they provide personal insights and advice to current/future physicians, highlight unique attributes women bring to medicine, and discuss career challenges women continue to face. A compilation of their answers follows.





Christine Franzese, MD, is a General Otolaryngologist and Allergist at the University of Missouri, Columbia, Missouri.



Betty M. Drees, MD, MSMA member since 2000, is an Endocrinologist and former Dean at University of Missouri - Kansas City School of Medicine and Contributing Editor for Missouri Medicine. She was recently appointed as President Stowers Institute Graduate School.



Debra Koivunen, MD, MSMA member since 1990, is a Surgical Oncologist at the University of Missouri, Columbia, Missouri.



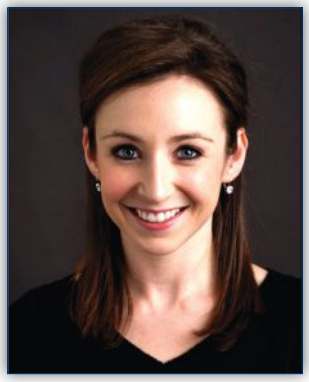
Laura Miller-Smith, MD, MSMA member since 2012, is a Pediatric Intensivist at Children's Mercy in Kansas City, Missouri.



Laura Dooley, MD, is a Head & Neck Surgical Oncologist at the University of Missouri, Columbia, Missouri.



Joanne Loethen, MD, MSMA member since 2016, is a Resident, Internal Medicine and Pediatrics, University of Missouri - Kansas City, Kansas City, Missouri.



Lauren Umstattd, MD, MSMA member since 2011, is a Resident, Department of Otolaryngology - Head and Neck Surgery, University of Missouri, Columbia, Missouri.

If you could give one piece of advice to a room full of female medical students or early-career physicians, what would it be?

- Find a variety of successful people at different stages in their careers and ask them to mentor/sponsor you. A sponsor is someone that promotes you and the things that you're doing/working on.
  -Dr. Franzese

- Know yourself well, including your strengths, weaknesses, values, and what brings you joy. If you do, you can set career and personal goals that align with both a successful career and a personally satisfying life. Find a career path that you enjoy so much that you still look forward to getting up and going to work every day when you're 50 and older.
  -Dr. Drees

- Be prepared to work hard.
  -Dr. Koivunen

- Awareness of the areas where you need improvement is not a bad thing, but it should always be put in the context of everything that has been and will be achieved. It's important that positivity takes up a bigger portion of your thoughts than negativity.
  -Dr. Miller-Smith

- Figure out what makes you happy – a lot is expected of you, so making sure you like what you are doing makes it doable.
  -Dr. Dooley

Are there any quotes you think of often or live your life by?

- My magic is never giving up. There will be obstacles and setbacks that we encounter, but we can overcome them. We shouldn't give up. There's always a way around these obstacles or another solution to the problem.
  -Dr. Franzese

- "Unless we change direction, we are likely to end up where we are headed," Chinese Proverb. Don't be afraid to make changes if what you are doing is not satisfying or not meeting your goals.
  -Dr. Drees

- "Do onto others as you would have them do onto you," or treat everyone like they were a beloved family member.
  -Dr. Koivunen

- "You can have it all, just not all at once," Oprah Winfrey. I try to be fully at work when I am at work so that when I am home I am fully at home.
  -Dr. Dooley

According to the AAMC Physician Workforce Data Report which analyzed physician workforce data by state, the median percentage of female physicians was approximately 33% in 2016. In your opinion, what more can the medical field (or specific specialties) do to enhance the participation of female physician in the workforce?

- Maternity and paternity leave. Childcare and childrearing are not just female things – there should be better available childcare options for both genders. Also, zero tolerance for any kind of harassment/discrimination.
  -Dr. Franzese

- Fair and transparent compensation and expectations across specialties and positions is important in enhancing women's participation in all aspects of the healthcare workforce.
  -Dr. Drees

- Thoughtful planning and working with their supervising faculty will find the correct balance to allow child-bearing to coincide with education/training. As our profession matures and the complement of younger physicians increases, the needed flexibility for female physicians is growing.
  -Dr. Koivunen

- Encouraging girls to pursue science at a young age, with mentorship about the career possibilities including medicine.
  -Dr. Miller-Smith

- We need to change the culture - support each other and advocate for each other.
  -Dr. Dooley

What unique challenges do women face in careers, such as medicine, that require advanced education and training?

- Childbearing and potential complications that go with it.
  -Dr. Franzese

- Perception bias of women's leadership ability that may result in them being overlooked for promotions and leadership positions. Leadership ability can be enhanced with training and experience.
  -Dr. Drees

- The demands of this profession are not going to change, but more flexibility will become evident.
  -Dr. Koivunen

- We are also still not thought of as the doctor or the surgeon when we walk into a room. Patients will trust a male intern immediately as the doctor while I just explained and am the one making the plan.
  -Dr. Dooley

What can women do today to better promote themselves within medicine?

- Speak up and support each other. Promote other women.
  -Dr. Franzese

- Without being overly assertive, women can still promote themselves…if you have accomplished something (such as a publication, etc.) make sure others know it. Don't be afraid to get into conversations and display your competence. Network.
  -Dr. Koivunen

- I think women are better listeners, and do exceedingly well at garnering information from multiple parties, but we also need to do better at speaking out with authority and confidence. It is people who present themselves with confidence and knowledge who are offered opportunities.
  -Dr. Miller-Smith

In your opinion, what unique attributes do women bring to the table as medical professions?

- Common sense, level headedness, compassion, and the ability to see both sides.
  -Dr. Franzese

- Women may facilitate a culture and environment of inclusivity in the workplace.
  -Dr. Drees

- Sometimes we are more prone to show our emotions (touching a patient, etc.) which makes us more approachable.
  -Dr. Koivunen

- Men and women both can be excellent physicians and what makes a good physician is not related to having the XX chromosomes. Patients may be able to open up to women physicians more and are more willing to share and connect.
  -Dr. Dooley

What impact, if any, did life-work balance play a role in your selection of specialty?

- Pick and choose the non-work activities carefully and outsource the chores and services you don't have time to do or don't like. It's important not to short-change the relationships you have outside of work with family, friends, and the activities that bring you inner joy.
  -Dr. Drees

- None. I wanted to be a surgeon, I still love being a surgeon, and I figured the rest would work itself out with the appropriate attention/planning on my part.
  -Dr. Koivunen

- It was important to me during residency to find a subspecialty that would allow me to have a favorable life-work balance that could be sustained through my career. Life-work balance is a personal thing, and is impacted by so many factors in life. But there are also so many different specialties/subspecialties that I think there is always a way to meet your own personal goals.
  -Dr. Miller-Smith



MSMA Women in Leadership. Front row, from left: Drs. Sandra Ahlum, Peggy Barjenbruch, Sharon Wallace, Ramona Behshad, Rebecca Hierholzer, and Lirong Zhu. Back row, from left: Drs. Joanne Loethen, Betty Drees, Amanda Turner, and Lisa Thomas. Below, from left: Drs. Sri Devi Kolli, Sarah Florio, and Jo-ellyn Ryall.







- I was drawn to ENT and knew that I had to find something that I was interested in and loved. You have to like/love your job and work to then be happy in life.
  -Dr. Dooley

How have you seen the presence and/or influence of women in medicine change from the start of your career to now?

- It's better but it still has a long way to go.
  -Dr. Franzese

- There are more role models for success across specialties. It is important for individuals to see people like themselves who are successful, so that they may more easily visualize themselves as successful, too. Expecting to succeed is very powerful in realizing that outcome.
  -Dr. Drees

- There are more women, more in leadership roles, and we are taken seriously by our male counterparts.
  -Dr. Koivunen

- In medical school I was exposed to women "mentors" who seemed to think that in order to compete with men, they had to act like them. More recently, the strong female physicians with whom I work recognize that they can be themselves, however feminine that may or may not be. It's not a man or woman's world – healthcare is inclusive of everyone and we perform best when we are true to ourselves.
  -Dr. Miller-Smith

- I see the great need for role models that are similar to you, not only in your field but in your situation in life. Just someone to look up to and say - they made it, I too will survive.
  -Dr. Dooley

What advice would you give your younger career self?

- Keep an open mind to new opportunities.
  -Dr. Drees

- Work hard, but take time to take care of yourself. Find a way to "give back"…volunteer activity, teaching, etc.
  -Dr. Koivunen

- Enjoy the journey more, and not be afraid to take some side roads. The goal of life is not some far off endpoint down the road, but living each individual day to its fullest.
  -Dr. Miller-Smith

Any additional thoughts or comments to share for Women in Medicine Month?

- Men and women are together in this and we need the support of both genders. So even in a "Women in Medicine month" there's still men there. You just have to look a little closer.
  -Dr. Franzese

- Better work environments are better for everyone, not just women.
  -Dr. Drees

- Medicine, regardless of the specialty, is a wonderful career. At the end of the day, the help you give to a patient (and the gratitude they express) outweighs the negatives.
  -Dr. Koivunen

For complete answers from their responses, visit: https://www.dropbox.com/s/pfhs99gu07j720q/Full%20Text.Women%20in%20Medicine.pages?dl=0

MM

NORCAL GROUP OF COMPANIES

NORCAL MUTUAL®

MEDICAL PROFESSIONAL LIABILITY INSURANCE

PHYSICIANS DESERVE

Offering top-tier educational resources essential to reducing risk, providing versatile coverage solutions to safeguard your practice and serving as a staunch advocate on behalf of the medical community.



Talk to an agent/broker about NORCAL Mutual today.

NORCALMUTUAL.COM | 844.4NORCAL

© 2016 NORCAL Mutual Insurance Company

nm5001

What We Owe To Each Other

by Frances Mei Hardin, MD

A starter kit of life-affirming ideas and suggestions beyond the hospital setting.

… That we take good enough care of ourselves that we are tolerable, even enjoyable, to work alongside. There is immense value in finding outlets to release some of the stress that accumulates over the course of the surgeon's day. Having hobbies and various outside interests can also play a critical role in building up resilience to workplace demands. The purpose of this writing is to emphasize the importance of finding stress-relieving activities, and to offer some suggestions about where to start, for those who are in search of ideas.

Batting Cages

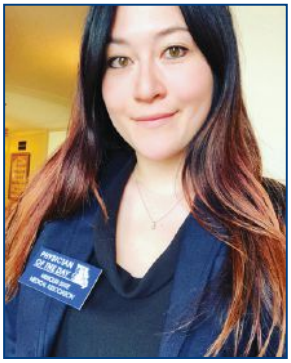
During my residency I have already graduated from having never swung a bat to the proud owner of an aluminum Easton. It turns out that America's favorite pasttime is also a phenomenal anger management technique. There's something satisfying about it on a visceral level.

Driving Range

Fun for even the golf-naive person. See reasoning above.

Salt Water

Best put by author Karen Blixen, "The cure for anything is salt water: sweat, tears or the sea."[1]



Frances Mei Hardin, MD, MSMA member since 2017, is in the Department of Otolaryngology, University of Missouri, Columbia, Missouri. Above, she is shown as MSMA Physician of the Day at the Missouri Capitol in 2018.
Contact: hardinf@health.missouri.edu



Edley in her (my) favorite Red Sox jersey.

Mindfulness Apps

As a benefit of this digital age, there are countless mindfulness apps such as Headspace and Calm. If there are five to ten minutes to spare at bedtime, for instance, the apps have modules that walk the listener through meditation and relaxation pathways. There is evidence that engaging in mindfulness practice even only a few times per week can lead to reduced rumination, increased focus, less emotional reactivity, and more cognitive flexibility. Who among us wouldn't benefit from that?

Pet Ownership

One of my greatest happinesses comes from the simple act of dressing my cat in a Red Sox jersey. While she does not derive similar enjoyment from the experience, it's a great way to bring some levity into the home.

Moisturizer

Lavender has long been known as a stress-reducing scent, so I make a point of searching out this ingredient in lotions. Moroccan oil products are currently having a moment in the sun, and can be applied broadly to the skin, hair, or nails.

Baking

My best work as a baker has been in honing a jumbo chocolate chip cookie recipe that I found on the internet. There's no going back to regular-size cookies at this point.

Local Alpacas

Sycamore Creek Farm, located in Rocheport, Missouri, is a truly magical place where the owners generously allow visitors to tour the grounds, feed the alpacas, and take selfies.



Selfie with Chloe the alpaca, from Sycamore Creek Farms.

New Writing Utensils

There is no limit to the fun I have looking for new, fine-tip pens. These are essentially objects of happiness that can be brought anywhere in the workplace. So far, I am most taken with the Pilot G-2 0.38mm tip numbers, and Pigma Micron pens 0.2mm.

Tequila Pineapple

Recommend Casamigos tequila or bust (with all things in moderation).

Coworkers and patients can sense, and certainly appreciate, a joie de vivre when it's there. There are a myriad of hobbies and interests that can buoy our sense of happiness and self in times that there is disruption of those things in the workplace.

Disclaimer

This article was not sponsored by Easton bats, Headspace, Calm, Sycamore Creek Farms, Pilot, or Casamigos, but if any of these institutions would like to reach out, I'll be available.

References

1. Blixen, K. Reader's Digest 1964.

MM

Missouri Medicine Annual Statement of Ownership, Management & Circulation

1. Publication Title: Missouri Medicine
2. Publication No.: 0355-3800
3. Filing Date: 9/28/18
4. Issue Frequency: Bi-Monthly
5. No. of Issues Published Annually: 6
6. Annual Subscription Price: $75
7. Complete Mailing Address of Known Office of Publication:
   113 Madison Street - Cole County
   Jefferson City, MO 65101
8. Complete Mailing Address of Headquarters or General Business Office of Publisher:
   113 Madison Street - Cole County
   Jefferson City, MO 65101
9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor:
   Publisher-Missouri State Medical Association
   113 Madison Street - Cole County
   Jefferson City, MO 65101
   Editor: John C. Hagan, III, MD
   113 Madison Street - Cole County
   Jefferson City, MO 65101
   Managing Editor: Lizabeth R. S. Fleenor
   113 Madison Street - Cole County
   Jefferson City, MO 65101
10. Owner: Missouri State Medical Association
    113 Madison Street - Cole County
    Jefferson City, MO 65101
11. Known Bondholders, Mortgagees & Other Security Holders: None
12. The purpose, function, and nonprofit exempt status for federal income tax purposes has not changed during the preceding 12 months.
13. Publication Name: Missouri Medicine
14. Issue Date for Circulation Data Below: July/August 2018
15. Extent and Average Actual number nature of number of copies of circulation copies each single issue during published preceding nearest to

	12 Months	Filing Date
15a. Total No. Copies (Net Press Run)	3076	2914
15b. Paid and/or Request Circulation		
(1) Paid/Requested Outside-County Mail Subscriptions	2953	2834
(2) Paid In-County Subscriptions	0	5
(3) Sales Through Dealers and Carriers, Street Vendors	1	0
(4) Other Classes Mailed Through the UPS	0	0
15c. Total Paid and/or Requested Circulation	2954	2839
15d. Free Distribution by Mail	0	0
15e. Free Distribution Outside the Mail	0	0
15f. Total Distribution	2054	2839
15g. Copies Not Distrib.	122	75
15h. Total	3076	2914
15i. Percent Paid	100%	100%
16. Electronic Copy Circulation		
16a. Paid Electronic Copies	45	45
16b. Total Paid Print Copies + Paid Electronic Copies	2999	2884
16c. Total Print Distribution + Paid Electronic Copies	2954	2839
16d. Percent Paid (Both Print and Electronic Copies)	100%	100%

This Statement of Ownership is printed in the September/October 2018 issue of this publication.

Sulla Strada di Nuovo... "On the Road Again"

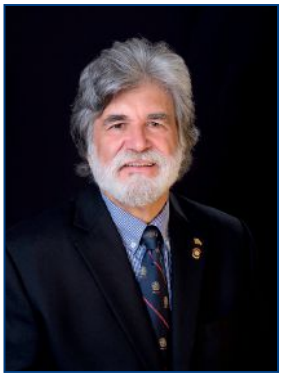
by Joseph A. Corrado, MD

As I continue my journey as your President of MSMA, I truly feel blessed to be representing my fellow physicians of Missouri. After I left the MSMA meeting at the Lake of the Ozarks in July, MSMA Executive Vice President Patrick Mills and I headed to Joplin and the new campus of the Kansas City University College of Osteopathic Medicine to join in their white coat ceremony. Several distinguished deans and faculty, including David E Tannehill, DO, President of MAOPS, and I presented white coats to over 150 budding physicians, the incoming class of 2022. You could see the excitement in their faces as they donned their white coats for the first time. It was quite inspiring, renewing the feelings of why I chose this profession. We were most cordially welcomed and learned that nearly 40% of KCU alumni practice in rural and underserved areas, and that 60% are in a primary specialty. We toured a modern, impressive campus with the students, who showed us one of the most advanced simulation labs in existence. It is gratifying to see how interested and eager these physicians-in-training were to become a part of organized medicine.

In mid-August, it was off to join our colleagues in West Central Medical Society in Nevada, Missouri. There we were escorted by our immediate past president, Warren Lovinger, MD, and his wife, Marilyn. We felt we were among friends. You know, just down the street from my home in Mexico is a sign on Highway 54 saying "Nevada 199" miles. Driving that whole road for the first time, we were awed by how beautiful and diverse our state is. We met with several assistant physicians, and found out, first-hand how valuable that program has been for them and their community.

At the end of August, my wife, Donna, and I drove to Louisville to the Kentucky Medical Association's 168th annual meeting. We attended their association leadership reception and watched as outgoing President Maurice Oakley, MD, installed Bruce A. Scott, MD, as their new president. Bruce, as you may know is the AMA Vice-Speaker of the House of Delegates. Their invited speaker was Frank Abagnale, Jr., the original 2002 Spielberg film "Catch Me if you Can." He gave a riveting expose of his life and how he had impersonated an airplane pilot and flew millions of miles, a lawyer, and a real physician, all before the age of 21. A great imposter! From his youthful escapades he turned to the right side of the law as an FBI trainer, enlightening us on an insider's knowledge of identity management. It's truly eye-opening and frightening to know how much the government and our electronic devices know about us. One interesting fact we learned was that our printer's hard drive retains information and should be destroyed. They had a wonderful display called "Beyond the White Coat," featuring their doctor's past-times outside of medicine. On display was art, books, jewelry, flowers, film, dance, music, even a hot air balloon! This gave a real feel for the diversity of personality of their physician members. Oh, did I tell you that Kentuckians know how to party and that the bourbon was flowing? Now I know why the Massachusetts and New Jersey Presidents were also there! Also joining us was Barbara McAneny, MD, current AMA President, part of a fireside chat on leadership.

Just recently, we joined Nebraska Medical Association in Omaha as members celebrated their 150th anniversary. Robert Rhodes, MD, handed the gavel to Britt Thedinger, MD, another ENT specialist. There, NMA reiterated that there is strength in



Joseph A. Corrado, MD, FACS, a surgeon from Mexico, Mo., and MSMA member since 1982, is MSMA President for 2018-2019.
Contact: bigdocjoe@sbcglobal.net

numbers which can make a difference at both the state and national levels. We heard of the physician burnout rate being as high as 54% and that there were 356 physician suicides in 2017. Learning that Nebraska does not have a physician's health program, of course, I touted the virtues of our excellent program, here in Missouri. They advocated for being agents of change, and that 9 of 10 adults want a physician in charge of their medical team. Their mantra was not to allow untrained providers get the power of the prescription pad. They were also quite proud of their new marketing campaign at Husker athletics: GO BIG RED -GO BIG MED with huge banners at the husker football games, and declaring how physicians in Nebraska care about patients, even an impressive radio media campaign with weekly medical panel discussions by their members. Medical students from Creighton and University of Nebraska School of Medicine were in the programs, showimg us their new curriculum changes, to include more about the ethics, business, and advocacy part of medicine. We heard from C.T. Lin, MD, of Colorado, a chief medical information officer of a seven-hospital 400-clinic system, who achieved HIMSS' highest achievement in EHR effectiveness, and how important a physician-patient communication was in improving health outcomes across the board.

Home at last, we met with our own Audrain County Medical Society and discussed how the possible hospital acquisition by the University of Missouri Health System may change our practice patterns and delivery of care here in Mexico. We wait patiently as negotiations unfold.

On the horizon, we have one more contiguous state to visit, that will make eight. Topeka, here we come! We look forward to joining many more of your local society meetings in the future. It never ceases to amaze me that wherever I go, our MSMA staff is so highly regarded. And so, for now…Ciao! **MM**



Kentucky: Maurice Oakley, MD, outgoing Kentucky President, Dr. Corrado, Bruce A. Scott, MD, incoming President.



Nebraska: Dr. Corrado, Britt Thedinger, MD (President, Nebraska) Michael Romano, MD (President, Iowa).



Massachusetts: Dr. Corrado and Alain A. Chaoui, MD, President, Massachusetts.

Missouri Medicine in the News

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

Missouri Medicine Accepted into PubMed Central, and Continues Posting in PubMed

Missouri Medicine: The Journal of the Missouri State Medical Association, is pleased to announce that after a thorough review, PubMed, the indexing service of the National Library of Medicine (NLM), will continue to index our Journal.

PubMed has indexed *Missouri Medicine* since 1966. Prior to 1966, *Missouri Medicine* articles were indexed by OLDMEDLINE, which consisted of journal article citations from two print indexes: *Cumulated Index Medicus* and the *Current List of Medical Literature,* and created by the National Library of Medicine from 1946 through 1965. OLDMEDLINE records, most of which are included in MEDLINE database, can be searched via PubMed

New technical requirements regarding uploading content in an XML format have been attained by using the services of Digital Conversion Labs.

After a separate review, PubMed Central, a free full-text archive of biomedical and life sciences journal literature at the NLM/NIH has also approved *Missouri Medicine* for inclusion. Previous (digital-only) issues dating from 2010 are in the process of being uploaded. These new and updated services are critical to our Journal to remain one of the foremost state medical journals in the United States, and to be certain all content is available at all world data bases and literature electronic literature searches.



Jessica D. Bauerle, MD, MSMA member since 2016, has been appointed the newly created position of Young Physician Contributing Editor to *Missouri Medicine*. She will begin a three-year term January 1, 2019. Dr. Bauerle is a practicing pediatric anesthesiologist in the St. Louis metropolitan area. Dr. Bauerle has an outstanding record of academic achievement, scientific publication, participation in medical education, and national and international community service. She has contributed chapters to three medical texts. She will represent the interests of young, early career physicians.



Charles Lederer, MD, MSMA member since 1982, former ophthalmology editorial board member for *Missouri Medicine*, received the Golden Medallion Award for Lifetime Achievement from the Missouri Society of Eye Physicians September 28, 2018. Dr. Lederer also recently received the Hal Foster Lifetime Achievement Award from the Kansas City Society of Ophthalmology & Otolaryngology. From left, residents under Dr. Lederer: Jonathan Drummond, MD, Denise Hug, MD, Charles Lederer, MD, Abraham Poulose, MD.



Esteemed physician and educator Betty M. Drees, MD, FACP, MSMA member since 2000, was recently appointed president of the Graduate School of the Stowers Institute for Medical Research. She is also a Contributing Editor to *Missouri Medicine.* Dr. Drees is Dean Emerita and the immediate past dean of the University of Missouri-Kansas City (UMKC) School of Medicine.



Frederick Fraunfelder, MD, MBA, MSMA member since 2014, has been appointed Assistant Dean for Faculty Affairs at the University of Missouri School of Medicine by Patrick Delafontaine, MD, Dean of the MU School of Medicine, and also an MSMA member.



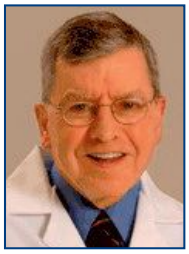
Congratulations, Raghav Govindarajan, MD, on receiving the 2018 Advocacy Award from the American Association of Neuromuscular & Electrodiagnostic Medicine for your longstanding work with electrodiagnostic medicine. MSMA appreciates your membership support since 2013.



Edmund Landry, MD, recently joined the Regional Physician Services team in Kennett. MSMA appreciates your membership since 2001.



MSMA is proud to have young physician, Melissa Rooney, MD, as a member since 2015. We'd like to wish her well in her new endeavor with Parkland Health Center of Bonne Terre, Mo.



MSMA would like to congratulate MSMA member since 1993, John Sanfelippo, MD, on joining SSM Health Medical Group in Jefferson City.



MSMA is proud of our member James Womack, MD, for utilizing advanced technology at Golden Valley Memorial Healthcare. Thank you for your membership since 2011.

EDITORIAL BOARD OPENING: PSYCHIATRY AND PULMONARY MEDICINE

Missouri Medicine has openings on its Editorial Board for Psychiatry and Pulmonary Medicine. Applicants must be board certified and a member in good standing of MSMA. Membership in state and national organizations is highly desirable. Duties will include peer-review of papers within the field of Psychiatry and Pulmonary Medicine. This generally will not occur more than once/year. There are no meetings but approximately once every other year editorial board members may be asked to either author a paper or help procure willing authors on specific subjects within Psychiatry and Pulmonary Medicine. Candidates that have published extensively or who are involved in research, education, or who have academic appointments are given special consideration. Appointments are for one calendar year and are annually evaluated by the Editorial Board. Please submit your CV to Lizabeth Fleenor (lfleenor@msma.org) by November 21, 2018.

TRI-STATE OCCUPATIONAL MEDICINE

Physicians Needed for Outpatient Exams

Tri-State Occupational Medicine, Inc. (TSOM) is looking for physicians to perform disability evaluations in MO.

Part-time. No treatment is recommended or performed. No follow up.

Travel within SE MO will be necessary.

Contact: Susan Gladys 866-929-8766 or susang@tsom.com

SteriPort Solutions
The Professional Medical Waste Service

Missouri Medical & Hazardous Waste Disposal

SteriPort Solutions offers:

- Flexible scheduling & on-call service
- No long-term contacts
- No hidden charges
- Cost effective to meet every budget and goal
- Online compliance seminars
- Fully licensed and insured

SteriPort Solutions
The Professional Medical Waste Service
www.steriportsolutions.com
573-442-5040

Greene County Medical Society

Always in Motion

The Greene County Medical Society seems to always be in motion. Ably led by GCMS Presidents Dan Pinheiro, MD, in 2017 and Matt Stinson, MD, in 2018, GCMS continually works, along with our colleagues at MSMA, to meet the challenge of supporting our physicians and the patients they serve in our communities, and in our state.

This past year has been particularly rewarding as we celebrated GCMS's own David Barbe, MD, as the first Missouri AMA President in ninety years. David, with his wife Debbie by his side, took the oath of office June 13, 2017. Several proud GCMS and GCMS Alliance members made the trip to Chicago to cheer him on.

Dr. Barbe is a practicing Family Physician in Mountain Grove Missouri and serves as Vice President for Regional Operations at Mercy Health in Springfield Missouri; he is also a former MSMA President.

In addition to his AMA duties and hectic speaking schedule nationwide, David found time to formally address the GCMS membership on two occasions. On October 24, 2017, he spoke on the Opioid Crisis at Jordan Valley Community Health Center; this GCMS meeting was hosted by Dr. Stinson and was attended by many community leaders, including the Mayor of Springfield. On March 20, 2018, Dr. Barbe along with his wife Debbie, spoke on Physician Burnout; this well attended GCMS dinner was sponsored by the GCMS Alliance.

Dr. Barbe has also written monthly articles for the GCMS Journal on topics ranging from Gun Violence in America (encouraging us to use an evidence-based approach and treat the issue as a Public Health crisis) to Physician Leadership, and Hypertension recognition and control. You may read Dr. Barbe's articles, along with reports of his presentations online by going to the GCMS web site at GCMS.us, and clicking on Journals. You will also find reports on GCMS activities and original articles from GCMS physicians of all specialties on various topics, along with GCMS supported ventures such as the Child Advocacy Center, the Victim Center, and the Family Justice Center.

The GCMS is currently attempting to update all member information in an online directory; we anticipate that this will take several months, but this endeavor will hopefully give us the opportunity to recruit new members as well. We also would like to work with the GCMS Alliance to increase our family friendly events for GCMS members and their families, in an effort to help prevent physician burnout. We have initiated an Opioid Crisis Committee to work both with our Springfield/Greene County Department of Health and a broad based community coalition.

GCMS Past President Dr. Pinheiro hosted our GCMS HPV 2017 Conference at the Metropolitan Grill the event was sponsored by the GCMS Van Smith Foundation. Our President Elect, Shannon Woods, MD, recently hosted a very successful Sports Medicine Conference at Cox, partially supported by the GCMS. Both conferences were open to all community physicians and health care professionals.

In addition to Dr. Barbe, we are also proud of our GCMS Executive Director Cathy Leiboult, who is our heart and soul, as well as the GCMS Alliance with their many accomplishments over the past year. Please read their report below.

At the AMA Alliance Annual meeting in Chicago in June, Greene County Medical Society Alliance won their third Health Awareness Promotion (HAP) Community



Matthew L. Stinson, MD
2018 GCMS President



David Barbe, MD, and 2017 President Dan Pinheiro, MD, at the Greene County Medical Society Opioid Conference.

Health Project award for our project "Taking Care of the Physician Family." We previously won for our Smoking Makes Me Ugly! and Pills Are NOT a Party! projects. This is the AMAA's top award and is given in three categories: Opioid Initiative, Fund Raising, and Community Health.

The Greene County Alliance has a passion for focusing their energies on health issues affecting the community. After hearing Dr. Kim Blackham speak at the 2015 AMAA meeting, they decided to focus their efforts on strengthening the physician family.

Physician burnout affects the health and happiness of the family, so in 2016 we changed the focus of their Doctors' Day celebration and received support from Ferrell Duncan Clinic and Mercy Health System to bring in a speaker at a catered dinner, open to all physicians and spouses in the area. At the first event in March 2016 Dr. Kim Blackham addressed strengthening the medical marriage, and our physician evaluations were all very positive.

After hearing Dr. Samantha Meltzer-Brody at the AMAA meeting in 2016, the Alliance immediately booked her for the next event in 2017. Dr. Meltzer-Brody is the founder and director of the Taking Care of Our Own Program, targeting physician burnout and strengthening the physician family.

She suggested increased social activities targeting physician families, noting that physicians need more down time and social activities with others in the same profession. Last fall the Alliance held a Smallin Cave tour and catered picnic, which included games for the children. In the winter, they held a Physician Family Night at the Museum, renting the Discovery Center after hours and featuring child-friendly food, and cookie decorating.

Fun, food, and fellowship with others who understand the stress of the profession resulted in the Alliance making a positive difference in the community of medicine. These events were open to all physician families regardless of membership and were actively publicized by the health systems in the community. The families that participated really seemed to enjoy themselves; many said they are looking forward to the next activity. They were happy for the opportunity to visit with other physician families, and the Alliance knows these events helped to strengthen the family bonds. A physician who is happy at home is often happier at work and better able to handle the pressures that medicine presents.

Our Alliance also has a social called Wine Time for physicians and their spouses on the third Tuesday of each month at a local wine bar. This is a casual, no reservation activity that is becoming increasingly popular.

AMA President Dr. Barbe and his wife Debbie were featured speakers at the Alliance's 2018 Doctors' Day dinner discussing their experience handling the stress of practice. The Doctors' Day events have all offered specific strategies to recognize, prevent, and mitigate physician burnout, which is important because studies show that physicians who suffer burnout are less able to connect with and serve their patients.

Membership in both the Medical Society and the Alliance increased because of interest in this topic. The Alliance has succeeded in strengthening the family of medicine - and by doing so, helping physicians better serve the community. **MM**



Stable protection. No assessments.

ProAssurance is the only medical professional liability insurer to serve Missouri uninterrupted since 1976. No moratoriums, and no retreats.

Our insureds have local contact with claims and underwriting services in our St. Louis and Springfield, Missouri offices. And in the event of a claim, we have defense experts that know Missouri law—winning with 87% of claims closed without indemnity.*

We deliver the financial strength and stability that has kept us on the Ward's Top 50® list for eleven years running and rated A+ (Superior) by A.M. Best.

You need coverage you can trust. For a no-obligation quote, contact Emil Pela at epela@proassurance.com or 205.903.4749.

**Source: internal company data 2015-2017*

PROASSURANCE®
Treated Fairly

SINCE 2007 WARD'S 50 SAFETY • CONSISTENCY • PERFORMANCE®

Financial Strength Rating A.M. BEST A+ Superior

Healthcare Professional Liability Insurance & Risk Resource Services

ProAssurance.com/Missouri • 800.282.6242

School of Medicine

A Triplicate Mission to Improve Lives

by Patrick Delafontaine, MD & Jerry C. Parker, PhD

When I joined the University of Missouri (MU) School of Medicine as dean in 2014, I became part of a medical school with a legacy rooted deeply in the history of our state. The MU School of Medicine has improved health, education, and research in Missouri and beyond since its founding in 1872. On behalf of the faculty, staff and students of our medical school, I am pleased to provide an update on our school's missions in the areas of research, education, and clinical care.

I am privileged to lead our medical school in pursuit of our vision of being a transformational leader in improving health. As part of Missouri's flagship academic health system, the School of Medicine works closely with our hospital and clinics, MU Health Care, in providing care for all Missourians. MU Health Care is a destination for patients who need access to all levels of care, including an extensive primary care network, a Level 1 trauma center, and stroke and cardiology programs that have been nationally recognized. MU Health Care is home to five hospitals and more than 50 primary and specialty clinics throughout the mid-Missouri region. Our health system is dedicated to providing patients with state-of-the-art health care technologies and infrastructure. MU Health Care recently opened a $40 million expansion of the Missouri Orthopaedic Institute (Figure 1); a $16 million expansion of the University Hospital emergency department is currently under construction. These expansions, and others, will ensure that our facilities are able to accommodate growing patient volumes into the foreseeable future. In fiscal year 2018, our School of Medicine clinical faculty treated more than 226,000 patients — an increase of nearly 24,000 patients since fiscal year 2016. This growth is facilitated by our partnership within the Health Network of Missouri and the multi-state MPact Health provider network. Through these strategic alliances, MU Health Care is well-positioned to improve access and coordinate care for patients throughout the state.

While our clinical enterprise has seen tremendous growth, I also am pleased to report that the educational programs inherent in our mission continue to thrive. The foundation of our undergraduate medical student curriculum continues to be patient-based learning, which is an approach to medical education that allows students to learn from actual clinical cases as they acquire their medical training. The MU School of Medicine recently celebrated our 25th anniversary of teaching through the patient-based learning model. Since our second year of using the curriculum, our medical student United States Medical Licensing Examination scores have consistently exceeded the national average. Indeed, our patient-based learning curriculum has been a model that has been emulated by several other medical schools across the nation. As a result of our class-expansion project, which includes a new Patient-Centered Care Learning Center (see Figure 2), students now have the option to spend their





Patrick Delafontaine, MD, MSMA member since 2016, (left), is the Hugh E. and Sarah D. Stephenson Dean, Professor of Medicine and Medical Pharmacology and Physiology, University of Missouri School of Medicine and Jerry C. Parker, PhD, is Associate Dean for Research, Professor of Physical Medicine and Rehabilitation, University of Missouri School of Medicine, Columbia, Missouri.
Contact: delafontainep@health.missouri.edu



Figure 1. Missouri Orthopaedic Institute



Figure 2. Patient-Centered Care Learning Center (PCCLC)

last two years of training at our Springfield Clinical Campus, which operates in partnership with CoxHealth and Mercy health systems. Each year since June 2016, eight to 12 MU medical students have completed their last two years of medical training in Springfield. Although we now have campuses in both Columbia and Springfield, we are truly one, unified medical school with a mission to train physicians for Missouri and beyond.

In addition to improving health and education, I have been working closely with School of Medicine leaders and faculty to enhance our research infrastructure and our standing as a research-intensive institution. Research funding at the national level remains highly competitive, but due to the efforts of our scientists, we are achieving sustained growth in both research awards and expenditures. Over the past four years, SOM research awards have increased by 37

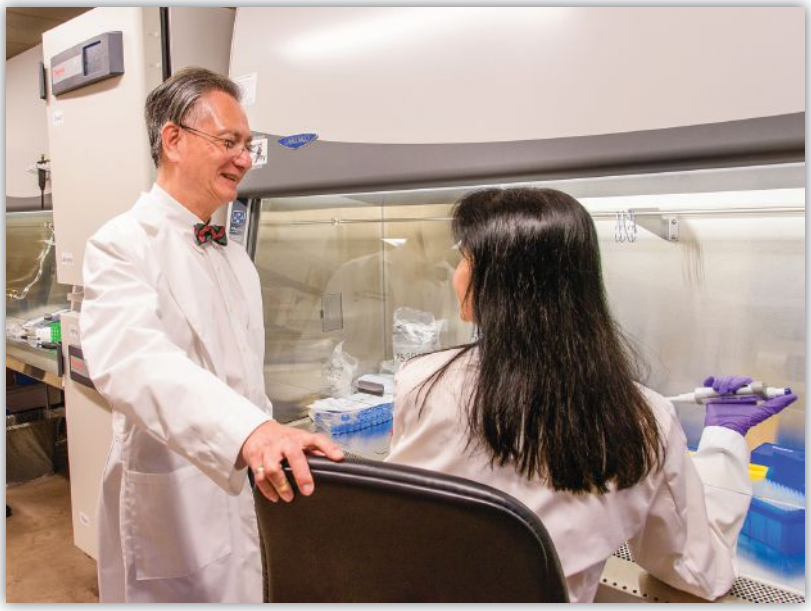


Figure 3. Edward T. H. Yeh, MD, Francis T. McAndrew Chair, Department of Medicine, Professor of Medicine

percent, and NIH awards have grown by 42 percent; our total research expenditures have increased by 17 percent over the last three years. Our faculty are devoting particular efforts to obtaining large multi-project research awards. Accordingly, we recently awarded five research teams with internally-funded Program Project Planning Grants; these grants are intended to help research teams prepare and submit extramural applications to the NIH or other federal agencies for multi-project grants.

MU School of Medicine researchers are working to address some of our nation's most prevalent and disabling health conditions; a short list of ongoing projects is as follows:

- Elizabeth Parks, PhD, is increasing our understanding of metabolism and diet, which has implications for preventing metabolic diseases.
- Studies led by Kevin Staveley-O'Carroll, MD, PhD, are seeking new, improved therapies for hepatocellular carcinoma.
- Timothy Domeier, PhD, is studying molecular mechanisms to prevent cardiac damage following heart attacks.

Dongsheng Duan, PhD, is working to develop gene therapy to prevent Duchenne muscular dystrophy. Dr. Duan's approach has shown tremendous promise in a canine model, and his work is now the foundation for a clinical trial to address the gene mutation in humans.

- Peter Tonellato, PhD, is using precision medicine techniques to ensure that patients on warfarin receive optimal anticlotting protocols. At the MU Center for Biomedical Informatics, Dr. Tonellato is developing mathematical models to simulate treatment outcomes.
- As Francis T. McAndrew Chair, Department of Medicine, Edward T.H. Yeh, MD, is advancing our understanding of the relationship between heart disease and cancer (Figure 3).

The emerging field of precision medicine recognizes that each patient is unique with regard to genes, lifestyle, and environmental exposures. Accordingly, the School of Medicine is a key partner in the MU effort to plan for the Translational Precision Medicine Complex (TPMC), which will bring scientists together from all across the campus to tackle a range of compelling health conditions. The TPMC will bring together multiple schools and colleges, industry partners, and the federal government to pursue a collaborative approach to the treatment and prevention of many diseases; the facility will be an exceptional resource to study cancer, neurological, and vascular diseases. The TPMC will be home to 32 principal investigators whose focus will be to seek breakthroughs in translational science and precision medicine; the facility will help MU attract funding from federal and industry sponsors.

In conclusion, our school has been in existence for more than 140 years, and we continue to be committed to improving health through the latest advances in clinical care, education, and research. As I look toward the future, I am excited by the possibilities for the MU School of Medicine and our ability to serve the citizens of Missouri and beyond. **MM**

Overview: Management of the Injured Patient

by Salman Ahmad, MD

School of Medicine

This Trauma Care update is for the rural healthcare provider and EMS first-responders who stand on the front lines of trauma care for Missouri.



Salman Ahmad, MD, FACS, is Assistant Professor of Surgery, Medical Director Surgical Intensive Care Unit, Acute Care Surgery Division, Department of Surgery, University of Missouri Healthcare, Columbia, Missouri.
Contact: ahmadsa@health.missouri.edu

The Acute Care Surgery Division at the University of Missouri in Columbia is honored to share our 2018 update on the management of the injured patient. Despite our patients' above-average injury acuity, our Trauma Quality Improvement Program (TQIP) risk-adjusted mortality rate continues to outperform the national average due in large part to a refined trauma system consisting of students, residents, advanced practice nurses, pharmacists, dietitians, social workers, and attending surgeons.

Many have earned research awards and grants for their commitment to the care of our injured patients. Our injured population mirrors trauma care in the state of Missouri and runs the spectrum from urban to rural, penetrating to blunt. A well-coordinated state EMS transport system is a crucial link in this chain of care. While many dedicated academic trauma centers are well-versed in the latest advances in the management of the injured patient, we have written our 2018 update for the rural healthcare provider and EMS first-responders who stand on the front lines of trauma care for Missouri.

We will share our thoughts on the initial management of the injured patient, focusing on the basics with an emphasis on rapid transport to higher levels of care. In reviewing the management of the bleeding patient, our update will discuss an aortic occlusion catheter, tranexamic acid and the latest massive transfusion protocols. Our pediatric review covers the management of traumatic brain and blunt solid organ injuries, updates imaging guidelines and discusses trauma-induced coagulopathy. We will share our institution's successful treatment of a severely burned patient while reviewing the management of severe burns. The latest in simulation training will be described as a safe environment for healthcare providers to learn and practice management skills. Finally, we will review the approach to mass casualty incidents in the context of lessons learned from recent events and discuss current research and development of a triage communication tool we are developing in conjunction with the department of computer engineering.

We hope this update encourages local and regional trauma systems to enhance their standard of practice and reiterate the importance of a collaborative state trauma system. Thank you for all you do for the injured in Missouri. **MM**

Initial Evaluation and Management of the Injured Patient

by Jeffrey Coughenour, MD

School of Medicine

Practice the concept of 'minimally acceptable care;' treating the patient within the hospital's capability and promptly transferring the more severely injured to a higher level of care.



Jeffrey Coughenour, MD FACS, is Associate Professor of Surgery, Trauma Medical Director, Division of Acute Care Surgery, Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri.
Contact: coughenourj@health.missouri.edu

Abstract

This update is a conversation with our trauma medical director about the initial evaluation and management of the injured patient. After a brief historical perspective, we discuss the immediate treatment of life-threatening injuries at local hospitals within the context of definitive care at a level 1 trauma center. Our journey is colored by recent cases we have treated at our institution with the hope that we save more Missourian lives.

Historical Perspective

The impact of medical history is often lost on the contemporary graduate, but I believe it is extraordinarily helpful to set the stage for our discussion. Have you read *Accidental Death and Disability: The Neglected Disease of Modern Society*[1]? Often referred to as the "white paper" of trauma care, the piece was published in the fall of 1966 by the National Academy of Sciences. If you haven't studied it, you should. The general public was insensitive to the trauma disease process. Prevention efforts and research were sparse. Medical training for responders was suboptimal if present at all. Organized rehabilitation didn't exist. Patients with long bone fractures died from an alarmingly high rate of venous thromboembolism, yet it was rarely documented in the medical record as a cause of death.[2] In short, we didn't know what we didn't know.

This visionary paper established standards for educating the lay public and training emergency responders. A foundation for data acquisition and gap analysis occurred at a regional and national level. A mechanism for emergency department and hospital accreditation was established; the precursor for today's American College of Surgeon's Committee on Trauma Verification Review Committee. It established "the system" and multiple works demonstrated improved outcomes.[3] I didn't steer off course unintentionally. Knowing your role in a trauma system becomes vitally important to survival, especially in the rural environment where geography and resource-scarce areas comprise the adversary of optimal care. Especially in a place like Missouri.

Initial Evaluation

Let's get down to the business at hand. Conjure up a typical scenario presenting at your institution where you are the only provider in a rural emergency department (ED). You have two nurses, a clerk, and a radiology/lab technician. There is no surgical capability in-house. The local EMS provider calls in with a young female injured in a car crash: lower extremity fractures, abdominal bruising, and she is "acting like a head injury." A farmer catches his leg in an auger – they've used trauma shears to complete the amputation and he's in shock. Perhaps a young man involved in an assault sustains gunshot wounds to the proximal thigh and left thoraco-

abdomen with significant trouble breathing. You've only dealt with these ten times or less in the previous year… so we need to buckle down and get to work.

First, I cannot say enough about standardization of practice. There is a best-practice model to follow: The Advanced Trauma Life Support Course (ATLS™)[4] is the most well-known and complete reference to a step-wise, safe approach to evaluating the seriously injured. This common approach means no matter who staffs the ED, physicians, nurses, and support personnel know the expectations. They understand the preparation, actions, and correct sequence for successful resuscitation. Standardization minimizes variation among providers and improves quality of care. It also helps develop a level of comfort to a potentially very stressful situation, keeping you in charge of the team and on the right track. For those of you practicing at a critical access facility, the College's Rural Trauma Team Development Course (RTTDC™) is an excellent alternative.

When the patient arrives, listen to your pre-hospital providers. They often provide clues that will direct your search for injury. However, resist the temptation to enter what I call a CSI interrogation of the EMT or paramedic… none of the sensational, often inaccurate details change the next steps; the primary and secondary survey. "Annie, I'm Dr. Coughenour. What happened to you; are you ok?" I say it while I feel for a radial pulse and scan the body for life-threatening bleeding. In less than 10 seconds I've assessed the patency of the airway, adequacy of breathing and ventilation, circulatory status and presence (or absence) of life-threatening hemorrhage and evaluated the patient's neurologic capability. A few additional details and we've completed the primary survey. Any immediate threats to life should be treated without delay. If there are none, proceed with adjuncts to the primary survey such as application of monitors, obtaining a manual blood pressure reading, and plain radiographs of the chest and pelvis. If ultrasound is available to you, focused assessment with sonography for trauma (FAST) assists in identification of cavitary hemorrhage, pericardial tamponade or pneumothorax. If there are still no injuries that require immediate attention, focus on a head-to-toe physical examination known as the secondary survey.

At completion, you now can summarize to the team:

1) what injuries are known or suspected

2) begin to develop a plan of care, and most importantly

3) can we take care of this patient or do we need to begin the transfer process? All less than 15 minutes from patient arrival! You're doing great, stay calm, and keep moving forward.

Allow me to address two misconceptions concerning the initial evaluation: lab tests and CT imaging. First, you don't need every lab test available. In fact, you only need three. First, arterial blood gas analysis signals the degree of cellular dysfunction and anaerobic metabolism; a venous sample is adequate and many ABG analyses can include a lactate, basic electrolytes, and a hemoglobin (if you just can't resist). Second, coagulation parameters evaluate for early post-traumatic coagulopathy, a very worrisome and often deadly finding. Third, if you have blood products available, a type and crossmatch will enable the patient to receive type-specific product as soon as possible. Everything else is of questionable benefit. The severely injured human hasn't had time to equilibrate to significant blood loss so a CBC will be deceiving. Electrolytes and renal function are not helpful. Liver function tests might add to the complexity of the billing, but they contribute nothing to saving the patient's life. Focus on guiding your resuscitation decision-making.

Patients demonstrating a clear reason to initiate the transfer process to a higher level of care do not require imaging. In fact, I would recommend against it.[5] Assuming you have begun treatment for injuries identified in your primary and secondary survey but find yourself needing more information to determine proper disposition for the patient, CT imaging can be considered. Radiation exposure, incidental findings, and appropriate study selection can make this a complicated decision. Let's focus on the major issue at hand; if you're going to scan the patient, get the appropriate information necessary for subsequent decision-making. If you aren't sure what to scan or how to do it, engage your regional trauma center. They will likely share imaging protocols so you can standardize the process. Omitting intravenous contrast and failing to scan certain areas (CT angiogram of the neck for instance) are the most common reasons we have to repeat studies at the trauma center. Interestingly, a recent study from Iowa noted no improvement in time from arrival at the trauma center to operative management for brain injuries when a CT was performed at the referring center.[6] Assure YOU need the test. Do not assume it is a requirement of the trauma center.



Figure 1. Trauma resuscitation.

Initial Management

Now that we've covered the principles that will allow for a rapid but accurate patient assessment, let's discuss what you might have to do. In reality, there are only a few procedures that will handle the majority of cases, but they can be anxiety-provoking and chaotic if you aren't prepared. Remember that earlier bit about standardization? As I said, when you find a problem during completion of the primary survey, act immediately. Airway management may consist of nasal or oral airway placement with bag-mask ventilation while equipment is prepared, followed by endotracheal intubation. A variety of rescue devices are available for the difficult airway – decide which ones your institution or group agrees to use and train often. Patients can sustain for quite a while in shock, but they'll only tolerate a few minutes of significant hypoxemia. Write out your approach for drug-assisted intubation and hang it on the wall. Avoid hypotension by volume resuscitating critically ill patients prior to airway intervention.

Quite possibly the most important initial management maneuver, and the most frightening, is the surgical airway. When a cuffed tube cannot be placed in the trachea, and rescue devices are ineffective, proceed immediately to cricothyroidotomy. I strongly advise the Three-Step Method, supported by literature for its economy of motion and success.[7] In cases where the anatomy cannot be discerned, make a vertical incision and divide the subcutaneous tissue with your finger, feeling for the anterior wall of the trachea. The anatomy should become apparent, and landmarks will guide you. Pass a bougie through the incised cricothyroid membrane and advance an endotracheal tube until the balloon disappears. Remove the bougie, inflate the cuff and begin ventilation. Most anatomy will accommodate tubes from 5.5mm (smallest that will still slide over a traditional adult bougie) to 7.0mm. Use caution as anxiety will promote mainstem intubation. Lastly, the small anterior jugular veins can bleed and will create quite a spectacle. Plan on doing the procedure by feel not by sight.

Once the airway is secure, breathing is next on our priority list. Needle decompression and tube thoracostomy are used to decompress pneumothoraces and hemothoraces following injury. While conventional teaching places a long, large-bore needle in the 2nd interspace along the mid-clavicular line, newer cadaveric studies promote a 5th interspace approach along the anterior axillary line.[8] Either is acceptable, but assure you've entered the pleural space to correct the problem. Because the catheter is prone to malposition following withdrawal of the needle, I advocate for a rapidly placed chest tube. Unfortunately, this may be a lost art in many emergency departments. That's right… I said it. Many physicians staffing EDs in our state can't place a chest tube. I've seen the attempts and I've listened to nurses who tearfully describe the weak effort put forth by physicians they work with. Be proactive and refresh your skills. Or take yourself off the ED schedule.

Vascular access is usually straight forward. Peripheral intravenous access with a 14 to 18 gauge catheter is still preferred. Using an ultrasound probe for the difficult stick or moving straight to an intraosseous device for patients in life-threatening shock is best. If you are comfortable with central venous access the subclavian position works well but carries a risk of inadvertent arterial puncture and pneumothorax. If you select central access, utilize an appropriate line – temporary dialysis catheters or pulmonary artery catheter introducers are short and have a large lumen, thus they can instill a large volume of fluid in a hurry. The traditional "triple-lumen" catheter has no place in the initial resuscitation following trauma.

I feel obligated to briefly discuss resuscitation. The literature has been clear since 1994 as the beginning of the movement away from crystalloid infusion towards earlier blood product transfusion.[9] Patients bleed whole blood. Packed cells are helpful, but the plasma component is equally vital. Have a system to mobilize what you have in a timely manner. If you don't have access to blood components, use crystalloid to maintain a radial pulse and mentation. Avoid the temptation to 'normalize' vital signs… and move the patient rapidly to a place capable of stopping the bleeding. Albumin and other colloids aren't worth the increased cost to stock, so we avoid them entirely. Since uncontrolled hemorrhage is implicated in as many as 20% of preventable deaths following trauma, we should discuss bleeding. Direct pressure, compression dressings with hemostatic gauze, and tourniquet application may be necessary. Reduce and stabilize open long-bone fractures. Yes, reduce them all! Returning the compartment to its normal anatomic alignment slows bleeding. "Splinting in position found" has a place in the medical archives, not present-day trauma care (joint dislocations being the one notable exception). Don't forget often overlooked sources of hemorrhage such as the scalp, especially in the anticoagulated medically-frail elderly. I like to say I've never seen a death related to hemorrhage shock from a scalp laceration…but I can't.

What about surgical capability? General or subspecialty surgeons should be willing to help plan your standardized approach to trauma. Use them as a resource. If you are a surgeon, please support your emergency care colleagues in their efforts to better prepare the hospital's response to major injury. Most importantly, discuss mobilization of the operating room and the necessary components to operate on a critically ill patient. Is it something the institution is willing and able to do? A hemorrhage control operation prior to transfer can be life-saving, demonstrating that complex surgical problems often demand simple surgical solutions. A gunshot wound to the trunk may require suture ligation of a single bleeding vessel. Packing and a temporary closure can then be followed by transfer to the trauma center for a second-look surgery and definitive closure. Splenectomy and surgical control of extremity hemorrhage are other examples of straight-forward operations that can have significant positive impact. Surgery at a non-designated hospital or lower-level trauma center (III or IV) is a vital component of a larger trauma system, and sadly it hardly ever occurs (Figure 1).

Decision to Transfer

Military trauma care has evolved around the concept of echelons of care, where far-forward surgical teams provide immediate care with limited resources. Patients are then moved to higher levels of care for definitive treatment and rehabilitation. A mature civilian trauma system should mirror this concept, where patients that need immediate intervention are taken to the local ED with subsequent transfer to a regional level 1 trauma center. The idea, coined 'minimally acceptable care', was described in a 2002 edition of *Missouri Medicine*

by one of my mentors, Thomas Helling.[10] A word of caution; moving patients through the "echelons" of care takes time. I rarely see a patient stop at the local ED and depart for the trauma center in under 90 minutes. Evaluate your local hospital and EMS resources and strive for an initial ED stay of less than 60 minutes. Plan which patients may be best served bypassing the nearest hospital to more rapidly arrive at a center capable of operative hemorrhage control. Always keep quality care in mind; rapid transfer of an untreated pneumothorax – still bad.

I visualize these patient transfer decisions in three basic categories. First, pre-hospital providers can provide enough information for the most severely injured to move to a higher level of care; you have no surgical or critical care capability and the patient has a GCS of 4, transfer without a CT scan. Second, some patients with minor injuries can and should be managed locally. Rib fractures requiring 24 hours of pain management or a ground-level fall that requires a medical evaluation are good examples. These patients will be happy to receive quality care close to home. Third, and often most difficult, are the patients that appear stable until they're not. Unrecognized bleeding or significant solid organ injuries may take time to identify. Follow the mantra of RTTDC™, and work to complete the primary and secondary survey and make a transfer decision within 15 minutes of patient arrival[11], understanding some patients may require additional diagnostics before demonstrating a need for transfer.

Allow me to make some statements on a few odds and ends. Consider what the EMTALA statutes say, but most importantly what they don't say. You are required to treat a patient based on your facility's available resources. It is perfectly acceptable to transfer a hypotensive patient with on-going bleeding if you have no surgeon. Be willing to have difficult discussions with families regarding end of life care. When a 93-year-old patient falls and suffers massive, non-survivable intracranial hemorrhage, a neurosurgeon doesn't necessarily need to be the one to relay that news. Especially when the family would decline surgical intervention if offered. In some cases, telephone or telehealth consultation may suffice. Lastly, demand quality from the providers moving your patients. Just as all hospitals are not created equal, all ambulances and helicopters aren't either. Work closely with your EMS folks to establish expectations and participate in their on-going education.

Summary

The patient with serious injury is a high-acuity, low-occurrence event. Material and human resources may be limited. Important adjuncts to optimal care such as experience, education, blood components, or surgical expertise are often unavailable. Standardize your institution's approach and train often. Perform a rapid primary and secondary survey, treating life-threatening injuries as they are identified. Airway management, tube thoracostomy, and various maneuvers to control hemorrhage may be necessary. Practice the concept of 'minimally acceptable care;' treating the patient within the hospital's capability and promptly transferring the more severely injured to a higher level of care. Engage your regional trauma centers and use them as a resource.

References

1. Accidental Death and Disability: The Neglected Disease of Modern Society. National Academy of Sciences and National Research Council Committee on Trauma, National Research Council Committee on Shock. Washington, DC. National Academies Press; 1966.
2 An analysis of 950 fatal injuries. Fitts WT, et al. Surgery 56:663-668; 1964.
3. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. Celso B, Tepas J, Langland-Orban B, Pracht E, Papa L, Lottenberg L, Flint L. J Trauma. 2006 Feb;60(2):371-8; discussion 378.
4. American College of Surgeons, Advanced Trauma Life Support. https://www.facs.org/quality-programs/trauma/atls
5. Imaging may delay transfer of rural trauma victims: a survey of referring physicians. Lee CY, Bernard AC, Fryman L, Coughenour J, Costich J, Boulanger B, Chang P, Kearney PA. J Trauma. 2008 Dec;65(6):1359-63.
6. Head CT before transfer does not decrease time to craniotomy for TBI patients. Sidwell RA, et al. Am Surg 2018 Feb 1;84(2):201-207.
7. Emergent surgical airway: comparison of the three-step method and conventional crico-thyroidotomy utilizing high-fidelity simulation. Quick JA, MacIntyre AD, Barnes SL. J Emerg Med. 2014 Feb;46(2):304-7.
8. Cadaveric comparison of the optimal site for needle decompression of tension pneumo-thorax by prehospital care providers. Inaba K, Karamanos E, Skiada D, Grabo D, Ham-mer P, Martin M, Sullivan M, Eckstein M, Demetriades D. J Trauma Acute Care Surg. 2015 Dec;79(6):1044-8.
9. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. Bickell WH, Wall MJ Jr, Pepe PE, Martin RR, Ginger VF, Allen MK, Mat-tox KL. N Engl J Med. 1994 Oct 27;331(17):1105-9.
10. Minimal acceptable care as a vital component to Missouri's trauma system. Helling, TS. Mo Med 2002 Jul;99(7):275-8.
11. American College of Surgeons, Rural Trauma Team Development Course, 4th Edition. https://www.facs.org/quality-programs/trauma/education/rttdc. Accessed 6 April 2018.

Disclosure

None reported. **MM**

New Advances in the Care of the Hemorrhaging Patient

by Tessa N. Woods, DO, Keela R. Scott, MS3 & Jacob A. Quick, MD

School of Medicine

Developing technological and pharmacological therapies present opportunities to improve care for patients, including at rural critical access hospitals.







Tessa N. Woods, DO, (top), PGY-6 Surgical Critical Care Fellow, Keela R. Scott, MS3, (bottom left), and Jacob A. Quick, MD, FACS, (bottom right), are in the Division of Acute Care Surgery, Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri.
Contact: woodstn@health.missouri.edu

Abstract

Thirty-three percent of early traumatic deaths are secondary to hemorrhage. In addition to timing to source control, the literature has seen a surge of research on adjuncts in hemorrhage control. This review focuses on three of the latest interventions in the management of the bleeding patient; an endovascular aortic occlusive balloon, tranexamic acid (TXA), and updates to the massive transfusion protocol.

Introduction

Timely hemorrhage control is the *sine qua non* of a successful traumatic resuscitation. Traditional methods of hemorrhage control remain a mainstay of treatment, however several advances have been made in recent years allowing for immediate cessation of hemorrhage via less invasive means. One of these methods, an aortic balloon catheter first used in the 1950s, has made a resurgence in the last few years as a temporizing adjunct to initial resuscitation in the emergency department. Recent research in acute trauma-induced coagulopathy has revealed multiple therapeutic targets within the complexities of coagulation cascade, opening the door to novel pharmacologic agents to restore homeostasis. In practice for over a decade, the balanced resuscitation massive transfusion protocol is also evolving with civilian research into the proper ratios of component therapy and consideration of whole blood transfusion. This review article will briefly summarize recent developments in these areas of resuscitation.

Resuscitative Endovascular Balloon Occlusion of the Aorta

Occlusion of the aorta to facilitate improved cardiac and cerebral perfusion in the setting of severe hemorrhagic shock has been utilized for many decades. Traditionally, this has been performed through a thoracotomy, often performed in the emergency department, to gain proximal control of the aorta. Resuscitative thoracotomy is associated with overall poor outcomes, with the highest mortality rates seen in blunt traumatic arrests. The dismal prognosis of patients requiring and undergoing resuscitative thoracotomy has remained static despite advances in resuscitation and surgical technique.[1] Efforts to decrease time and morbidity associated with thoracic aortic control, along with improvements in endovascular technology has resulted in rekindled interest in balloon aortic occlusion for immediate hemorrhage control. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) was originally described in 1954, in which aortic balloon occlusion was utilized in three soldiers with intra-

abdominal hemorrhage during the Korean War.[2] However, commercially available kits have not been available until recently, and as a result multiple studies have shown benefits to its use. The main advantage of balloon aortic occlusion, compared with resuscitative thoracotomy, is rapid deployment without the need for a large incision, via a familiar percutaneous Seldinger technique. Additional benefits include decreased morbidity and infectious complications.[3] Of course, potential complications of this new modality include arterial access complications, balloon positioning issues, complications from balloon inflation, and sheath complications.[4] Patient selection is a key component of success, with patients presenting with intraabdominal or pelvic hemorrhage showing the greatest benefit. Penetrating thoracic trauma is a clear contraindication as balloon occlusion may exacerbate blood loss and delay source control.[5]

Evolution in technique has been well-described and continues to be validated.[6-9] The latest iteration of the catheter uses a 7Fr sheath placed percutaneously into the femoral artery via a Seldinger technique. It is designed for deployment into two of three aortic zones; Zones 1 and 3. Zone 1 extends from the takeoff of the left subclavian artery to the celiac artery, allowing for proximal thoracic aortic control, similar to clamping through a thoracotomy incision. Zone 2 extends from the celiac artery to the lowest renal artery and is traditionally not utilized. Zone 3 extends from the lowest renal artery to the aortic bifurcation, providing control of pelvic hemorrhage, with sparing of renal vasculature. Prior to placement and deployment, the catheter is connected to an arterial waveform transducer which lies at the tip. Proper balloon positioning is suggested by a rapid spike in the systolic blood pressure read by the arterial transducer after the balloon is gently inflated. Thereafter, rapid transport to the operating or endovascular suite is necessary to gain definitive hemorrhage control and to address intraabdominal and pelvic injuries. The catheter should be removed in the operating room once surgical hemorrhage has been addressed.

The less invasive, rapid nature of the REBOA catheter has led to multiple studies showing its benefit in non-compressible truncal hemorrhage. [3,9,10] Improved survival rates of up to 30% have been shown in patients in extremis upon arrival. This represents a marked improvement from resuscitative thoracotomy, which at best has a less than 10 percent survival in penetrating trauma, and less than 1 percent survival in blunt trauma. Questions arise however, regarding the role of selection bias in many of these studies. The REBOA catheter is less-invasive, and relatively easy to deploy, leading to earlier use in the resuscitation bay. Contrasted with thoracotomy, which many physicians are reluctant to employ prior to full cardiovascular arrest. Ongoing studies aim to directly, and prospectively compare the outcomes of REBOA and resuscitative thoractomy.[3]

There remain questions regarding use of the catheter, including placement in the emergency department versus the operating room, open versus percutaneous approach, and physician specialty required for placement – emergency medicine versus surgeon. In the future, we may expect to see more data emerge regarding catheter use not only in arterial hemorrhage, but also in the setting of venous injury.[11,12] Despite these questions, it appears endovascular balloon occlusion is a viable alternative to resuscitative thoracotomy, though exactly how, when and where to use the catheter will continue to be defined with emerging studies.

Tranexamic Acid

Since its discovery in 1962, tranexamic acid (TXA) has been widely recognized for its use as an antifibrinolytic.[13] TXA is a synthetic lysine analog, most commonly intravenously administered, that acts to prevent plasmin degradation of fibrin, thereby preserving the fibrin clot matrix. Its antifibrinolytic action is currently approved for treatment in hemophilia but has seen widespread use as an adjunct to trauma resuscitation.

Prior to the CRASH-2 study in 2010, the use of TXA in bleeding trauma patients was relatively unexplored. The CRASH-2 trial was the first of its kind to assess the prehospital use of TXA in civilian trauma patients with significant hemorrhage. Findings from the trial, including over 20,000 patients, indicated a 1.5% decrease in all-cause mortality as well as a 0.8% decrease in mortality risk due to hemorrhage in patients given TXA. These findings were noted in the setting of no significant differences in quality/quantity of blood products used or number of thromboembolic

complications.[14] Several years later, the MATTERs study was undertaken as the first military examination of TXA. This retrospective study included severely injured combat patients requiring at least 1 unit of blood transfusion.[15] Outcomes of the study showed an increased survival benefit in the TXA group, despite the fact that these patients had higher Injury Severity Scores and greater incidence of hypotension. Multiple other studies have shown survival benefit to TXA use in trauma.[16-18]

The timing of administration and identification of appropriate patient subtypes are important factors to consider when deciding whom is appropriate for TXA administration. Data suggests a significant decrease in mortality due to bleeding when TXA is administered within 3 hours of injury, and an increase in mortality beyond that 3-hour mark.[19] Further, there appears to be a subset of patients with fibrinolytic shutdown, that are predisposed to increased mortality risk with empiric TXA administration. This has led to more in-depth physiologic studies to determine markers for patients who may benefit from TXA, and those who should not receive it.[20,21] Prehospital TXA administration is currently being studied, and at present there is insufficient evidence to support or refute prehospital TXA use.[22]

Massive Transfusion Protocols

Volume resuscitation continues to be a point of study in trauma research. Crystalloid resuscitation modalities have largely fallen out of favor, as multiple studies show increased mortality with crystalloid-based strategies. Whole blood resuscitation, as done more frequently in the military setting, has shown improvements in physiologic parameters and survival. However, it is impractical in the civilian setting governed by cost, storage, and logistical issues. Fixed-ratio blood component therapy has thus emerged as the mainstay of volume resuscitation in trauma.

Nomenclature has moved from "massive transfusion protocol" to "goal directed resuscitation" to "damage control resuscitation." Traditionally, massive transfusion protocols (MTP) have been utilized for patients in hemorrhagic shock. Massive transfusion has most commonly been defined as the use of 10 units of blood products given within 24 hours. Goal directed resuscitation, in comparison, is driven by tailoring blood products to physiologic deficits. The newer term of "damage control resuscitation" originated in the U.S. military and was applied to resuscitation in patients suffering from hemorrhagic shock in Iraq and Afghanistan. This manner of resuscitation typically follows a fixed transfusion pattern of packed red blood cells, fresh frozen plasma and platelets, with minimization of crystalloid and permissive hypotension.[23,24]

The PROMMT study, published in 2013, sought to better validate this new manner of resuscitation in the civilian setting, noting improved outcomes when the ratio to blood and platelets neared 1:1.[24] Expanding on these results, the PROPPR trial noted earlier hemostasis, fewer complications and lower mortality in patients receiving a 1:1:1 ratio of blood, plasma and platelets.[25] Success of these studies was believed to be, in-part, to earlier initiation of fixed ratio protocols, with an emphasis on early platelet transfusion. Early activation of fixed ratio transfusion modalities has spawned concern over appropriate usage of the limited supply of blood products, although these concerns have yet to be proven in the literature.

Rapid scoring systems based upon physical parameters present on admission have emerged to aid in the decision to initiate massive transfusion protocols. The Assessment of Blood Consumption score utilizes four easily attainable parameters and has demonstrated the ability to correctly identify patients in need for massive transfusion approximately 85% of the time.

As we move toward more targeted blood component resuscitation, it appears that early administration of platelets and plasma portend survival benefit in severely-injured trauma patients. Accurate and timely assessment for the need of massive transfusion is paramount, and institutions are urged to develop evidence-based protocols to drive its use.

Conclusion

While limitations exist for smaller health care institutions in caring for severely-injured trauma patients, developing technological and pharmacological therapies present opportunities to improve care for patients, including at rural critical access hospitals. The REBOA catheter, with proper training and understanding may allow for early, temporary hemorrhage control prior

to definitive hemorrhage control. Early administration of TXA has the ability to stop hyperfibrinolysis and result in decreased hemorrhage related to trauma-induced coagulopathy. Development of massive transfusion protocols that include the early administration of plasma and platelets may lead to less physiologic derangement with improved mortality.

References

1. DuBose J, Fabian T, Bee T, et al. Contemporary utilization of resuscitative thoracotomy: Results from the AAST Aortic Occlusion for Resuscitation in trauma and Acute Care Surgery (AORTA) Multicenter Registry. Shock 2017 Dec 26. Epub ahead of print.
2. Hughes CW. Use of an intra-aortic balloon catheter tamponade for controlling intra-abdominal hemorrhage in man. Surgery. 1954;36(1):65-68.
3. Dubose JJ, Scalea TM, Brenner M, et al. The AAST prospective Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) registry: Data on contemporary utilization and outcomes of aortic occlusion and resuscitative balloon occlusion of the aorta (REBOA). J Trauma Acute Care Surg. 2016;81(3):409-419.
4. Davidson JD, Russo RM, Reva VA. The pitfalls of resuscitative endovascular balloon occlusion of the aorta: Risk factors and mitigation strategies. J Trauma Acute Care Surg. 2018;84(1):192-202.
5. Joseph B, Ibraheem K, Haider AA, et al. Identifying potential utility of resuscitative endovascular balloon occlusion of the aorta: An autopsy study. J Trauma Acute Care Surg. 2016;81(5):S128-S132.
6. Stannard A, Eliason JL, Rasmussen TE. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) as an Adjunct for Hemorrhagic Shock. 2011;71(6):1869-1872.
7. Brenner M, Hoehn M, Pasley J, Dubose J, Stein D, Scalea T. Basic endovascular skills for trauma course: Bridging the gap between endovascular techniques and the acute care surgeon. J Trauma Acute Care Surg. 2014;77(2):286-291.
8. Villamaria CY, Eliason JL, Napolitano LM, Stansfield BR, Spencer JR, Rasmussen TE. Endovascular Skills for Trauma and Resuscitative Surgery (ESTARS) course: curriculum development, content validation, and program assessment. J Trauma Acute Care Surg. 2014;76(4):929-936.
9. Gamberini E, Coccolini F, Tamagnini B, et al. Resuscitative endovascular balloon occlusion of the aorta in trauma: a systematic review of the literature. World J Emerg Surg 2017;12:42.
10. Moore LR, Martin CD, Harvin JA, Wade CE, Holcomb JB. Resuscitative endovascular balloon occlusion of the aorta for control of noncompressible truncal hemorrhage in the abdomen and pelvis. Am J Surg. 2016;212(6):1222-1230.
11. Bisulli M, Gamberini E, Coccolin F, Scognamiglio G, Agnoletti V. Resuscitative endovascular balloon occlusion of vena cava: An option in managing traumatic vena cava injuries. 2017;84(1):211-213.
12. Reynolds CL, Celio AC, Bridges LC, Mosquera C, et al. REBOA for the IVC? Resuscitative balloon occlusion of the inferior vena cava (REBOVC) to abate massive hemorrhage in retrohepatic vena cava injuries. 2017;83(6):1041-1046.
13. Watts G. Utako Okamoto. Lancet. 2016;387(10035):2286.
14. Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): a randomized, placebo-controlled trial. Lancet. 2010;376(9734):23–32.
15. Morrison JJ, Dubose JJ, Rasmussen TE, Midwinter MJ. Military application of tranexamic acid in trauma emergency resuscitation (MATTERs) study. Arch Surg-chicago. 2012;147(2):113–119.
16. Neeki MM, Dong F, Toy J, et al. Efficacy and safety of tranexamic acid in prehospital traumatic hemorrhagic shock: outcomes of the Cal-PAT study. West J Emerg Med. 2017;18(4):673–683.
17. Dewan Y, Komolafe EO, Mejía-Mantilla JH, Perel P, Roberts I, Shakur H, et al. CRASH-3 - tranexamic acid for the treatment of significant traumatic brain injury: study protocol for an international randomized, double-blind, placebo-controlled trial. Trials. 2012;13(1):1–14.
18. Harvin JA, Peirce CA, Mims MM, et al. The impact of tranexamic acid on mortality in injured patients with hyperfibrinolysis. J Trauma Acute Care Surg. 2015;78(5):905-911.
19. Wafaisade A, Lefering R, Bouillon B, Böhmer AB, et al. Prehospital administration of tranexamic acid in trauma patients. Crit Care. 2016; 20:143.
20. Moore HB, Moore EE, Liras IN, et al. Acute fibrinolysis shutdown after injury occurs frequently and increases mortality: a multicenter evaluation of 2,540 severely injured patients. J Am Coll Surg. 2016;222(4):347-355.
21. Roberts I. Fibrinolytic shutdown: fascinating theory but randomized controlled trial data are needed. Transfusion. 2016;56(Suppl 2): S109-S114.
22. Fischer PE, Bulger EM, Perina DG, et al. Guidance document for the prehospital use of tranexamic acid in injured patients. Preh Emer Care. 2016;20(5):557-559.
23. Johansson PI, Sorenson AM, Larsen CF. Low hemorrhage-related mortality in trauma patients in a Level 1 trauma center employing transfusion packages and early thromboelastography-directed hemostatic resuscitation with plasma and platelets. Transfusion. 2013; 53:3088-3099.
24. Del Junco DJ, Holcomb JB, Fox EE: PROMMTT Study Group. Resuscitate early with plasma and platelets or balance blood products gradually: findings from the PROMMTT study. J Trauma Acute Care Surg. 2013;75(1) (suppl. 1): S24-S30.
25. Holcomb JB, Tilley BC, Baraniuk S. Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients with Severe Trauma - The PROPPR Randomized Clinical Trial. JAMA. 2015;313(5):471-482.

Disclosure

None reported.

MM

Pediatric Trauma Update

by Dane C. Paneitz, MS3 & Salman Ahmad, MD

School of Medicine

This article reviews the evaluation and management of the pediatric trauma patient while focusing on recent updates.





Dane C. Paneitz, MS3, and Salman Ahmad, MD, FACS, Assistant Professor of Surgery, are in the Division of Acute Care Surgery, Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri.
Contact: ahmadsa@health.missouri.edu

Abstract

Trauma is the leading cause of mortality in children, accounting for over 11,000 deaths and more than 8 million nonfatal injuries in 2015 for ages 1-19 years.[1] Current issues garnering particular attention and research efforts include traumatic brain injury (TBI), blunt solid organ injuries, imaging guidelines and trauma-induced coagulopathy. This article reviews the evaluation and management of the pediatric trauma patient while focusing on recent updates.

Traumatic Brain Injury

Head injuries are the most common fatal injury in children and account for approximately 435,000 emergency department visits each year.[2] Compared with adults, children have a number of anatomical differences that may predispose them to injury including thinner cranial bones, a larger head-to-torso ratio, an immature immune system and differences in thermoregulation.[3] After evaluating the airway, breathing, circulation and disability of the injured child, evaluation for TBI should include a complete neurologic exam including a Glasgow Coma Score (GCS), pupil size, inspection of the head and spine, including the anterior fontanel, for gross deformity along with funduscopic and otoscopic evaluation. The pediatric GCS is modified for age-appropriate verbal development and should be used for children under two years of age. Children over two years should be evaluated with the standard GCS measurement.[4] (Table 1.)

Neuroimaging

Imaging of head injuries is an important focus of research as we are learning more about the effects of radiation exposure in children. A study by Rice et al. reported one lethal case of cancer for every 1,000 computed tomography (CT) scans of a child.[5] The CT scan is the preferred imaging modality for moderate to severe head injuries as it quickly provides detailed images that can guide management. However, for minor head trauma, fewer than 10% of children sustain a TBI. This has led to the creation of several clinical decision tools for neuroimaging, including CATCH, PECARN and CHALICE, to reduce unnecessary radiation exposure.[3] The CATCH study identified high-risk individuals who require CT scan as those who fail to reach GCS of 15 within two hours of injury, suspicion of open skull fracture, worsening headache and irritability, while moderate-risk individuals had a large scalp hematoma, signs of basilar skull fracture or a dangerous mechanism of injury. MRI and transcranial Doppler (TCD) are two other valuable modalities that are frequently used. TCD was shown to have high sensitivity for detecting intracranial hemorrhage (ICH) and abnormal cerebral perfusion pressure (CPP) after severe TBI in children.[6]

Table 1. Glasgow Coma Score

Pediatric GCS[4]	
Eye Opening	
Spontaneous	4
Speech	3
Pain	2
None	1
Verbal Response	
Coos, Babbles	5
Irritable cries	4
Cries to pain	3
Moans to pain	2
None	1
Motor Response	
Normal spontaneous movement	6
Withdraws to touch	5
Withdraws to pain	4
Abnormal flexion	3
Abnormal extension	2
None	1

Interventions

Walker and colleagues published an excellent update on the management of pediatric TBI in 2017 that highlighted a few modern interventions including controlled hypothermia and hypertonic saline (HTS) infusion. Controlled hypothermia has been shown to decrease mortality and improve neuronal function, presumably by decreasing neuronal metabolism. Current literature supports initiation within 24 hours of trauma and lasting up to 48 hours. HTS has been shown to decrease intracranial pressure (ICP) thereby increasing cerebral blood flow and providing neuroprotection. This mechanism is similar to that of mannitol; however, in a rat study, HTS was better at decreasing ICP and neurotoxicity than mannitol. A dosing range of 3 to 5 mL/kg is commonly used, but future randomized prospective trials with mannitol are needed before it is accepted as standard of care.[7]

Blunt Solid Organ Injury

Intraabdominal injury (IAI) is the third leading cause of pediatric trauma mortality with the majority of injuries sustained by a blunt mechanism (85%) versus penetrating (15%).[8] Motor vehicle crashes (MVC) are the major cause of blunt abdominal trauma, and a common physical exam finding that has been associated with IAI is the "seat belt sign" (SBS), which has been defined as an area of ecchymoses, erythema or abrasions sustained as a result of seat belt use. However, Chidester and colleagues did not find SBS to be significantly associated with IAI in a retrospective review of 331 children involved in an MVC. Fifty-four (16%) of the 331 children had SBS, but only 12 (22%) of those children had an IAI identified by CT scan or with an operation. Of the three children who required an operation, two had bowel injuries and one had a negative laparoscopy. They found the SBS to have a sensitivity of 25% and a specificity of 85%, concluding that SBS may not be as predictive of IAI as historically reported in adults.[9]

Notricia and Linnaus published an excellent update on the nonoperative management of blunt solid organ injury (SOI) in pediatric surgery.[10] Solid organ injury includes the spleen, liver and kidneys; is more common than hollow organ injury and is most often treated nonoperatively. In the 1990's, the increasing utilization of the CT scan led to the development of organ injury scales (OIS) by the American Association for the Surgery of Trauma (AAST) as a means to guide SOI management. However, in recent years, studies have found hemodynamic status to be a better guide of management than OIS. For those with hemodynamic instability, attempts should first be made to restore adequate perfusion with isotonic fluid followed by blood products. If unsuccessful, a massive transfusion protocol should be considered along with operative exploration or interventional angiography. The current recommendation for maximum transfusion volume is 40 mL/kg based on a retrospective study of children injured in a combat zone. Children who respond to early resuscitation should be evaluated with CT scan and monitored for further hemodynamic instability. Patients admitted to the ICU may be transferred to a lower level of care after 24 hours with a stable hemoglobin and may be discharged the following day if the child is tolerating oral intake with minimal abdominal pain and stable vital signs. This recommendation replaces the initial guidelines of OIS grade plus one day for the length of hospitalization based on recent data demonstrating very low rebleeding rates in hemodynamically stable patients with a median time to rebleeding of 10 days.[11]

Blunt Liver and Splenic Injury

Nonoperative management (NOM) is the standard for blunt liver and splenic injury with a retrospective study by Holmes and colleagues showing a NOM failure rate of 3% for isolated liver injuries and 4% for isolated spleen injuries. Though rare, it is important to recognize failure of NOM quickly. Identified risk factors for NOM failure

include higher ISS, higher organ injury grade, multiple organ injuries and lower GCS on presentation. In two separate studies, the main cause of failure was hemorrhage. Holmes and colleagues found the median time of failure to be 2 hours with 76% of failures occurring within 12 hours of injury. Children with contrast extravasation from splenic injury are often treated successfully with nonoperative management but may benefit from angioembolization if conservative treatment fails. Angioembolization is rare for liver injury as very few of these injuries demonstrate contrast extravasation.[11]

Blunt Renal Injury

Most blunt renal injuries are successfully managed with conservative treatment, which may include percutaneous drainage, endourologic stenting and angioembolization. However, there is no consensus on the management of high-grade injuries. A systematic review by LeeVan and colleagues reported a success rate of 80% to 100% with nonoperative management for grades IV and V.[12] Therefore, it is recommended for all patients with renal trauma to initially be treated using a conservative protocol, while immediate surgical intervention is reserved for those with hemodynamic instability. LeeVan and colleagues also found minimal evidence to support ICU care for high-grade renal injury patients, urinary catheter placement, prophylactic antibiotics or mandatory bed rest. They recommend using ultrasound for assessment of injury progression as opposed to routine CT imaging. In cases of urinomas, two thirds of these will resolve spontaneously, and intervention should be reserved for large (greater than 4 cm), symptomatic or persisting urinomas.[11] The initial intervention should be ureteral stenting as isolated percutaneous drainage alone has repeatedly failed in several studies. For renal artery pseudoaneurysms and renal hemorrhage, angioembolization has been found to be a great tool in the conservative approach. Finally, discharge can be made on the basis of symptomatic control and stability as opposed to the commonly used criteria of resolution of gross hematuria.[12]

Pancreatic and Duodenal Injuries

Although solid organ injuries rarely necessitate an operation, pancreatic and duodenal injuries are more likely to require operative intervention. In a multicenter retrospective study of 1,823 patients with blunt abdominal trauma, Mattix and colleagues identified 173 (9.5%) patients who sustained pancreatic injury, of which 43 (26%) required operative intervention. The pancreas was cited as the cause of operation in 57.8% of all patients. This study found pancreatic ductal injury, defined as grades III to V, to be a predictor of nonoperative management failure with 23 of the 53 patients sustaining a ductal injury requiring an operation. Importantly, those with ductal injuries who were taken to the OR within 24 hours of injury experienced reduced rates of complications. Consequently, early identification of ductal injury by CT, MRI, or ERCP (endoscopic retrograde pancreatography) is critical. ERCP is an appropriate alternative diagnostic and potentially therapeutic study if CT imaging is equivocal.[13] Blunt duodenal injuries are rare and often occur with other abdominal injuries, most commonly the pancreas.[14] Their management is based on the hemodynamic stability of the patient with options of damage control and delayed repair, drainage or immediate definitive repair. The utility of duodenal diversion has been questioned in several studies and may be useful in a few specific situations. Antegrade and retrograde tube duodenostomies might be beneficial in cases requiring tenuous repair with mild contamination. There is no Level 1 evidence to support the routine use or nonuse of peri-duodenal drains. Moreover, Malholtra et al. do not recommend drains for Grade I or II injuries, rather they place them in the setting of a tenuous repair requiring a protective maneuver like a pyloric exclusion. Although uncommon, duodenal injuries can be a significant source of morbidity leading to fistula formation and obstruction and are often associated with multiple organ injuries which contribute to the overall outcome.[15]

Radiation Exposure and Imaging Guidelines

Imaging studies have an increasingly important role in the evaluation and management of trauma patients. CT scan utilization has increased from 3 million scans per year in the early 1980s to over 60 million in 2006. However, the radiation exposure produced by CT scans is not trivial, especially in the pediatric population. A retrospective review by Brunetti and colleagues calculated the total effective dose of radiation received by 719 injured children who underwent 4,603 radiographic studies (67.3% x-rays, 31.7% CT scans). The mean dose for all children was 12.8 mSv $\pm$ 12.0 mSv. For comparison, the average ionizing radiation exposure a person receives each year from the environment is 3 mSv.[16] While CT scans only accounted for 31.7% of the total radiographic studies, they produced 91% of the total radiation dose. One study found that a total radiation exposure dose of 50 to 60 mGy to the head and bone marrow resulted in a threefold-increased risk for brain tumors and leukemia, respectively.[17] For perspective, two to three head CT scans from a current scanner on

typical settings would provide a dose of 50 to 60 mGy to the brain.[18] Unsurprisingly, guidelines are being developed to limit the unnecessary radiation exposure. The Pediatric Trauma Society supports the Level 2 recommendations by Rozzelle et al. for clearing children of the need for cervical spine imaging. They report cervical spine imaging is not recommended for injured children greater than 3 years of age who are alert, have no neurological deficit, have no midline cervical tenderness, have no painful distracting injury, do not have unexplained hypotension and are not intoxicated. Children under 3 years of age must meet the above criteria as well as a GCS greater than 13 and were not involved in an MVC, fall greater than 10 feet or non-accidental trauma.[19] Children who have experienced trauma and do not meet either set of criteria should have cervical spine radiographs or high resolution CT scan.

Trauma-Induced Coagulopathy

Trauma-induced coagulopathy (TIC) is a complex process resulting from tissue injury and ischemia that is further exacerbated by dilution, acidosis and hypothermia. It is well known that children have different hemostatic systems that mature with age. The majority of trauma patients become hypercoagulable and can benefit from coagulation monitoring devices. In addition to conventional coagulation tests (CCT), coagulation screens including thromboelastography (TEG®) rotational thromboelastometry (RoTEM®) and impedance aggregometry are being implemented in the acute evaluation of the injured child and are necessary to better inform clinicians on TIC. These devices monitor the viscoelastic properties of whole blood and the endothelium along with platelet function testing. TEG® and RoTEM® are able to evaluate all of the stages of clotting.

An important mechanism associated with TIC in children is TBI, which may have a different pathophysiology than TIC of hemorrhage. A study by Vavilala and colleagues reported fibrin degradation product levels over 1000 μg/mL on admission predicted a poor outcome in children less than 16 years with an isolated brain injury and GCS between 7-12.[20] A retrospective 10-year review of 803 children after severe trauma with an INR of 1.2 or greater at presentation was an independent predictor of mortality, especially in those with TBI.

Treatment strategies for TIC

Early identification of coagulopathy with the screens mentioned above facilitate a targeted approach to blood product resuscitation. Christiaans and colleagues published an excellent review on coagulopathy after severe pediatric trauma focusing on novel hemostatic adjuncts.[21] Massive blood transfusion has evolved in recent years to include the early and liberal use of blood products, often with a goal of a 1:1:1 ratio of PRBC to FFP to platelets for severely injured patients. However, massive transfusion occurs less commonly in children than adults in large part due to their greater physiological reserve and tolerance to blood loss. Although a definition for massive transfusion in children is difficult due to varying body volumes by age, gender and weight, a commonly cited definition is 40ml/kg. Interestingly, in a single center study of 55 children by Chidester and colleagues, mortality was not significantly different between children who received massive transfusion protocol and children who were given blood at the physician's discretion.[22] Randomized prospective trials are needed to better evaluate the role of massive transfusion, optimal blood product ratios and blood component therapies in pediatric trauma patients.[21]

FFP (Fresh Frozen Plasma) is the most common blood component used to treat coagulopathy, but it is associated with several risks including transfusion-related acute lung injury (TRALI), transfusion associated circulatory overload (TACO) and adverse immunological reactions. It is recommended that FFP be used only in cases of active bleeding and not for abnormal coagulation screens alone. A retrospective study of patients receiving FFP alone and patients receiving coagulation factor concentrates without FFP showed the patients receiving FFP alone had an increased frequency of multi-organ failure.[21]

Recombinant Factor VIIa (rFVIIa) has gained support for off-label use in pediatric trauma patients in addition to its use in patients with hemophilia and acquired inhibitors. In one case series of 135 pediatric patients who received rFVIIa for off-label use, there was a decrease in the 24-hour median transfusion volume after receiving rFVIIa, and the mortality rate was significantly lower in surgical/trauma patients (16%) versus medical patients (58%). Dosing for rFVIIa has been extrapolated from adult literature and the pediatric hemophiliac population with bolus doses ranging from 40-100 μg/kg in the non-hemophiliac population and repeat dosing intervals reported from two to six hours. An analysis of the Western Trauma Association web-based registry suggests that rFVIIa may be most beneficial when given early in the setting of hemorrhage as acidosis (pH $<$ 7.2), thrombocytopenia (platelets $<$100,000) and hypotension (systolic $\leq$ 90) were indicators of poor response to rFVIIa.[21]

Prothrombin complex concentrate (PCC) is another blood product garnering attention for treatment of TIC, although very few studies exist for the pediatric trauma population as it was developed for treatment of hemophilia B and consequently also known as factor IX complex. PCC contains 25-30 times the concentration of clotting factors as FFP and can be a three or four factor concentrate. Three factor PCC contains factors II, IX and X while four factor PCC also includes factor VII. PCC has Level 2C evidence for its use in patients with massive bleeding who also receive FFP. Several guidelines and recommendations provide a recommended dosing range of 20-50 units/kg with a risk of thromboembolism at doses greater than 50 units/kg.

Tranexamic acid (TXA) acts to prevent the breakdown of a fibrin clot by competitively inhibiting tissue plasminogen activator (tPA), which converts plasminogen to plasmin. Plasmin then degrades fibrin, which is responsible for the clot stability. TXA has been well studied in the adult population and even the non-traumatic pediatric population.[23] The Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage (CRASH-2) study demonstrated a significant decrease in mortality from bleeding when TXA was given early after trauma. Beno and colleagues feel that TXA should be considered for adolescent trauma patients with the same indications and dosing regimen as adults.[23] They also suggest younger children with hemodynamic instability and ongoing risk of hemorrhage may also benefit from TXA with recognition that evidence in this population is lacking. Dosing recommendations for children over 12 years of age is the same as the adult protocol which is a 1-gram loading dose over 10 minutes within 3 hours of injury followed by a 1-gram infusion over 8 hours. For children 12 years and younger, the dosing recommendation is a loading dose of 15 mg/kg (max 1g) over 10 minutes followed by 2 mg/kg/h for at least 8 hours or until bleeding stops.[23]

Conclusion

While many lessons learned from the management of adult trauma patients can be applied in the pediatric population, due diligence must be practiced in the areas of TBI, blunt solid organ injury, radiographic imaging and traumatic coagulopathy in the context of age-specific research that is briefly summarized here. Randomized prospective trials are needed to better evaluate current methods of treatment and produce pediatric-specific guidelines.

References

1. Fatal Injury Data | WISQARS | Injury Center | CDC. https://www.cdc.gov/injury/wisqars/fatal.html. Accessed January 30, 2018.
2. Walker PA, Harting MT, Baumgartner JE, Fletcher S, Strobel N, Cox CS. Modern Approaches to Pediatric Brain Injury Therapy. doi:10.1097/TA.0b013e3181ad323a
3. Alexiou G a, Sfakianos G, Prodromou N. Pediatric head trauma. J emergencies, trauma Shock. 2011;4(3):403-408. doi:10.4103/0974-2700.83872
4. Badjatia N, Carney N, Crocco TJ, et al. Guidelines for prehospital management of traumatic brain injury 2nd edition. Prehosp Emerg Care. 2008;12 Suppl 1:S1-S52. doi:10.1080/10903120701732052
5. Rice HE, Frush DP, Farmer D, Waldhausen JH. Review of radiation risks from computed tomography: essentials for the pediatric surgeon. J Pediatr Surg. 2007;42(4):603-607. doi:10.1016/j.jpedsurg.2006.12.009
6. Amyot F, Arciniegas DB, Brazaitis MP, et al. A Review of the Effectiveness of Neuroimaging Modalities for the Detection of Traumatic Brain Injury. J Neurotrauma. 2015. doi:10.1089/neu.2013.3306
7. Brenkert T, Estrada C, McMorrow S, Abramo T. Intravenous Hypertonic Saline Use in the Pediatric Emergency Department. Pediatr Emerg Care. 2013;29(1):71-73. doi:10.1097/PEC.0b013e31827b54c3
8. Drexel S, Azarow K, Jafri MA. Abdominal Trauma Evaluation for the Pediatric Surgeon. Surg Clin North Am. 2017;97(1):59-74. doi:10.1016/j.suc.2016.08.004
9. Chidester S, Rana A, Lowell W, Hayes J, Groner J. Is the "seat belt sign" associated with serious abdominal injuries in pediatric trauma? J Trauma. 2009;67(1 Suppl):S34-6. doi:10.1097/TA.0b013e3181a93630
10. Notrica DM, Linnaus ME. Nonoperative Management of Blunt Solid Organ Injury in Pediatric Surgery. Surg Clin North Am. 2017. doi:10.1016/j.suc.2016.08.001
11. Notrica DM, Linnaus ME. Nonoperative Management of Blunt Solid Organ Injury in Pediatric Surgery. Surg Clin North Am. 2017;97(1):1-20. doi:10.1016/j.suc.2016.08.001
12. LeeVan E, Zmora O, Cazzulino F, Burke R V., Zagory J, Upperman JS. Management of pediatric blunt renal trauma: A systematic review. J Trauma Acute Care Surg. 2016;80(3):519-528. doi:10.1097/TA.0000000000000950
13. Mattix KD, Tataria M, Holmes J, et al. Pediatric pancreatic trauma: predictors of nonoperative management failure and associated outcomes. J Pediatr Surg. 2007;42(2):340-344. doi:10.1016/j.jpedsurg.2006.10.006
14. Siboni S, Benjamin E, Haltmeier T, Inaba K, Demetriades D. Isolated blunt duodenal trauma: Simple repair, low mortality. Am Surg. 2015;81(10):961-964.
15. Malhotra A, Biffl WL, Moore EE, et al. Western Trauma Association Critical Decisions in Trauma: Diagnosis and management of duodenal injuries. J Trauma Acute Care Surg. 2015;79(6):1096-1101. doi:10.1097/TA.0000000000000870
16. Brunetti M a, Mahesh M, Nabaweesi R, Locke P, Ziegfeld S, Brown R. Diagnostic radiation exposure in pediatric trauma patients. J Trauma. 2011;70(2):E24-E28. doi:10.1097/TA.0b013e3181e80d8d
17. Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet (London, England). 2012;380(9840):499-505. doi:10.1016/S0140-6736(12)60815-0
18. Radiation Risks and Pediatric Computed Tomography - National Cancer Institute. https://www.cancer.gov/about-cancer/causes-prevention/risk/radiation/pediatric-ct-scans. Accessed March 10, 2018.
19. Rozzelle CJ, Aarabi B, Dhall SS, et al. Management of pediatric cervical spine and spinal cord injuries. Neurosurgery. 2013;72(SUPPL.2):205-226. doi:10.1227/NEU.0b013e318277096c
20. Vavilala MS, Dunbar PJ, Rivara FP, Lam AM. Coagulopathy predicts poor outcome following head injury in children less than 16 years of age. J Neurosurg Anesth. 2001;13(1):13-18. doi:10.1097/00008506-200101000-00003
21. Christiaans SC, Duhachek-Stapelman AL, Russell RT, Lisco SJ, Kerby JD, Pittet J-F. Coagulopathy after severe pediatric trauma. Shock. 2014;41(6):476-490. doi:10.1097/SHK.0000000000000151
22. Chidester SJ, Williams N, Wang W, Groner JI. A pediatric massive transfusion protocol. doi:10.1097/TA.0b013e318265d267
23. S. B, A.D. A, J. C, S. R. Tranexamic acid in pediatric trauma: Why not? Crit Care. 2014;18(4):1-5. doi:10.1186/cc13965

Disclosure

None reported.

MM

Evaluation and Management of the Burn Patient: A Case Study and Review

by Jeffrey S. Litt, DO

School of Medicine

Care of the patient with a large body-surface area burn is complex, lengthy, and fraught with potential complications.



Jeffrey S. Litt, DO, FACS, is Assistant Professor of Surgery, Burn Director, Division of Acute Care Surgery, Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri.
Contact: littjs@health.missouri.edu

Abstract

Advances in the management of burn patients have contributed to significant improvements in morbidity and mortality over the last century. The physiologic insult from this injury pattern, however, still requires extensive surgical intervention, resuscitation and multidisciplinary care. This paper will review the standard of care of these patients in the context of a recent case study from our institution.

Introduction

In spite of a decreasing frequency of burn-related injuries in the 21st century due to improved manufacturing production of commercial goods, thermal injury in the United States is still a major injury pattern. Over 200,000 patients in the United States alone were burned between 2005 and 2016, resulting in over 6000 deaths.[1] Mankind has been dealing with thermal injuries for thousands of years, yet "modern" burn care has evolved exponentially over the last 50-60 years. Advances in resuscitation, operative care and grafting techniques, infection prevention and treatment, and mitigation of hypermetabolism have all improved survival and recovery. In spite of these advances, however, questions and controversies regarding best practices are still prevalent, and numerous burn centers and laboratories across the United States continue to research various aspects of burn care, from the resuscitative phase to the reconstructive and recovery phase.

These advances in burn care have improved burn survival from a near 100% mortality seen with a burn size of 30% in the early 1900s,[2] to survival estimates over 50% in young, healthy patients with burn sizes up to 95%.[3] Nonetheless, the acute phase of resuscitation still generates significant controversy and is not a standardized process. One can query the resuscitation protocols of various burn units throughout the country and find many variations, from the usage of crystalloid-only formulae to adding colloid at various time points in the acute period, to the usage of "rescue therapies" and what they constitute and when to use them. While this review will not go into great detail of the variations, we will describe our initial burn evaluation, subsequent resuscitation, and overall management plan in caring for a seriously thermally-injured patient.

Case Presentation

A 58-year-old female patient was activated as a Level 1 trauma alert after being involved in a house explosion with resultant fire. She was awake and alert with no loss of consciousness at the scene but sustained significant thermal injuries per EMS report. She was intubated pre-hospital for "airway protection" out of concern

for inhalation injury with facial burns. Initial evaluation revealed an older woman, orally intubated with bilateral breath sounds, mildly tachycardic in the 100s, moderately hypertensive in the 160s/90s, with readily apparent full-thickness burns to the face, neck, anterior torso, bilateral arms, and bilateral legs (Photos 1 and 2). Secondary survey and imaging revealed no further injuries. At this juncture, it's important to remember and remind the non-burn or trauma center practitioner that a thermally-injured patient is still a "trauma" patient. While a large, third degree burn certainly elicits a significant morbid response in many observers, spending significant time managing the burn wounds while neglecting potential internal hemorrhage will invariably lead to a delay in treatment and worse outcomes.

The patient was immediately taken to our specialized Burn Operating Room once other injuries were ruled out and both non- and -excisional debridement of her burn wounds occurred, with resultant wound dressing application. Her upper body burns were debrided and dressed with antimicrobial dressings. She then resuscitated for the next 48 hours, ultimately receiving approximately 3.3 mL/kg/%TBSA in the first 24 hours post-injury based on a TBSA of 63%, primarily full-thickness (third degree). Resuscitation continued over the first 48 hours, and the patient underwent serial excisional debridement and wound preparation procedures over the next few weeks. Given the size of her burns, we opted to utilize cultured epidermal autografts for assistance with skin/wound coverage. It is important to note that during the entirety of our patient's two-month hospitalization she received attentive multi-disciplinary care including efforts from nutrition services, therapy services, social work, as well as the nursing and physician teams. After continued local wound and graft care the patient was discharged on HD61 to a rehabilitation facility, where she stayed for approximately three weeks until discharge home, where she now lives independently and is continuing to improve.

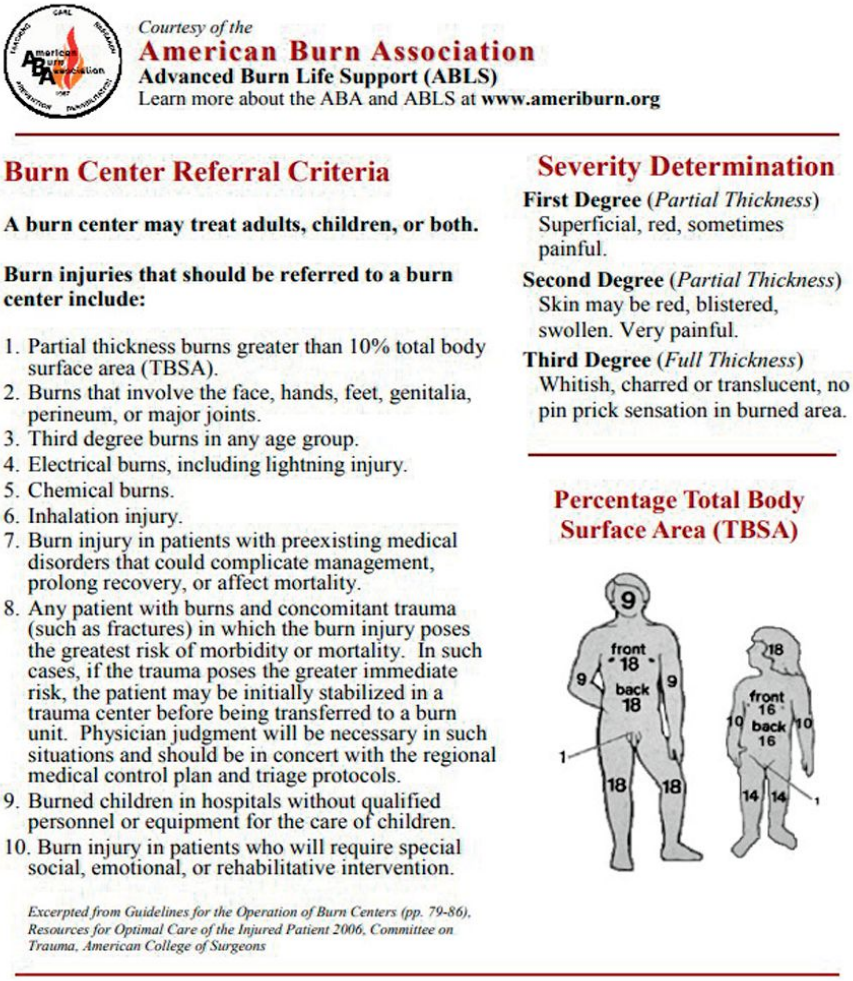
Discussion

Evaluating overall burn size can, likewise, be difficult to the untrained. While we expect that many in the medical field have heard of "the rule of 9s", establishing the rule in practice is trickier. Many studies have evaluated overall accuracy of pre-burn center size estimates from both EMS and referring hospitals, many of which are incorrect. What is perhaps more troubling is that the inaccuracies run in both direction, i.e. overestimating burn size is as frequent as underestimating. The American Burn Association (ABA) has a list of Burn Center Referral Criteria as well as a helpful

Photos 1 and 2. Patient Initial Burns







Courtesy of the
American Burn Association
Advanced Burn Life Support (ABLS)
Learn more about the ABA and ABLS at **www.ameriburn.org**

Burn Center Referral Criteria

A burn center may treat adults, children, or both.

Burn injuries that should be referred to a burn center include:

1. Partial thickness burns greater than 10% total body surface area (TBSA).
2. Burns that involve the face, hands, feet, genitalia, perineum, or major joints.
3. Third degree burns in any age group.
4. Electrical burns, including lightning injury.
5. Chemical burns.
6. Inhalation injury.
7. Burn injury in patients with preexisting medical disorders that could complicate management, prolong recovery, or affect mortality.
8. Any patient with burns and concomitant trauma (such as fractures) in which the burn injury poses the greatest risk of morbidity or mortality. In such cases, if the trauma poses the greater immediate risk, the patient may be initially stabilized in a trauma center before being transferred to a burn unit. Physician judgment will be necessary in such situations and should be in concert with the regional medical control plan and triage protocols.
9. Burned children in hospitals without qualified personnel or equipment for the care of children.
10. Burn injury in patients who will require special social, emotional, or rehabilitative intervention.

Excerpted from Guidelines for the Operation of Burn Centers (pp. 79-86), Resources for Optimal Care of the Injured Patient 2006, Committee on Trauma, American College of Surgeons

Severity Determination

First Degree (*Partial Thickness*)
Superficial, red, sometimes painful.

Second Degree (*Partial Thickness*)
Skin may be red, blistered, swollen. Very painful.

Third Degree (*Full Thickness*)
Whitish, charred or translucent, no pin prick sensation in burned area.

Percentage Total Body Surface Area (TBSA)

Figure 1. ABA Burn Referral Criteria

guide to the "Rule of 9s for public usage on their main website, reprinted in this summary (Figure 1).

Historically, "burn surgery" consisted of reconstruction and scar release if the patient survived. Lieutenant Colonel C.P. Artz, in 1955, discussed "exposing" the burn wounds to air until eschar forms, "[i]n full-thickness burns there is dehydration of the pearly white or charred dead skin, and it is converted into a protective eschar....This eschar serves as a temporary physiological cover until liquefaction occurs beneath it in 14 to 21 days."[4] It wasn't until the 1970s that a Yugoslavian surgeon, Zora Janzekovic, described her experience tangentially excising deep partial- and full-thickness burn wounds in over 1,600 patients that "burn surgery" truly developed into a surgical subspecialty.[5] Most modern burn units excise deep-partial and full-thickness burn wounds "early," typically 24-72 hours post-injury. In our experience, "early" means at or near admission, as burned tissue is a nidus of the inflammatory cascade that potentially leads to the "burn shock" phenomenon.[6]

Fluid resuscitation of the thermally injured patient is, in many ways, the most important early aspect of burn care, and likely contributes most to overall improvement in burn survival. The need for fluid resuscitation was first recognized in modern times in the 1920s. A physiologist at Yale Hospital, Dr. Frank Underhill, while caring for 20 burn-injured patients, discovered upon evaluation of burn-blister fluid a composition quite similar to plasma. He correctly theorized that "burn shock," or the hemodynamic instability that occurs after a major burn injury, was a hypovolemic state and that an intravascular volume-based treatment was necessary.[7] In 1942 the "Cocoanut Grove" nightclub, a popular, Pacific-Island themed club in Boston, Ma., caught fire. Drs. O. Cope and F. D. Moore cared for a majority of the patients between Boston City and Massachusetts General Hospitals, and in so doing helped codify the relationship between patient size and overall burn size as they related to fluid resuscitation. This resuscitation work was further advanced by C. Baxter and T. Shires at Parkland Hospital in Dallas, Texas, in the 1960s and 70s, ultimately leading to the Parkland™ formula, or 4mL/kg/%TBSA of Lactated Ringers solution, which is the most common burn resuscitation formula used in the United States.[8]

Large body-surface area burns are typically very difficult to close in an expedited manner, primarily due to lack of donor site autograft to use. To combat this issue numerous tissue substitutes have been developed over the last several decades. C. P. Artz, described earlier, relates using "postmortem homografts," "removed from the body of a deceased person under aseptic conditions soon after death…".[4] In modern times, "postmortem homografts" are now standardly called allografts and are typically utilized in a cryopreserved rather than fresh fashion. These are nearly always temporary dressings meant for wound

coverage and desiccation prevention. Concerns of disease transmission, skin supply, and expense make the use of allografts somewhat problematic. Bioengineered "skin substitutes" have been utilized in large body surface area burns for decades. The first, and perhaps most widely used is a bilaminar product called Integra.™ Developed in the 1980s, it combines bovine collagen and shark cartilage-derived chondroitin-6-sulfate, and allows for vascularization and formation of a neodermis when placed on full-thickness burns. The outer layer is a Silastic silicone-based material that acts like an epidermis and allows for protection of the fragile underlying collagenous material. Once the collagen is engrafted in a few weeks, it allows for placement of an ultra-thin split-thickness skin graft. Similar materials have been developed for use in burn care, including another bovine collagen product called Primatrix™ as well as a Hyaluronic acid derivative called Hyalomatrix.™ In very large burns with extremely limited donor sites, cultured "skin" has been utilized with great success at wound closure. Called Epicel,™ confluent sheets are grown into epidermis within two to three weeks from a sample of patients' full-thickness skin sample by a company in Cambridge, Massachusetts. These sheets can then be implanted on a prepared wound and are FDA-approved for compassionate use in large burns. The end-result is a closed but imperfect wound as the thin epidermal layer offers little resistance to blistering or shearing. The expense associated with its usage is also considerable. An offshoot of "cultured" skin is a product commonly called "spray-on skin" in social media and by the public. ReCell™ is a real-time non-cultured skin graft alternative that is presently being evaluated by the FDA. By obtaining a small full-thickness skin sample, a clinician prepares a suspension containing basal keratinocytes using a proprietary kit in real-time that may be "sprayed" on an excised and prepared wound bed in an approximate 80:1 expansion, which is truly donor-site sparing.[9] Thus, on HD2 a 6 x 2 cm full-thickness skin sample from our patient was sent for growth of epidermal sheets which were implanted without complication approximately one month after injury.

Burn care is a true "team effort," and, in fact, was likely the first "team-centered" surgical subspecialty developed after more than 500 people were killed and 3,000 injured in the "Texas City Disaster" in 1947, still considered to be America's "worst industrial accident."[10] The injured were cared for by Dr. T. Blocker and the University of Texas Hospital in Galveston, and during their convalescence were cared for by a team comprising nurses, physicians, therapists, nutritionists, and social workers to maximize outcomes. The team recognized the need for early nutrition, early mobilization, and aggressive wound care. These concepts are still followed today.

Conclusion

Care of the patient with a large body-surface area burn is complex, lengthy, and fraught with potential complications. These complications can be anticipated and minimized in burn centers accustomed to the complexities of major burn care; ultimately yielding improved survival and functional outcomes. The patient in this article, in spite of an anticipated initial mortality approaching 70% on admission, survived to discharge with only a few treatable complications, and is currently home, driving, and otherwise living independently. Her burn scars are being managed with outpatient scar exercises such as moisturization, massage, and compression. This positive outcome is the norm in burn centers, and an excellent example of why patients with major burn injuries should be cared for in these specialized centers. Any patient with a significant burn, even if not delineated on the ABA referral list, warrants discussion with a burn-trained surgical team.

References

1. Mosier, MJ; Bernal, N; et al. National Burn Repository (2016). Report Dataset Version 12.0. pp 8-12; retrieved from Ameriburn.site-ym.com
2. Cancio, LC.; Pruitt Jr, BA. (2012) Historical Perspective and the Development of Modern Burn Care. In Phillips, BJ. editor Pediatric Burns (p. 1). Amherst, NY: Cambria Press
3. Branski LK.; Herndon, DN.; Barrow, RE. A Brief History of Acute Burn Care Management. In Herndon, DN. Editor (4th Ed) Total Burn Care (p. 1). Elsevier
4. Artz, CP.; Soroff, HS. Modern Concepts in the Treatment of Burns. JAMA. (1955); 159(5):411-417
5. Janzekovic, Z. A New Concept in the Early Excision and Immediate Grafting of Burns. The Journal of Trauma. (1970); 10(12):1103-1108
6. Lee, JO.; Dibildox, M.; et al. Operative Wound Management. In Herndon, DN. Editor (4th Ed) Total Burn Care (p. 157-158). Elsevier
7. Underhill, FP.; The Significance of Anhydremia in Extensive Superficial Burns. JAMA. (1930); 95(12):852-57
8. Warden, GD; Fluid Resuscitation and Early Management. In Herndon, DN. Editor (4th Ed) Total Burn Care (p. 117-118).
9. Wood FM, Giles N, Stevenson A, et al. Characterization of the Cell Suspension Harvested from the Dermal Epidermal Junction Using a ReCell Kit. Burns (2012);38:44–51.
10. Branski LK.; Herndon, DN.; Barrow, RE. A Brief History of Acute Burn Care Management. In Herndon, DN. Editor (4th Ed) Total Burn Care (p. 1). Elsevier

Disclosure

J. Litt received Acelity/KCI Speaker Honoraria. **MM**

Simulation Training in Trauma

by Jacob A. Quick, MD

School of Medicine

Trauma simulation training has become a key component in the education of practitioners caring for acutely-injured patients.



Jacob A. Quick, MD, FACS, is Assistant Professor of Surgery, Division of Acute Care Surgery, Department of Surgery, University of Missouri School of Medicine, Columbia, Missouri.
Contact: quickja@health.missouri.edu

Abstract

Trauma care is the classic high-acuity event for which simulation training has the potential to greatly improve outcomes. While not a new concept, the variability and availability of training modalities in trauma continues to rapidly multiply. Spanning the continuum of fidelity, simulation extends from simple trauma scenario discussion, to advanced virtual reality experiences. The choice of simulation is largely dependent upon the desired outcome, which is broadly divided into either task-oriented or non-technical skill acquisition.

Introduction

Infrequent, high-acuity events, such as those involved with caring for injured patients, require rapid identification and management of life-threatening injury via a thorough, systematic, and expeditious approach. These characteristics of trauma care make it a near-ideal setting to benefit from simulation training, which is inherently low-risk and repeatable.[1] Trauma care has been at the forefront of simulation training for many years. For more than 40 years, the Advanced Trauma Life Support (ATLS®) course has employed a variety of simulation modalities to streamline and improve trauma care worldwide.[2] Since that time, a variety of strategies, techniques and courses aimed at trauma-specific training have emerged, and now provide a plethora of learning opportunities for trauma providers. From low-fidelity trainers, such as tube thoracostomy mannequins, to high-fidelity simulators with immediate and realistic feedback, to virtual reality constructs that provide an immersive experience, there are a wide range of available simulation methodologies directed at improving trauma care and reducing errors at every stage of the process.

Standardized Patients

Standardized patients are either volunteers or paid participants that function as a real patient during simulation exercises. Participants assess the patient and appropriately manage simulated injures. This method of simulation is widely utilized by medical schools and has been embraced by the National Board of Medical Examiners.[3] Inexpensive and often easily recruited, standardized patients offer many benefits to trauma simulation training. Live human interaction is one of the chief benefits to standardized patient encounters, and has been shown to greatly improve learning and retention, secondary to increased participant engagement.[4,5] An added benefit of simulated human patients, is that they also may provide feedback for the learners from a layman's perspective.

Non-technical skill training is an area of simulation particularly suited to standardized patient encounters. The American College of Surgeons utilizes

standardized patients, complete with simulated blood, open fractures and other injuries, during ATLS® courses. After dressing in appropriate garb and moulage, they are given scripts related to their assigned traumatic event, and answer questions of the participants accordingly.

Low-Fidelity vs. High-Fidelity Simulators

Simulation training exists along a continuum, from low to high. Low-fidelity simulations are typically more artificial, less-complex and less realistic. Low-fidelity trainers generally omit factors that participants may experience in real-life. A scenario read aloud for participants to discuss is an example of a low-fidelity educational method. Another example includes a tube thoracostomy task trainer without physiologic simulated feedback. To contrast, a high-fidelity simulation may include standardized patients or a complex synthetic mannequin with physiologic feedback to participant actions. Low-fidelity training modalities can be extremely effective, and "low" should not convey a sense of inadequacy. Conversely, a high-fidelity simulator, while complex, may not afford benefit in all situations. Each simulated task requires careful thought and choosing of the appropriate simulator.[6]

Trauma training typically employs both low- and high-fidelity training modalities. Low-fidelity simulators, geared toward finite educational goals, form the basis for many task trainers. Popular low-fidelity methods include task trainers, such as those designed to teach central venous access, cricothyroidotomy, intubation and focused assessment with sonography in trauma (FAST). These are often inexpensive to purchase and maintain, and may even be homemade, and are thus frequently utilized for a variety of teaching scenarios where concise goals are sought. The TraumaMan© (Simulab Corporation, Seattle, WA) simulator is one such trainer designed for tube thoracostomy, needle thoracostomy, criothyroidotomy, tracheostomy, pericardiocentesis and diagnostic peritoneal lavage (DPL) that has been shown to be comparable to live tissue models.[7] Ultrasonographic evaluation after injury is a growing field of study, and several trainers exist, including SonoSim® (SonoSim, Santa Monica, CA), to improve image acquisition time and accuracy during FAST examinations.[8]

High-fidelity simulators are also frequently utilized in trauma training. The ability to incorporate more of the real-life patient experience allows high-fidelity simulations to invoke higher order thought processes and management of the entire patient or patients. The Apollo© (CAE Heathcare, Sarasota, FL) and SimMan 3D© (Laerdal, New York, NY) are two mannequin simulators that provide a wide variety of physiologic input which favor full-scale trauma simulation scenarios. These types of simulators have features that incorporate all body systems so that the facilitator can customize each patient encounter. For example, the simulator may be tachycardic, hypotensive, and with an altered mental status secondary to hemorrhage from a penetrating wound to the thigh. With tourniquet application, intravenous access gained and blood product resuscitation the simulator will respond just as a live patient. If other injuries are not identified, the simulator may mimic a transient responder, and prompt additional interventions. The ability of high-fidelity simulators to incorporate nearly all facets of caring for real trauma patients, make them highly effective educational tools.[9] In addition to technical skill training, high-fidelity simulators offer the benefit of teaching non-technical skills and team training.[10]

Virtual Reality

Immersive, highly visual and often 3D, virtual reality simulators closely replicate real-life with incorporation of physical interfaces and haptic feedback. Virtual reality simulators are technically advanced, and available in a range of sizes and shapes. Some incorporate gaming-industry headsets and cellular phones, while others involve large-scale simulators resembling carnival rides. The field of virtual reality training in trauma is growing exponentially. Downloadable apps are currently being developed that, with the addition of a $20 headset, can provide an immersive trauma scenario experience.[11] Additionally, virtual reality simulations have the ability to connect multiple users at multiple locations to increase availability to centers with limited resources.[12]

Cadaver Training

Cadavers have long-been employed to teach anatomy and surgical technique and continue to be an excellent training tool. The Advanced Surgical Skills for Exposure in Trauma (ASSET™) course currently utilizes fresh cadavers to address difficult and rarely performed trauma surgical exposures.[13] Recent advancements in technology have allowed cadavers to more closely replicate living human tissue. Perfused cadaver models replicate bleeding tissue, and therefore closely mimic traumatic injuries.[14,15]

Although useful as a trauma training analog, access to these models is expectedly limited.

Live-Tissue Training

Despite technological advancements leading to the development of complex and interactive high-fidelity and virtual reality simulators, they lack the realism that can be portrayed with live tissue models. Learner engagement is a key concept when debating the effectiveness of simulation in education, and live tissue has been shown to increase engagement substantially.[16] Start-up costs are high, and facilities are few, however the benefits of live tissue training cannot be overlooked. The Advanced Trauma Operative Management (ATOM™) course utilizes live tissue to train surgeons and surgical residents during a 1-day course designed specifically to address operative penetrating trauma. Studies aimed at assessing the effectiveness of the course show improved knowledge retention and confidence in approaching life-threatening penetrating injury.[17,18]

Trauma Non-Technical Skills

While many of the above methods are designed with specific tasks in mind, non-technical skills training in trauma is of equivalent importance. Most errors in the care of trauma patients are not technically-oriented, and arise from improper triage, indecisive team leadership and failed recognition of evolving life-threatening injury.[19] Several long-standing courses offered through the American College of Surgeons, including ATLS®, are specifically designed to improve recognition of serious injuries. Courses are offered to physicians frequently at several institutions across the state in an intense 2-day format. Less robust, Trauma Evaluation and Management (TEAM®) courses provide medical students a short, 90-minute overview of how to identify and treat common potentially lethal traumatic conditions. For those already in practice, the Rural Trauma Team Development Course (RTTDC™) improves care through a 1-day course aimed at improving care at rural facilities. This course addresses the importance of communication and role definition through interactive lectures and simulated scenarios.

Effective leadership appears to be a defining characteristic of successful trauma resuscitation.[20,21] For this reason, trauma team simulation curricula have focused on developing leadership qualities. A typical trauma team simulation follows crew resource management techniques taught most notably in the airline industry, where lectures are combined with practical stations and interactive discussions, all guided to improve leadership and closed-loop communication.[22] Team simulations frequently utilize high-fidelity mannequins to present physiologic and traumatic maladies to a multidisciplinary team. Virtual reality and live tissue simulations provide increased levels of engagement and are increasingly utilized for trauma team and leadership training. Additionally, standardized patients may be utilized via Objective Structured Clinical Examination (OSCE) methods. Video-based debriefings are frequently utilized and provide insight for participants to improve non-technical skills.

Emergency Medical Services Simulation

With changing paradigms regarding domestic terrorism and increasing frequency of mass casualty and disaster events, a focus on community readiness has emerged. Preparing emergency medical services (EMS) for large-scale events requires extensive planning and preparation to adequately manage patients during surge scenarios. To do this, simulated exercises have become more commonplace. Often involving multiple facets of emergency care, such as police, fire, ambulance, and hospital personnel, these sometimes massive simulation events have proven vital to the success of municipalities in addressing rare, high-acuity events like mass shootings.[23]

Simulation scene training for EMS has historically been focused on logistical simulation. However, evolving methods have begun to incorporate existing infrastructure, such as actual helicopters and ambulances to create mock scenarios targeted toward scene-specific issues, such as early identification and management of life-threatening injuries. Utilizing existing elements decreases costs and provides true-to-life practicum for participants who work within the exact environment in which they trained.[24] Utilizing high-fidelity mannequins during scene simulation adds an element of complexity that affords increased realism and scenario dynamics. Video monitoring of the events may be employed to provide instructors and participants the ability to view and debrief, adding educational value.

Technical procedure simulation has shown clear benefits for a variety of medical specialties. EMS procedural simulation is frequently performed with both low- and high-fidelity trainers. Some centers have the unique ability to expand procedural training to live tissue. However, local political climates and budgets may

preclude its use. Emergency life-saving procedures, such as cricothyroidotomy and tube thoracostomy, are well-suited to live tissue training for EMS providers.[16] The ability of high-fidelity and virtual reality simulation to replicate the austere EMS environment, has resulted in a shift toward more high-tech training methodologies.[24-26] Virtual-reality environments afford manipulated conditions that may be easily repeated to the desired task at hand.[27] Fully-immersive technologies allow for simulated medical care within the treatment bay of a realistic ambulance or helicopter while underway – adding in complexities such as wind, elevation and noise – which create lifelike training environments.

Simulation Challenges

Trauma simulation training has become a key component in the education of practitioners caring for acutely-injured patients. While a steady stream of technological advancements improve trauma simulation, modalities will continue to be challenged by innate shortcomings, such as realism and authenticity.[9] Additionally, high levels of learner engagement, and long-term knowledge retention with simulation have not been consistently demonstrated in the literature. Finally, start-up costs can be quite high, and thus prohibitive to smaller centers.

References

1. Ruesseler M, Weinlich M, Muller MP, Byhahn C, Marczi I, Walcher F. Simulation taining improves ability to manage medical emergencies. Emerg Med J 2010;27(10):734-738.
2. Carmont MR. The Advanced Trauma Life Support course: a history of its development and review of related literature. Postgrad Med J 2005;81(952):87-91.
3. Papadakis MA. The Step 2 Clinical Skills examination. N Engl J Med 2004;350:1703-1705.
4. Ali J, Adam R, Pierre I, et al. Comparison of performance 2 years after the old and new (interactive) ATLS courses. J Surg Res 2001;97(1):71-75.
5. Alsaad AA, Davuluri S, Bhide VY, et al. Assesing the performance and satisfaction of medical residents utilizing standardized patient versus mannequin-simulated training. Adv Med Educ Pract 2017;8:481-486.
6. Lee KHK, Grantham H, Boyd R. Comparison of high- and low-fidelity mannequins for clinical performance assessment. Emerg Med Australasia 2008;20(6):508-514.
7. Berkenstadt H, Munz Y, Trodler G, et al. Evaluation of the TraumaMan® simulator for training in chest drain insertion. Eur J Trauma 2006;32(6):523-526.
8. Chung GKWK, Gyllenhammer RG, Baker EL, Savitsky E. Effects of simulation-based practice on focused assessment with sonography for trauma (FAST) window identification, acquisition, and diagnosis. Mil Med 2013;178(S10):87-97.
9. Cherry RA, Ali J. Current concepts in simulation-based trauma education. J Trauma 2008;65:1186-1193.
10. Amiel I, Simon D, Merin O, Ziv A. Mobile in situ simulation a s a tool for the valuation and improvement of trauma treatment in the emergency department. J Surg Educ 2016;73(1):121-128.
11. Harrington CM, Kavanagh DO, Quinlan JF, et al. Development and evaluation of a trauma decision –making simulator in Oculus virtual reality. Am J Surg 2018;215(1):42-47.
12. McGrath JL, Taekman JM, Dev P, et al. Using virtual reality simulation environments to assess competence for emergency medicine learners. Acad Emerg Med 2018;25(2):186-195.
13. Bowyer MW, Kuhls DA, Haskin D, et al. Advanced Surgical Skills for Exposure in Trauma (ASSET): the first 25 courses. J Surg Res 2013;183(2):553-558.
14. Carey JN, Minneti M, Leland HA, et al. Perfused fresh cadavers: method for application to surgical simulation. Am J Surg 2015;210(1):179-187.
15. Minneti M, Baker CJ, Sullivan ME. The development of a novel perfused cadaver model with dynamic vital sign regulation and real-world scenarios to teach surgical skills and error management. J Surg Educ 2017 Oct 13. Epub ahead of print.
16. Barnes SL, Bukoski A, Kerby JD, et al. Live tissue versus simulation training for emergency procedures: Is simulation ready to replace live tissue? Surgery 2016 160(4):997-1007.
17. Kaban JM, Stone ME, Dayama A, et al. Does resident trauma exposure affect Advanced Trauma Operative Management course experience? Am Surg 2016;82(3):212-215.
18. Jacob LM, Burns KJ, Luk SS, Marshall WT. Follow-up survey of participants attending the Advance Trauma Operative Management (ATOM) course. J Trauma 2005;58:1140-1143.
19. Doumouras AG, Keshet I, Nathens AB, et al. Trauma non-technical training (TNT-2): the development, piloting and multilevel assessment of a simulation-based, interprofessional curriculum for team-based trauma resuscitation. Can J Surg 2014;57(5):354-355.
20. Hjortdahl M, Ringen AH, Naess AC, Wisborg T. Leadership is the essential non-technical skill in the trauma team – results of a qualitative study. Scan J Trauma Resusc Emerg Med 2009;17:48.
21. Briggs A, Raja AS, Joyce MF, et al. The role of nontechnical skills in simulated trauma resuscitation. J Surg Educ 201572(4):732-739.
22. Shapiro MJ, Morey JC, Small SD, et al. Simulation based teamwork training for emergency department staff: does it improve clinical team performance when added to an existing didactic teamwork curriculum? Qual Saf Heath Care 2004;13:417-421.
23. Albert E, Bullard T. Training, drills pivotal in mounting response to Orlando shooting. ED Manag 2016;28(8):85-89.
24. Dotson MP, Gustafson ML, Tager A, Peterson LM. Air medical simulation training: a retrospective review of cost and effectiveness. Air Med J 2018;37(2):131-137.
25. Winkelmann M, Friedrich L, Schroter C, et al. Simulator-based air medical training program Christoph Life: from concept to course. Air Med J 2016;35:243-246.
26. Wright SW, Lindsell CJ, Hinckley WR, et al. High fieldity medical simulation in the difficult environment of a helicopter: feasibility, self-efficacy and cost. BMC Med Educ 2006;6:49.
27. Whalen D, Harty C, Ravalia M, et al. Helicopter evacuation following a rural trauma: an emergency medicine simulation scenario using innovative simulation technology. Cureus 2016;8(3):e524.

Disclosure

None reported.

MM

Mass Casualty Incident Management

by Salman Ahmad, MD

School of Medicine

Sponsor integrated live-action exercises with the intention of breaking the system, finding weaknesses and improving your plan.



Salman Ahmad, MD, FACS, is Assistant Professor of Surgery, Medical Director Surgical Intensive Care Unit, Acute Care Surgery Division, Department of Surgery, University of Missouri Healthcare, Columbia, Missouri.
Contact: ahmadsa@health.missouri.edu

Abstract

A mass casualty incident (MCI) by definition can overwhelm local and regional resources. Preparation and training is required by any health system to minimize the loss of life and maximize patient recovery. This update will review lessons learned from recent events and discuss current research that healthcare providers should be familiar with when managing MCI's.

Introduction

The Hospital Preparedness Program (HPP) was established after September 11, 2001 to "enhance the ability of hospitals and healthcare systems to prepare for and respond to bioterror attacks…and other public health emergencies, including pandemic influenza and natural disasters".[1] An interim 2007 progress report on the state of U.S. hospital preparedness highlighted considerable progress made in the area of healthcare coalitions contributing to collaboration and networking between all levels of providers from first responders to hospitals and public health agencies. Evolving areas for improvement include planning for catastrophic emergencies requiring drastic changes in infrastructure and response systems, and their ability to respond to unconventional mass casualty incidents (MCI) as measured by surge capacity.[1] In 2015 the federal government updated its National Preparedness Goal, "A secure and resilient Nation with the capabilities required across the whole community to prevent, protect against, mitigate, respond to, and recover from the threats and hazards that pose the greatest risk".[2] The document outlines core capabilities which include quick disaster response in the aftermath of an incident. It also emphasizes the mitigation of risk at the local level with preparation and coordination.

Lessons Learned from Recent Events

In 2011, the deadliest single tornado recorded in the U.S. since the beginning of recordkeeping in 1950 struck Joplin, Missouri. It destroyed 7,000 homes, resulted in 162 fatalities and over 1,000 injured, and cost an estimated $3 billion in insured losses. In their review of the MCI, Bimal Paul and Mitchel Stimers collected data from first responders, survivors and the Federal Emergency Management Agency (FEMA) to determine reasons for the high fatality rate.[3] They concluded that in addition to the intensity of the tornado and the large size of damage area, other contributing factors included ignoring the warning sirens or having less than 15 minutes to seek shelter, structural weakness in area homes and disproportionate damage to a hospital and area business where more people were gathered. A component of delayed recognition of a rare fungal infection also contributed to late deaths.[4] Some of these patients were transferred to our institution only to succumb to the widely disseminated infection.

An after-action review published by the Boston Trauma Center Chief's Collaborative discusses key lessons learned from the 2013 Boston Marathon bombings' MCI response, the scale of which had not been seen since the Cocoanut Grove fire.[5] Representing six area trauma centers



Boston Marathon Finish Line Bombing.
Source: Time, Inc.

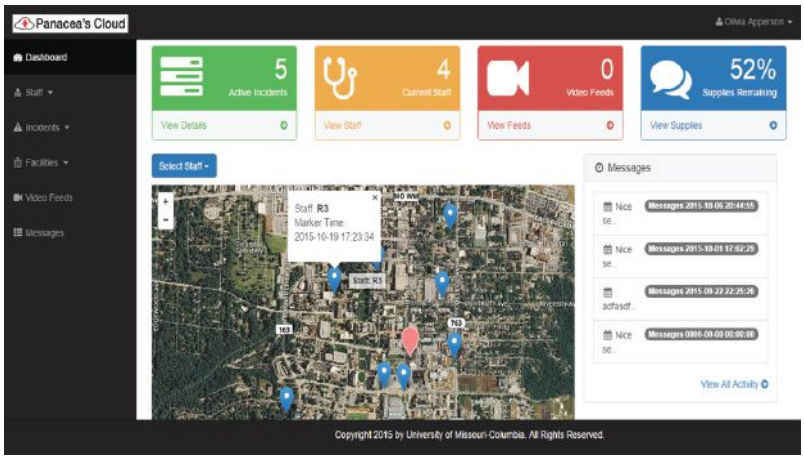
that cared for the injured, the review credits the work of first responders and healthcare providers for the 100% survival rate for any patient that arrived at a trauma center. Field triage only tagged 50% of patients arriving at trauma centers and patients in extremis were unevenly distributed among the six area trauma centers, where one level 1 center received none of these patients. Multiple transport mechanisms were used including ambulances, police vehicles and private automobiles. A central EMS Command Center coordinated triage among area hospitals but law enforcement occasionally redirected ambulance traffic. Several first responders and healthcare providers were already staffing the marathon to render medical assistance and proved invaluable after the bombing in providing bleeding control with tourniquets and stabilizing victims prior to transport. While most trauma centers were already aware of the event via the media before Boston EMS radio contact, all sites reported difficulty with communication among their own staff members, reflecting shortcomings with their center's MCI communication plan. Key lessons learned are summarized in these points:

- Resist complacency and perform ongoing MCI training to enhance preparedness.
- Establish robust communication systems that utilize the modern cellular telephone network and insure reliable backup systems.
- Enhance situational awareness of the scene to provide closed-loop feedback between first responders, law enforcement and trauma centers to ensure appropriate triage and victim allocation.
- Military-grade tourniquets should be standard issue on all emergency vehicles and incorporated into the national first-aid curriculum.
- Improve planning of system-wide resource sharing during MCI and non-MCI emergencies.

Current Research

In 2009 the Institute of Medicine (IOM) sponsored a workshop on medical surge capacity.[6] Participants defined standard terminology and metrics, discussed the state of the art in MCI management and offered strategies for the future. Surge or crisis capacity was defined as a "systematic change into a system in which standards of care are significantly altered…", prompting "…the institution to either get the right resources in, transfer the excess patients out, or look for additional relief." The IOM workshop also discussed several legal issues including suspension of EMTALA and state licensing and credentialing requirements during MCI's, allowing for reciprocity of out-of-state responders and healthcare providers as well as drafting of mutual medical aid agreements. One of the most critical themes in their executive summary is the integration of care. Captain Deborah Levy from the CDC described the "…preferred framework [as] one in which the established healthcare system (hospital administrators and emergency departments, physicians, emergency medical services, community health clinics, pharmacists, and other caregivers) works closely with the public health community (local departments of public health), then explicitly brings the

local emergency management agency into the process…", while the alternative of silo-based independent goals and objectives is ineffective and inefficient.[6] They also briefly shared the Israeli example of alternative sites of triage for minor injuries, reserving the hospital for the most severely injured that require the highest level of medical care. Given its size at just slightly smaller than the state of New Jersey, Israel's MCI model is analogous to a state-level trauma system. In a prospective study during live simulation exercises in Israel, using de-identified real trauma patient data facilitated more accurate triage knowing the exact resources that were required for successful treatment of those patients.[7] Their experience emphasizes centralization of hospital triage and delegation of leadership roles to nursing and other staff. Prehospital triage includes identification and documentation and reliance on ultrasound over CAT scanning to rule out intraabdominal hemorrhage. Israeli trauma hospitals also establish an emergency public information site (EPIS) headed by social workers to communicate with the public about their loved ones. Hospital security in controlling access is also paramount for the safety of patients, staff and family.[8]





Figures 1 and 2. MCI triage communication platform called Panacea's Cloud©.

Using federal grant funding, a coalition of eight counties in south central Pennsylvania, with a catchment population of 1.9mil, engaged seventeen hospitals and healthcare systems in a prospective performance improvement project.[9] Their coalition's goals were to demonstrate improvements in six areas:

- Situational awareness of capabilities and assets.
- Development and testing of advanced regional planning and exercise events.
- Augment mutual medical aid agreements (MMAA) between regional healthcare facilities especially hospitals.
- Strengthen partner relationships through joint planning, communication, simulation and evaluation of preparedness.
- Ensure compliance with the National Incident Management System (NIMS).
- Develop and test plans for more effective utilization of the state's emergency volunteer registry.

The coalition expanded these goals to 59 specific, measurable, achievable, realistic and time-framed (SMART) objectives they used as performance metrics. Their interventions included teleconferences and webinars, enhancement of the radio-based emergency response system to include the internet, creation of a web-based portal to catalogue real-time available resources across the coalition and brief web-based surveys to assess changes in measured variables. After a 24-month evaluation period, the coalition reported improvements in all measured goals including a 100% response rate to emergency notifications, 16 training exercises performed, 14 out of 17 mutual medical aid agreements formulated, 4,651 trained employees available 24/7 at each facility and near universal registry tracking of volunteers with an overall 97% SMART objective completion rate.[9]

In their recent editorial response to MCI's, Knudson et al. connected lessons learned from the battlefield to contemporary civilian experience.[10] They emphasized the evolution of damage control resuscitation, formerly the massive transfusion protocol, in treating life-threatening hemorrhage. Recent MCI's were highlighted from the Boston Marathon bombing to the crash of Asiana Airlines Flight 213 in San Francisco with take home lessons including dual command triage, communications and CAT scanning for triage, the latter acknowledged as contrary to the standard practice of ultrasound triage for intraabdominal hemorrhage. They concluded with the Hartford Consensus on providing the public with the skills

and tools needed to control hemorrhage as bystander first responders through the "Stop the Bleed" program at www.bleedingcontrol.org (see Sidebar next page).[11]

Ongoing research is also improving MCI communication systems. Jokela et al. described their incorporation of RFID tagging systems with conventional cellular networks to improve situational awareness in a military training exercise.[12] Their initial results encouraged civilian adoption and testing. More recently, the University of Washington Harborview Medical Center in Seattle described their novel approach in staff notification in the setting of difficulties with cellular networks during the Boston Marathon bombing.[13] Leveraging their unique Disaster Management Control Center (DMCC), researchers created a system that utilized a combination of text, voice and e-mail coupled with conference calls to communicate with staff in their system. Their premise behind using text messaging was the higher likelihood of successful transmission than voice calls.

Since 2014, our institution has been testing an MCI triage communication platform called Panacea's Cloud©. A collaboration between the Acute Care Surgery Division and the Department of Computer Engineering, Panacea© is being developed as a situational awareness operating system whose common operating picture (COP) includes communication with and tracking of patients, first responders, healthcare providers and incident commanders. The prototype system consisted of an ad-hoc resilient and self-sustaining battery-powered Wi-Fi™ mesh network covering a two-scene lake boating crash simulation.[14] The original dashboard provided video calling capabilities for the incident commander with both scenes via Google Glasses™ donned by the paramedics over the mesh network and has recently been enhanced to include staff and victim tracking capabilities[15–17] (Figure 1). Our latest experiment was conducted with Missouri's Task Force One search-and-rescue team during a training simulation. We compared Panacea© with their standard of care Iron Sights© GPS system used for geotracking of incident markers and found our system to be more efficient in providing real-time actionable intelligence for remote commanders[18] (Figure 2). Our goal is to enhance Panacea's capabilities through real-world testing with collaborative city-wide exercises.

Conclusion

Take advantage of the lessons learned from recent MCI's in developing, implementing and testing your own MCI disaster plan. Sponsor integrated live-action exercises with the intention of breaking the system, finding weaknesses and improving your plan. Statewide initiatives can improve integration of care and raise the state of preparedness for MCI's. Research continues into novel systems-based solutions to MCI management.

References

1. Center for Biosecurity of UPMC. Hospitals Rising to the Challenge: The First Five Years of the U.S. Hospital Preparedness Program and Priorities Going Forward. 2007;(March). http://www.upmc-biosecurity.org.
2. Department of Homeland Security U. National Preparedness Goal - Second Edition. 2015. https://www.fema.gov/media-library-data/1443799615171-2aae90be55041740f97e8532fc680d40/National_Preparedness_Goal_2nd_Edition.pdf. Accessed March 12, 2017.
3. Paul BK, Stimers M. Exploring probable reasons for record fatalities: The case of 2011 Joplin, Missouri, Tornado. Nat Hazards. 2012;64(2):1511-1526. doi:10.1007/s11069-012-0313-3.
4. Neblett Fanfair R, Benedict K, Bos J, et al. Necrotizing Cutaneous Mucormycosis after a Tornado in Joplin, Missouri, in 2011. N Engl J Med. 2012;367(23):2214-2225. doi:10.1056/NEJMoa1204781.
5. Boston Marathon bombings: An after-action review. J Trauma Acute Care Surg. 2014;77(3):501-503. doi:10.1097/TA.0000000000000397.
6. Altevogt BM, Stroud C, Nadig L. Medical Surge Capacity: Workshop Summary; Forum on Medical and Public Health Preparedness for Catastrophic Events.; 2010.
7. Ashkenazi I, Ohana A, Azaria B, et al. Assessment of hospital disaster plans for conventional mass casualty incidents following terrorist explosions using a live exercise based upon the real data of actual patients. Eur J Trauma Emerg Surg. 2012;38(2):113-117. doi:10.1007/s00068-011-0154-x.
8. Admi H, Eilon Y, Hyams G, Utitz L. Management of Mass Casualty Events: The Israeli Experience. J Nurs Scholarsh. 2011;43(2):211-219. doi:10.1111/j.1547-5069.2011.01390.x.
9. Terndrup T, Leaming J, Adams RJ, Adoff S. Hospital-Based Coalition to Improve Regional Surge Capacity. West J Emerg Med. 2011;13(5):445-452. doi:10.5811/westjem.2011.10.6853.
10. Knudson MM, Velmahos G, Cooper ZR. Response to mass casualty events : from the battle fi eld to the Stop the Bleed campaign. Trauma Surg Acute Care Open. 2016;1(1):1-3. doi:10.1136/tsaco-2016-000023.
11. Jacobs LM, Wade D, Mcswain NE, et al. Hartford Consensus: A Call to Action for THREAT, a Medical Disaster Preparedness Concept. J Am Coll Surg. 2014;218:467-475. doi:10.1016/j.jamcollsurg.2013.12.009.
12. Jokela J, Simons T, Kuronen P, et al. Implementing RFID technology in a novel triage system during a simulated mass casualty situation. Int J Electron Healthc. 2008. doi:10.1504/IJEH.2008.018923.
13. Morris, MD, MPH SC, Pelley JK, Mitchell, MD, FACEP SH. Using a novel technology for disaster staff notification. Am J Disaster Med. 2017;12(1):63-65. doi:10.5055/ajdm.2017.0260.
14. Gillis J, Calyam P, Bartels A, et al. Panacea ' s Glass : Mobile Cloud Framework for Communication in Mass Casualty Disaster Triage. IEEE Mob Cloud. 2015. doi:10.1109/MobileCloud.2015.39.
15. Gillis J, Calyam P, Apperson O, Ahmad S. Panacea's Cloud: Augmented reality for mass casualty disaster incident triage and co-ordination. In: 2016 13th IEEE Annual Consumer Communications and Networking Conference, CCNC 2016. ; 2016. doi:10.1109/CCNC.2016.7444772.
16. Vassell M, Apperson O, Calyam P, Gillis J, Ahmad S. Intelligent Dashboard for augmented reality based incident command response co-ordination. In: 2016 13th IEEE Annual Consumer Communications and Networking Conference, CCNC 2016. ; 2016. doi:10.1109/CCNC.2016.7444921.
17. Demir F, Ahmad S, Calyam P, Jiang D, Huang R, Jahnke I. A Next-Generation Augmented Reality Platform for Mass Casualty Incidents (MCI). J Usability Stud. 2017;12(4):193-214. http://www.upassoc.org. Accessed September 4, 2017.
18. Cheng E, Meiss K, Park K, et al. Contextual geotracking service of incident markers in disaster search-and-rescue operations. In: Proceedings - 2016 IEEE 15th International Symposium on Network Computing and Applications, NCA 2016. ; 2016. doi:10.1109/NCA.2016.7778586.

Disclosure

None reported. **MM**

SIDEBAR *by John C. Hagan III, MD*

Stop the Bleed Program

Public education directed by physicians has been enormously successful in the past. Especially notable were the efforts to teach the general public to perform cardio-pulmonary resuscitation and the Heimlich maneuver to clear blocked airways.

Launched in October of 2015 by the White House, Stop the Bleed is a national awareness campaign and a call to action. Stop the Bleed is intended to cultivate grassroots efforts that encourage bystanders to become trained, equipped, and empowered to help in a bleeding emergency before professional help arrives.



Background

No matter how rapid the arrival of professional emergency responders, bystanders will always be first on the scene. A person who is bleeding can die from blood loss within five minutes, so quickly stopping the bleeding is critical. Those nearest to someone with life threatening injuries are best positioned to provide immediate care if they are equipped with the appropriate training and resources.

What's Happening Now

The Stop the Bleed initiative brought together a number of Federal agencies, non-profit organizations and corporations to develop and disseminate resources to train the public in bleeding control. Hosted by the Department of Homeland Security, the Stop the Bleed website (https://www.dhs.gov/stopthebleed) offers posters and other materials that explain how to control life-threatening bleeding and links to information, such as where to find courses on bleeding control and how to offer them in your community.

Who's Involved?

The Stop the Bleed initiative began as a collaborative effort headed up by the White House that included a number of Federal agencies, including the NHTSA Office of EMS, as well as national organizations and corporations. Missouri organizations teaching Stop The Bleed Courses include: University of Missouri SOM, Washington University SOM, Kansas City Medical Society, a large coalition of partners in Springfield and many others.

What You Can Do?

Offer training on bleeding control in your community to increase bystander engagement and willingness to act during an emergency. The Stop The Bleed website has information on offering courses, training medical personnel to be instructors, educational material and kits to stop bleeding.

Reference: Some of this material is taken verbatim from the Stop The Bleed Website.

A Cross-Sectional Study of Firearm Injuries in Emergency Department Patients

by Heather de Anda, MD, Taylor Dibble, Charles Schlaepfer, Randi Foraker, PhD & Kristen Mueller, MD

Our data demonstrate that patients presenting to the ED for firearm injury were predominately young, African American males. Patients who had been shot previously were more likely to be African American, male, uninsured, unemployed, and have a history of other non-accidental trauma.



Heather de Anda, MD, Taylor Dibble, Charles Schlaepfer, Randi Foraker, PhD, and Kristen Mueller, MD, (above), are affiliated with the Washington University in Saint Louis School of Medicine, St. Louis, Missouri.
Contact: Kristen.Mueller@wustl.edu

Synopsis

This is a single-center cross-sectional study of consecutive patients who presented to an urban emergency department (ED) with firearm injuries between July 1, 2014 and June 30, 2016. The objective of this study was to describe the characteristics of patients in this cohort and identify those at risk of firearm re-injury to inform future interventions. Patients in this cohort with both initial and recidivistic firearm injures were found to be predominately young, African American men.

Abstract

Objective

To describe the characteristics of patients who present to the emergency department (ED) with firearm injuries and identify those at risk of firearm re-injury.

Methods

This is a single-center cross-sectional study of consecutive patients who presented to the ED with firearm injuries between July 1, 2014 and June 30, 2016. We collected data on patient demographics, history of previous traumatic injury including firearm injury, and whether the firearm injury was self-inflicted. We also evaluated characteristics of patients in this cohort who returned to the ED with firearm re-injury within a one year follow-up period.

Results

This study included 1226 unique patients. Our data demonstrate that patients presenting to the ED for firearm injury were predominately young, African American males. Fourteen percent had a history of a previous firearm injury and 20% had a history of other non-firearm assault. Patients who had been shot previously were more likely to be African American, male, uninsured, unemployed, and have a history of other non-accidental trauma. Eight percent of firearm injuries were self-inflicted. All 35 patients who sustained a new firearm injury within 1 year of the index injury were African American males with a median age of 23.

Conclusions

Among patients treated in the ED for firearm injuries, young, African American males are disproportionately at risk of firearm injury and re-injury. ED visits for traumatic injury represent an opportunity to provide social work, case work, and counseling-based interventions to help disrupt the cycle of violence in high-risk individuals.

Introduction

Background

Firearm injuries are a significant public health issue in the United States (US). Between 2010 and 2015 there were 422,907 violent firearm injuries

and deaths in the US.[1,2] In 2016 the rate of violent firearm deaths in the US was 3.85/100,000.[3] Annually, firearm assault generated $389 million in healthcare expenses from over 30,000 reported hospital admissions for firearm injuries between 2003 and 2013.[4]

Interpersonal violence disproportionately affects the African American population. Homicide is the leading cause of death for African American males ages 15-34.[5] In 2014, homicide accounted for 48% of deaths among African American males ages 15-24.[5] In contrast, homicide accounted for 7.6% of deaths among white males aged 15-24, although it was still the third leading cause of death in that population.[6] In a study of children injured by firearms in the US, young African American males were admitted to the hospital for firearm injury 10 times as often as their white male counterparts.[7]

In St. Louis City the incidence of violent crime and firearm injury is significantly higher compared to the rest of the US. In 2016 the rate of violent firearm deaths was more than 14 times that of the national average.[8,9] In 2016, 1,601 firearm assaults occurred in St. Louis City,[10] and the violent crime rate was five times the US average.[11] In 2014, the rate of violence perpetrated against African Americans in Missouri was double that of the national average.[12]

Firearm injuries in the local pediatric population are also high. St. Louis City ranks second in firearm mortality in the 10 to 19 year old age group (50/100,000 people annually), while St. Louis County and surrounding suburbs ranked ninth in the nation.[13] A study performed at the two pediatric Level I Trauma Centers in St. Louis over a period of five years in children aged 16 and younger revealed that most non-accidental pediatric firearm injuries occurred among children aged 14 to 16 years, of whom 91% were African American. Over one-third of the firearm injuries were localized in seven of 94 ZIP Codes in St. Louis City and County.[14]

Additionally, victims of assault and penetrating trauma are likely to be re-victimized and to perpetrate violence against others.[15] Patients affected by penetrating trauma are more likely to return to the ED with new penetrating trauma than those presenting with blunt trauma; re-presentation for penetrating trauma correlates with an increased likelihood of death with each subsequent ED visit.[16] Multiple studies have also shown that re-victimization rates for patients presenting to a Level I Trauma Center for penetrating trauma range from 44-52%, with an average of 2.6 traumatic incidents.[17,18,19] Patients who have two presentations for penetrating trauma have a re-victimization rate as high as 77%.[16] Furthermore, patients admitted for firearm injuries were found to have a 15% likelihood of arrest for violence-related crime versus 1% for patients hospitalized for non-violent injuries over a five year follow-up period.[20]

Importance

The leading cause of death for African American males aged 15-34 in the Midwest is homicide.[21] Given the societal and financial costs of firearm violence and death, there is a need to better characterize the patients who sustain firearm injuries in our region, as they are likely at high risk for re-victimization and perpetration of violence. Currently there is a dearth of data describing victims of firearm violence in St. Louis, particularly among the adult population. Multiple professional organizations have called for additional research and intervention into firearm injury and death,[22] culminating in a 2017 call for a consensus-driven agenda for emergency medicine firearm injury prevention research from the Annals of Emergency Medicine.[23]

Goals of this Investigation

The goal of this investigation was to better describe characteristics of patients who present to the ED with firearm injury, and to compare our local population with previous data on violently injured patients.

Our secondary objective was to identify both patients who had sustained previous firearm injuries and those who re-presented to the ED with new firearm injuries within one year of index injury. By identifying this cohort at highest risk for recidivistic firearm injuries, hospitals and health care systems can use the ED as an access point to provide social work, case work and counseling-based interventions to help disrupt the cycle of violence.

Methods

Study Design and Setting

This is a single-center cross-sectional study of patients aged 14-81 in an urban, academic, Level I Trauma Center tertiary care ED with more than 95,000 patient visits per year in St. Louis, Missouri. This hospital serves St. Louis City, St. Louis County and the surrounding region.

This observational study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies.[24] This study was approved by the institutional review board at Washington University in St. Louis.

Selection of Participants

We reviewed the medical records of 1386 consecutive patients who presented to the Barnes-Jewish Hospital ED between July 1, 2014 and June 30, 2016 with a triage chief complaint or ICD-9 or ICD-10 diagnosis code of "gunshot wound" (our institution transitioned from ICD-9 to ICD-10 during the study period). Inclusion criteria required that the firearm injury occurred within 72 hours of initial presentation. Our sample included patients who were transferred from other hospitals. Participants were included whether the firearm injury was thought to be accidentally or intentionally self-inflicted or inflicted by another person. Patients who presented with firearm injuries multiple times during the study period were included in this patient series once at the time of their first ED presentation.

Data were collected on patients identified by query of the ED electronic medical record (EMR). Variables were defined before data extraction and placed in a standardized format during the data collection process. All data were collected by two medical students (TD, CS) who were blinded to the primary outcomes of this study.

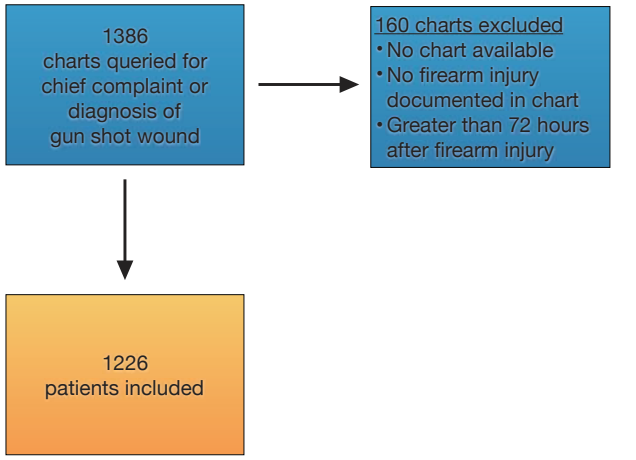
Measurements

The following data points were collected: gender (male, female), race (African American, Caucasian, Asian), age, psychiatric history (yes, no), insurance status (none, Medicare/Medicaid, private, local temporary healthcare program), employment status (unemployed, employed, student, retired, disabled), religious affiliation (none, Protestant/Baptist, Catholic, Jewish, Muslim), whether the firearm injury was self-inflicted (intentionally or accidentally), number of prior firearm injuries (zero, one, two, three or more), other previous traumatic injuries (yes, no), history of non-firearm assault (yes, no), disposition from the ED (discharged, operating room, intensive care unit, floor, expired, left against medical advice, transferred), and ZIP Code of residence. Data point sources included any physician, nursing, social work or administrative documentation present in the EMR. If the ED chart from the index visit did not contain all data points of interest, previous records from the EMR were reviewed in reverse-chronologic order to complete data collection. Outcome data comprised subsequent ED visits for a new firearm injury within one year of the initial firearm injury.

Analysis

Categorical variables were presented as counts and percentages. The only continuous variable, age, was presented as the median and inter-quartile range due to its non-normal distribution. We compared demographic and follow-up parameters between patients with and without a history of a firearm injury. Univariate odds ratios were calculated with 0.5 added to cells with a count of 0, and p-values reported correspond to chi-squared (c^2) and Fisher exact tests. Statistical analyses for this paper were generated using SAS software, Version 9.4 of the SAS System for Windows. Copyright © 2013 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks of SAS Institute Inc., Cary, NC, USA.

Figure 1. Cohort inclusion matrix of 1226 patients who presented to the ED for firearm injury between July 1, 2014 and June 30, 2016.



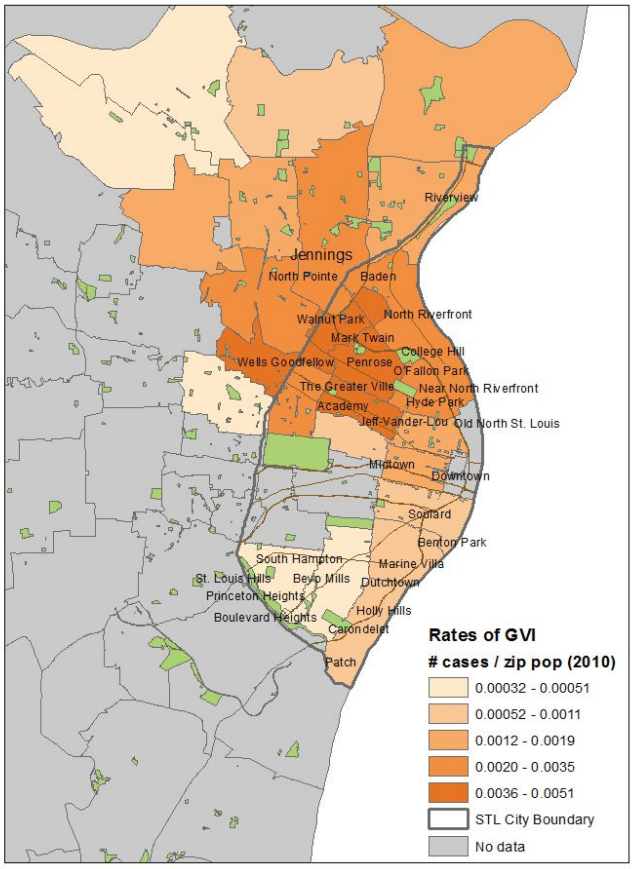
Outcomes

The study's primary outcome was to describe the demographic and clinical history of patients presenting to the ED with firearm injuries. Secondary outcomes included identifying risk factors for re-presentation to the ED with a new firearm injury within one year of the index injury.

Results

Query of the EMR resulted in 1386 unique records; 1226 patients met criteria for inclusion in our study (Figure 1). We excluded 160 charts for the following reasons: (1) no documentation or chart present within the EMR; (2) no firearm injury was documented in the chart; or (3) ED presentation was not related to a firearm injury within the last 72 hours. Inter-rater reliability was calculated for all data points from a sample of the first and last 10% of patients in this dataset; the overall inter-rater reliability was 93%. For the primary outcomes of sex, age, race, whether the firearm injury was self-inflicted or not, and number of prior firearm injuries, the inter-rater reliability score was 96%.

Figure 2. Firearm injuries by ZIP Code of 1226 patients who presented to the ED for firearm injury between July 1, 2014 and June 30, 2016.



Characteristics of Study Subjects

Patient demographics are described in Table 1. Eighty-eight percent of patients presenting to the ED for firearm injury were male and 89% were African American. The median age was 26 years. Ninety percent of patients had no documented psychiatric history. Just over half of patients did not have medical insurance, and less than half identified a religious affiliation. Twenty-three percent were unemployed, although employment data was not documented in the EMR on 41% of patients.

Eight Percent of Firearm Injuries Were Self-Inflicted

Forty-eight percent of patients had a history of other prior accidental injury, which included non-assault related trauma such as motor vehicle accidents, and 20% of patients had history of another non-firearm assault. Forty-seven percent of patients in the study cohort were discharged home from the ED and 93% of patients survived their hospitalization (Table 2). Many patients in this cohort lived in a concentrated geographic region in north St. Louis (Figure 2).

Table 1. Demographics and characteristics of 1226 patients who presented to the ED for firearm injury between July 1, 2014 and June 30, 2016.

Sex, No. (%)	
Male	1076 (88)
Female	150 (12)
Race, No. (%)	
African American	1097 (89)
Caucasian	113 (9)
Asian	2 (0)
Not documented	14 (1)
Age	
Age, median (IQR), y	26 (22-35)
Age range, y	14-81
Psychiatric history, No. (%)	
No	1100 (90)
Yes	96 (8)
Not documented	30 (2)
Insured status, No. (%)	
None	644 (53)
Medicare/Medicaid	203 (17)
Private	221 (18)
Local temporary healthcare program	21 (2)
Not documented	137 (11)
Employment, No. (%)	
Unemployed	286 (23)
Employed	366 (30)
Student	40 (3)
Retired	11 (1)
Disabled	25 (2)
Not documented	498 (41)
Religion, No. (%)	
None	665 (54)
Protestant/Baptist	380 (31)
Catholic	32 (3)
Jewish	1 (0)
Muslim	12 (1)
Not documented	136 (11)
Self-inflicted firearm injuries, No. (%)	
Injury not self-inflicted	1132 (92)
Injury self-inflicted, unintentional	73 (6)
Injury self-inflicted, intentional	21 (2)
Number of prior firearm injuries, No. (%)	

History of Firearm Injury

Table 3 describes the 173 patients who had a history of prior firearm injury and risk factors for firearm injury. Patients in this group were more likely to be male (98%) African American (99%), uninsured (67%), and unemployed (34%). Those with previous firearm injury were also more likely to have experienced other accidental trauma and non-firearm related assault compared to those without a history. Five of these patients had sustained three or more separate prior firearm injuries. There was

Table 2. Disposition from the ED of 1226 patients who presented to the ED for firearm injury between July 1, 2014 and June 30, 2016.

	No. (%)
Discharged	581 (47)
Operating room (OR)	270 (22)
Intensive care unit (ICU)	88 (7)
Floor	223 (18)
Expired	55 (4)
Left against medical advice	8 (1)
Transferred	1 (0)

*3% of patients died in the OR or ICU after disposition from the ED

more lifetime firearm injuries). Patients in this subgroup were more likely than those without a history to re-contact the health care system again through outpatient follow up (69%) and repeat ED visits (43%).

Discussion

Firearm injuries are now an endemic public health threat in the US. Firearm violence is among the leading causes of death for young adults.[25] Recent research has shown that gun violence spreads through a community in a similar manner to contagious disease.[26] St. Louis is at the epicenter of this disease progression.[8,10,11]

Our data correlate with previous work that indicate young, African American men are disproportionately more likely to be shot and more likely to die from firearm injuries than their white male counterparts. Previous work in our region cited an average of 80 children aged 16 and younger presenting with firearm injury to the pediatric Level I Trauma Centers per year.[27] Over seven times as many adult patients present to our institution's ED per year, and these data do not include adults who have presented to other regional trauma centers. The majority of these patients are under the age of 35, indicating that risk for firearm injury increases from adolescence. The results of our research can be generalized to other large, urban academic EDs, especially those in areas with higher rates of interpersonal violence.

Table 3. Comparison of demographics between patients who had prior history of firearm injury and those who did not in 1226 patients who presented to the ED for firearm injury between July 1, 2014 and June 30, 2016.

	History of prior firearm injury (No. = 173)	No history of prior firearm injury (No. = 1053)	OR (95% CI)	P value
Age, median (IQR), y	26 (26-31)	26 (22-36)		
Male, No. (%)	169 (98)	907 (86)	6.8 (2.5-19)	<0.001
African American, No. (%)	171 (99)	925 (88)	11.8 (2.9-48)	<0.001
Prior psychiatric history, No. (%)	10 (6)	86 (8)	0.7 (0.3-1.3)	0.24
Uninsured, No. (%)	116 (67)	528 (50)	2.0 (1.4-2.8)	< 0.001
Unemployed, No. (%)	59 (34)	227 (22)	2.1 (1.4-3.2)	<0.001
No religious affiliation, No. (%)	99 (57)	566 (54)	1.0 (0.7-1.4)	0.86
Injury not self-inflicted, No. (%)	170 (98)	962 (91)	5.4 (1.7-17)	0.001
History of other accidental trauma, No. (%)	110 (64)	482 (46)	2.1 (1.5-2.9)	<0.001
History of non-firearm assault, No. (%)	54 (31)	188 (18)	2.1 (1.5-3.0)	<0.001
Returned for outpatient follow-up visit, No. (%)	98 (57)	496 (47)	1.3 (0.9-1.9)	0.15
Returned to ED for any reason (except new firearm injury) within 90 days of index visit, No. (%)	69 (40)	281 (27)	1.7 (1.2-2.4)	0.001

no difference in psychiatric history or religious affiliation between these groups. Patients with a previous firearm injury were more likely to return to the ED (40%) compared to those with no history of a previous firearm injury.

Re-Injury

Of the 1,139 patients who survived their initial hospital visit, 35 (3%) returned to our ED within one year with a new firearm injury (Table 4). All these patients were African American males, with a median age of 23 years old. One patient suffered three separate firearm injuries within the one-year follow-up period. Although the number of patients in this group was small, they also skewed towards a higher prevalence of uninsured (66%), unemployed (31%), and without religious affiliation (69%) compared to those who did not return to the ED with a new firearm injury. There was no difference in psychiatric history between the groups. Nine of these patients with firearm re-injury had a history of previous non-firearm assault. A different subset of nine patients had a history of previous firearm injury (three or

Violence Begets Violence

Our data support the supposition that some patients who present with firearm injury return with penetrating trauma on subsequent ED visits.[16] The literature suggests that urban trauma victims are more likely to need hospitalization and thus incur further healthcare expenses for subsequent violence-related injuries.[28] Our data also support

Table 4. Comparison of demographics and follow-up between patients who sustained a new firearm injury within one year of index injury and those who did not in the 1138 patients who survived initial hospital presentation for firearm injury between July 1, 2014 and June 30, 2016.

	History of new firearm injury (No. = 35)	No history of new firearm injury (No. = 1103)
Sex, No. (%)		
Male	35 (100)	963 (87)
Female	0 (0)	140 (13)
Race, No. (%)		
African American	35 (100)	982 (89)
Caucasian	0 (0)	106 (10)
Asian	0 (0)	2 (0)
Not documented	0 (0)	13 (1)
Age		
Age, median (IQR), y	23 (21-26)	26 (22-35)
Age range, y	17-43	1-81
Insured status, No. (%)		
None	23 (66)	591 (54)
Medicare/Medicaid	7 (20)	189 (17)
Private	4 (11)	209 (19)
Local temporary healthcare program	0 (0)	21 (2)
Not documented	1 (3)	93 (8)
Employment, No. (%)		
Unemployed	11 (31)	262 (24)
Employed	15 (43)	341 (31)
Student	1 (3)	39 (4)
Retired	0 (0)	11 (1)
Disabled	1 (3)	24 (2)
Not documented	7 (20)	426 (39)
Religion, No. (%)		
None	24 (69)	610 (55)
Protestant/Baptist	8 (23)	357 (32)
Catholic	1 (3)	31 (3)
Muslim	0 (0)	11 (1)
Not documented	2 (6)	94 (9)
Psychiatric history, No. (%)		
No	33 (94)	1017 (92)
Yes	2 (6)	85 (8)
Not documented	0 (0)	1 (0)
Self-inflicted firearm injuries, No. (%)		
Injury not self-inflicted	33 (94)	1021 (93)
Injury self-inflicted, unintentional	2 (6)	71 (6)
Injury self-inflicted, intentional	0 (0)	11 (1)

previous work that young, African American males who are victims of firearm injury are at higher risk for recurrent violent injury and death than victims in other racial and age demographics.[17,29] We found that these young men often lack potentially protective factors such as employment, health insurance and religious affiliation. However, there continues to be a paucity of firearm research at the regional, state and national level. Additional data are needed to understand the factors that contribute to firearm injury and re-injury in our region.

By characterizing the patients who present to the ED with firearm injury, we enable hospital-based violence intervention programs targeted at reducing violent re-injury in high-risk patients. In previous studies young males living in disadvantaged demographic areas or areas which experienced high levels of firearm violence were at higher risk of injury and re-injury; these findings were supported by our work which identified that a majority of patients presenting to the ED with firearm injuries lived in a concentrated geographic area in north St. Louis.[34,35]

Five hundred and ninety-two (48%) patients in this sample had contact with the health care system for a traumatic injury prior to their index firearm injury. ED visits for traumatic injury represent an opportunity to provide social work, case work, and counseling-based interventions to help disrupt the cycle of violence in high-risk individuals. Moving forward, these data will inform the launch of a St. Louis region-wide hospital-based violence intervention, Life Outside of Violence, which will provide such interventions to patients at risk for violent injury. This program will begin enrolling patients in the summer of 2018.

Limitations

This study was limited by its single center, retrospective design as availability of relevant data depended upon thorough documentation in the EMR by physicians, nurses, social workers and other hospital workers. Re-injury rates were likely underestimated, as data were not available on patients who presented to other hospitals with new injuries or those who died from their injuries in the pre-hospital environment. Additionally, one year post-index presentation is a narrow window to evaluate for firearm re-injury as compared to existing literature. Further region-wide study is needed to better delineate the burden of firearm disease and areas for targeted intervention.

References

1. [dataset] Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). Assault Firearm Gunshot Nonfatal Injuries and Rates per 100,000, 2010 - 2015, United States, All Races, Both Sexes, All Ages. Atlanta, GA: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, https://www.cdc.gov/ncipc/wisqars.

2. [dataset] Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). Homicide Firearm Deaths and Rates per 100,000, 2010-2015, All Races, Both Sexes, All Ages. Atlanta, GA: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, https://www.cdc.gov/ncipc/wisqars.

3. Naghavi M, Abajobir A, Abbafati C, et al. Global, regional, and national age-sex specific mort ality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;10100:1151-1210. DOI: https://doi.org/10.1016/S0140-6736(17)32152-9.

4. Peek-Asa C, Butcher B, Cavanaugh JE. Cost of hospitalization for firearm injuries by firearm type, intent, and payer in the United States. Injury Epidemiology. 2017;4:20. doi:10.1186/s40621-017-0120-0.

5. [dataset] Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). All Victims Death Counts and Rates per 100,000, 2010-2015, All Intents, Mechanism: Firearm, All Races, Both Sexes, All Ages. Atlanta, GA: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, https://www.cdc.gov/ncipc/wisqars.

6. [dataset] Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). All Victims Death Counts and Rates per 100,000, 2010-2015,
Suicide, Mechanism: Firearm, All Races, Both Sexes, All Ages. Atlanta, GA: National

1 Picture = 1000 Words

Murder Rate & Violent Crime in USA Much Lower Than 1990-1992

These statistics from 2016 are the latest available from FBI data. Violent crime rate follows a similar dramatic fall from 1990-1992. World-wide, "There was an annualized decrease of 0.9% in the global rate of age-standardized firearm deaths from 1990-2016"

Source: Global Mortality From Firearms, 1990-2016 JAMA 2018;320:792-814



Center for Injury Prevention and Control, Centers for Disease Control and Prevention, https://www.cdc.gov/ncipc/wisqars.
7. Elnour AA, Harrison J. Lethality of suicide methods. Injury Prevention. 2008;14(1):39-45. doi:10.1136/ip.2007.016246.
8. [dataset] Centers for Disease Control and Prevention (2018). Stats for the State of Missouri. Firearm Deaths 2014-2015. Atlanta, Georgia: National center for Health Statistics. https://www.cdc.gov/nchs/pressroom/states/missouri/missouri.htm
5. [dataset] Centers for Disease Control and Prevention (2017). Leading Causes of Death (LCOD) by Age Group, Black Males-United States, 2014*. Hyattsville, Maryland: Office of Minority Health & Health Equity (OMHHE), https://www.cdc.gov/healthequity/lcod/men/2014/black/index.htm.
6. [dataset] Centers for Disease Control and Prevention (2017). Leading Causes of Death (LCOD) by Age Group, White Males-United States, 2014*. Hyattsville, Maryland: Office of Minority Health & Health Equity (OMHHE), https://www.cdc.gov/healthequity/lcod/men/2014/white/index.htm.
7. Leventhal JM, Gaither JR, Sege R. Hospitalizations due to firearm injuries in children and adolescents. Pediatrics. 2014;133(2):219–225.
8. [dataset] St. Louis Metropolitan Police Department. 2016 Uniform Crime Reporting Homicide Analysis. St. Louis, Missouri. http://www.slmpd.org/images/2016_Homicide_Stats_for_Website.pdf.
9. [dataset] US Census Bureau (2016). Annual Estimates of the Resident Population: April 1, 2010 to July 1, 2016. U.S. Census Bureau, Population Division. https://factfinder.census.gov/faces/nav/jsf/pages/community_facts.xhtml.
10. [dataset] St. Louis Metropolitan Police Department. Crime Comparison Based on UCR Reporting All Neighborhoods, 2015 & 2016. St. Louis, Missouri. http://www.slmpd.org/crimestats/CRM0013-BY_201609.pdf
11. [dataset] FBI Uniform Crime Reporting. 2016 Crime in the United States: Missouri, Offenses Known to Law Enforcement by City, 2016. Federal Bureau of Investigations. https://ucr.fbi.gov/crime-in-the-u.s/2016/crime-in-the-u.s.-2016/tables/table-6/table-6-state-cuts/missouri.xls
https://ucr.fbi.gov/crime-in-the-u.s/2016/crime-in-the-u.s.-2016/topic-pages/violent-crime
12. [dataset] Langley M, Sugarmann J. Black Homicide Victimization in the United States: an analysis of 2011 Homicide data. Violence Policy Center (2014). http://www.vpc.org/studies/blackhomicide14.pdf
13. [dataset] Centers for Disease Control and Prevention (2011). Violence-related firearm deaths among residents of metropolitan areas and cities. http://www. cdc.gov/mmwr/preview/mmwrhtml/mm6018a1.htm?s_cid=mm6018a1_w.
14. Choi PM, Hong C, Bansal S, et al. (2016). Firearm injuries in the pediatric population. J Trauma Acute Care Surg. 2016; 80(1);:64-69. doi:10.1097/ta.0000000000000893
15. Kubrin CE, Weitzer R. Retaliatory homicide: Concentrated disadvantage and neighborhood culture. Soc Probl. 2003;50(2):157-180.
16. Brooke BS, Efron DT, Chang DC, et al. Patterns and Outcomes Among Penetrating Trauma Recidivists: It Only Gets Worse. J Trauma. 2006;61(1):16-20. doi:10.1097/01.ta.0000224143.15498.bb.
17. Morrissey TB, Byrd CR, Deitch EA. The incidence of recurrent penetrating trauma in an urban trauma center. J Trauma, 1991. 31(11): p. 1536-8.
18. Sims DW, Bivins BA, Obeid FN, et al. Urban trauma: a chronic recurrent disease. J Trauma, 1989. 29(7): p. 940-6; discussion 946-7.
19. Goins WA, Thompson J, Simpkins C. Recurrent intentional injury. J Natl Med Assoc, 1992. 84(5): p. 431-5.
20. Rowhani-Rahbar A, Fan MD, Simonetti JA, et al. Violence perpetration among patients hospitalized for unintentional and assault-related firearm injury. Ann Intern Med. 2016;165(12):841. doi:10.7326/m16-1596.
21. [dataset] Centers for Disease Control and Prevention (2017). Leading Causes of Death (LCOD) by Age Group, Black Males-United States, 2014. Hyattsville, Maryland: Office of Minority Health & Health Equity (OMHHE), https://www.cdc.gov/healthequity/lcod/men/2014/black/index.htm
22. Weinberger SE, Hoyt DB, Lawrence HC, et al. Firearm-related injury and death in the united states: a call to action from 8 health professional organizations and the American Bar Association. Ann Intern Med. 2015;162:513–516. doi: 10.7326/M15-0337
23. Ranney ML, Fletcher J, Alter H, et al. A Consensus-Driven Agenda for Emergency Medicine Firearm Injury Prevention Research. Ann Emerg Med. 2017;69(2):227-240. doi:10.1016/j.annemergmed.2016.08.454.
24. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147(8):573-7.
25 .Wintemute GJ. The Epidemiology of Firearm Violence in the Twenty-First Century United States. Annual Review of Public Health. 2015;36(1):5-19. doi:10.1146/annurev-publhealth-031914-122535.
26. Green B, Horel T, Papachristos AV. Modeling Contagion Through Social Networks to Explain and Predict Gunshot Violence in Chicago, 2006 to 2014. JAMA Intern Med. 2017;177(3):326–333. doi:10.1001/jamainternmed.2016.8245
27. Choi PM, Hong C, Bansal S. Firearm injuries in the pediatric population. Journal of Trauma and Acute Care Surgery. 2016;80(1):64-69. doi:10.1097/ta.0000000000000893.
28. Buss T, Abdu R. (2018). Repeat Victims of Violence in an Urban Trauma Center. Violence Vict, 1995;10(3):183-94.
29. Strong B, Greene C, Smith G. Trauma Recidivism Predicts Long-term Mortality. Ann Surg, 2017; 265(5), pp.847-853.
34. Carter, P., Cook, L. and Macy, M. (2017). Individual and Neighborhood Characteristics of Children Seeking Emergency Department Care for Firearm Injuries Within the PECARN Network. Academic Emergency Medicine, 24(7), pp.803-813.
35. Gibson P, Ippolito J, Shaath M. Pediatric gunshot wound recidivism. Journal of Trauma and Acute Care Surgery. 2016;80(6):877-883. doi:10.1097/ta.0000000000001072.

Disclosure

None reported.

MM

The Potential of Quantum Computing and Machine Learning to Advance Clinical Research and Change the Practice of Medicine

by Dmitry Solenov, PhD, Jay Brieler, MD & Jeffrey F. Scherrer, PhD

We may be at the dawn of a revolution in computing. At this time we can only point to experiments and speculate how quantum computing could improve imaging, diagnosis, treatment, and population health.



Dmitry Solenov, PhD, (above), is in the Department of Physics, Saint Louis University, St. Louis, Missouri. Jay Brieler, MD, and Jeffrey F. Scherrer, PhD, are in the Department of Family and Community Medicine, Saint Louis University School of Medicine, St. Louis, Missouri.
Contact: dmitry.solenov@slu.edu

Introduction

We may be at the advent of a revolution in computer applications in clinical care and medical research. Quantum computing can exponentially advance computational power and promises to usher in a new epoch in computing technology. Quantum computing compared to current computing could be what the first personal computer was to Charles Babbage's 1833 primitive computer the 'difference engine".

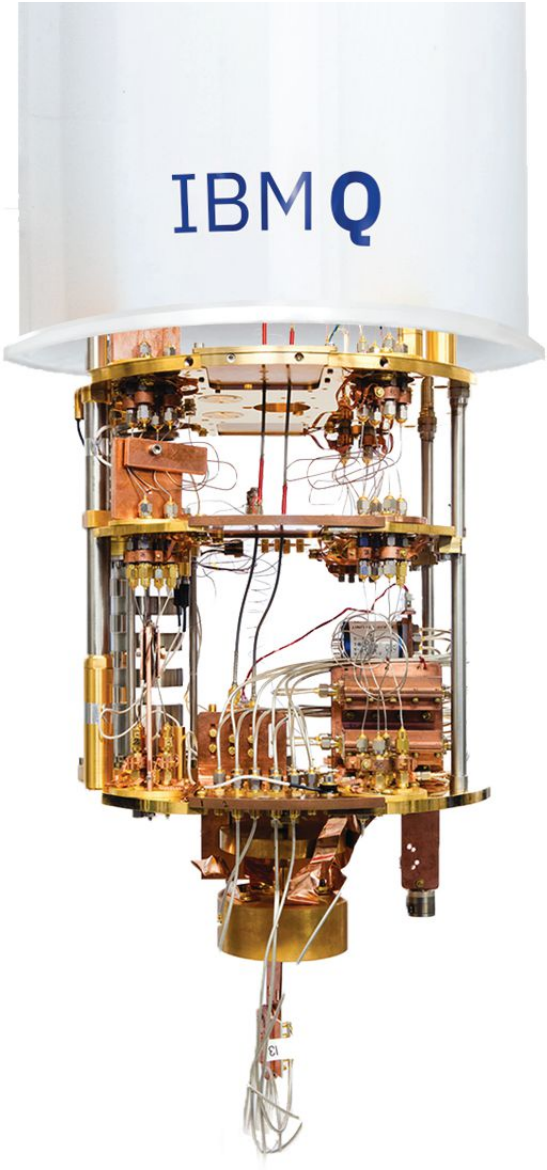
A Patient Encounter in the Age of Quantum Computing

Ms. Jones is at her annual follow-up for long term cancer screening. She had tissue sparing breast cancer surgery 20 years ago and has since been cancer free. Today she goes to the high speed imaging center and meets with her physician, Dr. Doe, 20 minutes after the scan. Dr. Doe brings up results of her imaging on the electronic health record. Ms. Jones is calm as all her medical records are secured with unbreakable quantum encryption. The quantum imaging software identified a $1/10^{th}$ mm square cluster of cancer cells near her original surgery site. Due to her history and after confirmation by the radiologist, Ms. Jones is scheduled for high precision radiation treatment the following week. A quantum computer is used to direct a radiation beam that destroys the cancer cells with extreme precision and spares all surrounding tissue. This rapid detection of a tiny cluster of cancer cells and their destruction is one of many potential advances in medicine that could occur pending the realization of quantum computing.

Many people are familiar with IBM's Watson computer which famously beat past Jeapordy! champions in 2011, or Google's AlphaZero machine learning chess algorithm that soundly defeated the best brute force computer chess champion in 2017. In 2018, IBM Watson Health now promises to provide more efficient patient care, population health, improved quality and earlier diagnoses, such as finding cancer at an early stage.[1] These services are possible because Watson has been fed the American College of Physician Medical Knowledge Self-Assessment study guide and the Merk Manual of Diagnosis and Therapy.[2] The

computational power to generate diagnoses in real time or to increase the precision of imaging to detect early stages of cancer may soon push beyond the limits of the standard binary 0/1 system available to Watson. Private industry (Google, IBM, etc.) and government agencies are already investing into quantum computing and artificial intelligence systems to make this happen. Thus, IBM may be one of the first to impact health care through quantum computing or artificial intelligence.

Figure 1. An IBM Quantum Computer
Source: https://www.research.ibm.com/ibm-q/network/



What is Quantum Computing and Why is it Different than Our Current Computer Technology?

Quantum computing is a revolutionary concept in digital data processing based on the fundamental principles by which nature operates, i.e. quantum mechanics. With advancements in physics in the early 20th century, methods of observation and purity of materials reached the level at which some quantum phenomena became detectable. The best example of this is a regular transistor present in every modern computer or device. It operates by directing large clouds of carriers of electrical current using engineered materials and quantum-based principles (band structure, localized states, etc.). They produce behavior unusual for naturally found materials – an ability to precisely control current with current, or current via light, or light via current.

Recently, miniaturization of transistors, detectors, and, at the same time, access to extremely low temperatures (such as -273C) have opened the possibility to operate, observe, and, most importantly, isolate individual particles with their inherently quantum properties. These properties are one reason the desktop or laptop computers we use have little resemblance to quantum computers (see Figure 1). Even though theoretically established for over 100 years, these properties have only recently been observed and verified over a wide range of particles and systems. While being nonsense in our daily experience, quantum mechanics has already led to dramatic advances in a few specific areas in medicine (e.g., MRI, laser surgery) with potential to revolutionize medical research and clinical care.[3] Because modern computers have largely saturated computational power and no longer grow exponentially as occurred in the last century, quantum computing, if realized, is the most promising technology for major advancements in processes currently beyond the reach of existing computing power.[4]

All currently known and beneficial quantum algorithms that can run on quantum computers are based on the ability of the quantum system, upon certain rearrangement, to behave in unison. The system of many (quantum) particles, each holding a bit of information, behave as one – a property based

on so-called quantum entanglement. For this reason, large chunks of data can be processed at once, operating essentially on only a few particles, that is, in a massively parallel manner. This will allow tasks[5-7] that would require centuries of computing on a standard computer to require only a few minutes on a quantum computer.

A key challenge for quantum computers is to provide and maintain isolation of individual quantum particles (qubits, illustrated in Figure 2) involved in computation. Extreme and stable cooling is required to make wire circuits (or circuits made of other materials) behave in a quantum fashion. Cooling superconducting systems to about a 10 thousands of a degree above absolute zero creates the needed degree of isolation[8] to form computational quantum particles (qubits). Operated by electrical signal from a classical computer, these systems must be maintained at these extreme low temperatures by a large refrigeration apparatus involving a rare helium-3 isotope. In these extreme conditions, quantum particles (qubits) remain sufficiently isolated, or coherent, for about 0.1 ms – a 10 thousands of a second.[9] Some other systems based on natural and artificial atoms rather than metal wires have also reached similar isolation and operability.[10,11]

At this time quantum computing is an academic domain with users able to access and run programs in the cloud using 'IBM Q'. Yet larger and larger quantum computing devices have become commercially available[12] and can perform a small number of operations on a relatively small number of quantum particles (qubits). Most of these systems are based on superconducting technology and can contain up to about 100 qubits. Some quantum computational devices have even been made publically available for the research community to test and investigate small quantum codes via web interfaces (e.g., IBM Q). All currently available quantum computational devices, however, are far from a functioning quantum computer as they are not yet able to run large codes or work with 'big data'.

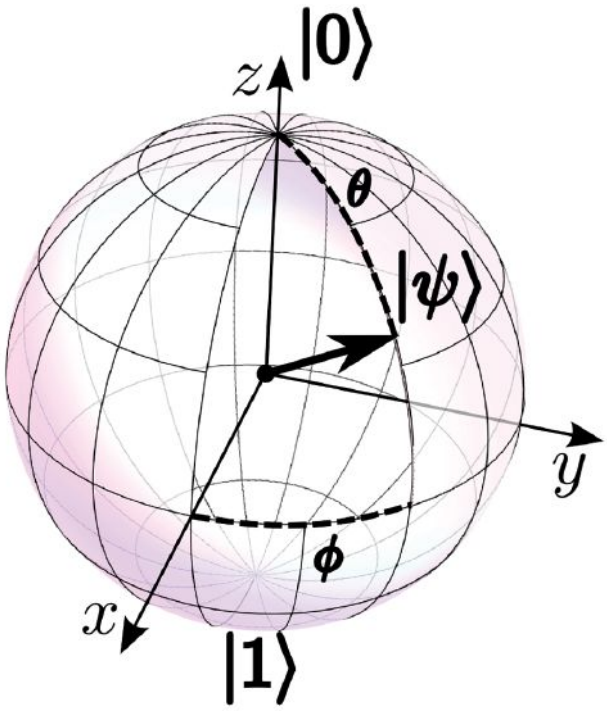


Figure 2. A computational quantum particle – qubit – represented as a unit (Bloch) sphere. Unlike regular bit that takes values of 0 or 1, a qubit can take any values on a sphere, as represented by two angles. The poles correspond to classical 0/1 bit values.

An important exception is one area of quantum computing - quantum cryptography.[13] With significant government investments (NSA, DOD, DOE), quantum cryptography is being already used to secure communications.[14-16] Standard encryption methods rely on a keycode for the user to access encrypted data. However, the key must be shared and can be decoded by unauthorized persons seeking to 'hack' a system. With quantum computing, the key and the data can be secured indefinitely with guaranteed unbreakable encryption. Such strong security is possible because quantum encryption relies on the laws of nature (quantum mechanics) to furnish it. Thus, cryptography is expected to be the first application of quantum computing to enter medical practice to secure medical records and communication.

If Quantum Computing Becomes Available for Daily Use What Can We Expect to Change in Medical Research and Delivery of Care?

Big data research and machine learning is likely to be one of the fields to advance quickly with the advent of real world functional quantum computers. Beam and Kohane[17] provide an excellent description

of machine learning, noting that there is a machine learning spectrum which runs from how much a predictive algorithm is driven by human decisions vs. decisions based on data. A statistical model requires human decisions about variable definitions and their inter-relationships. In machine learning, there are few assumptions and algorithms are derived by computer programs that evaluate millions of data elements and all their potential directions of effect and interactions. The more an algorithm is derived from raw data and with less human input, the more it fits into machine learning. Machine learning that informs clinical practice in real time depends on growing databases containing constantly updating medical record information and linked to other sources of data (e.g. wearable technology). To deal with this complexity future machine learning programs will require computational power of quantum computing to deliver results in real time. With more data informing predictive models and quantum computer power, the clinician may be able to select a therapy perfectly suited to an individual patient based on models continuously running and updated to predict treatment response while accounting for the numerous patient characteristics (race, age, gender, comorbidities, co-medications, genetic make-up, etc.) which contribute to outcomes.

With the first quantum computing devices becoming operational in around 2000, Parsons[18] speculated that quantum computing applications would generate a new era in medical imaging. It is expected that a quantum MRI machine will generate extremely precise imaging allowing visualization of single molecules.[3] Using artificial intelligence, quantum computing can be applied to interpreting diagnostic images. Not only will image detail be exponentially improved but the physician can be aided in interpreting results because efficient machine learning can train a quantum computer to identify abnormal findings with precision better than the human eye.[2]

In cancer treatment, quantum computing will contribute to improved therapies. Computers are currently used to deal with the thousands of variables used to develop a radiation plan that targets cancer cells without damaging healthy ones.[19] Quantum computers would allow rapid and more precise radiation plans and allow comparisons between all possible approaches. The end result would be an ideal radiation dose pointed at the right target and thus lead to more effective treatment with reduced side effects.[19,20]

Machine learning and artificial intelligence have been used with traditional computing resources to interpret CT scans, aid surgical procedures and to analyze big data to develop predictive models of disease. Gulshan et. al.[21] used machine learning and nearly 10,000 retinal images to create an algorithm that can detect diabetic retinopathy with high sensitivity and specificity. The authors note that this is an experimental design with no known clinical utility. If programs such as the one created by Gulshan and colleagues[21] had the computational power of quantum computing, one could imagine running an algorithm in real time to help physicians accurately detect retinopathy, possibly at an earlier stage.

Machine learning holds great promise in eliminating most diagnostic errors related to reading imaging. Dilsizian and Siegel[2] describe how artificial intelligence can overcome the source of diagnostic errors in medical imaging. Computers overcome human sources of error such as: being stuck on initial impression, over-reliance on context, drawing quick conclusions based on a previous case and failure to consider other answers once a conclusion is made.

The volume of material and speed of new research discoveries is overwhelming. Even the best attempts at providing guideline driven, evidence-based medicine are challenged by the rapid creation of new evidence. Combining big data with quantum computing will provide access to the current evidence and enable meaningful use of the electronic data continuously generated in the delivery of care. Realization of personalized medicine will need to draw on analysis of mega-data and bring together measures of physiology, imaging, genomics, wearable technology, screening measures, patient records, environment measures and more.[20]

Quantum computing holds no value to medicine

without the parallel increase in availability of clinically meaningful data from numerous sources. Challenges to realizing a healthcare system where quantum computing uses decades of data from billions of clinical encounters and recommends a specific medication for a patient presenting with new onset depression, cancer, diabetes or any condition, will be overcome when data can be merged from multiple sources including existing patient data networks, bio-banks, and wearable health devices, etc.

Will the future include visits to virtual physicians? Most patients expect more than a pill when they seek care. Particularly when treatment involves greater risk as in surgery and when treatment effectiveness requires patient adherence to complex regimens. Quantum computing does not replace the doctor-patient relationship, transparency and trust required in shared decision making. Nor will a computer replace the ability of a physician to offer encouragement, empathy, social support and most importantly providing words of encouragement and a pat on the back, a handshake, a smile and even a hug. We must never underestimate the power of the social contract patients make with physicians and the support of doctors, nurses, staff play in healing. Computer algorithms, whether run on a "traditional computer" or a future quantum laptop computer, do not have feelings and will never be able to provide the impact of a surgeon's promise to "get you through this procedure" or the reinforcing effects of a primary care provider's encouragement to "walk just another 5 minutes" to enhance your health.

Summary

We may be at the dawn of a revolution in computing. At this time we can only point to experiments and speculate how quantum computing could improve imaging, diagnosis, treatment, and population health. It is yet to be determined if and when quantum computers will be accessible for daily use in medicine and research. We have numerous examples of machine learning algorithms and artificial intelligence that may leverage the power of quantum computing to deliver real time results. Until this level of access is available, quantum computing will remain the domain of researchers, not physicians.

References

1. IBM Watson Health: Enable Effective Care. https://www.ibm.com/watson/health/value-based-care/enable-effective-care/. Accessed April 1, 2018, 2018.
2. Dilsizian SE, Siegel EL. Artificial Intelligence in Medicine and Cardiac Imaging: Harnessing Big Data and Advanced Computing to Provide Personalized Medical Diagnosis and Treatment. Curr Cardiol Rep. Jan 2014;16(1).
3. Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and medicaid insurance plans: The TROUP Study. Pain. Aug 2010;150(2):332-339.
4. M.A. N, I.L. C. Quantum Computation and Quantum Information. Cambridge: Cambridge University Press; 2010.
5. L.K. G. A fast quantum mechanical algoristhm for database search. STOC: ACM; 1996:212.
6. Shor PW. Polynomial-time algorithms for prime factorization and discrete logarithms on a quantum computer. Siam J Comput. Oct 1997;26(5):1484-1509.
7. Cleve R, Ekert A, Macchiavello C, Mosca M. Quantum algorithms revisited. P Roy Soc a-Math Phy. Jan 8 1998;454(1969):339-354.
8. Devoret MH, Martinis JM. Implementing Qubits with Superconducting Integrated Circuits. Quantum Inf Process. Oct 2004;3(1-5):163-203.
9. Rigetti C, Gambetta JM, Poletto S, et al. Superconducting qubit in a waveguide cavity with a coherence time approaching 0.1 ms. Phys Rev B. Sep 24 2012;86(10).
10. Kennedy TA, Colton JS, Butler JE, Linares RC, Doering PJ. Long coherence times at 300 K for nitrogen-vacancy center spins in diamond grown by chemical vapor deposition. Appl Phys Lett. Nov 17 2003;83(20):4190-4192.
11. Koehl WF, Buckley BB, Heremans FJ, Calusine G, Awschalom DD. Room temperature coherent control of defect spin qubits in silicon carbide. Nature. Nov 3 2011;479(7371):84-U108.
12. Sullivan MD. Who gets high-dose opioid therapy for chronic non-cancer pain? Pain. Dec 2010;151(3):567-568.
13. Bennett CH, Brassard G. Quantum cryptography: Public key distribution and coin tossing. Theor Comput Sci. Dec 4 2014;560:7-11.
14. B. K, C.C.W. L, R. H, et al. Provably secure and practical quantum key distribution over 307 km of optical fibre. Nat Photonics. 2015;9:163-168.
15. Pugh CJ, Kaiser S, Bourgoin JP, et al. Airborne demonstration of a quantum key distribution receiver payload. Quantum Sci Technol. Jun 1 2017;2(2).
16. Yin J, Cao Y, Li YH, et al. Satellite-based entanglement distribution over 1200 kilometers. Science. Jun 16 2017;356(6343):1180-1184.
17. Beam AL, Kohane IS. Big Data and Machine Learning in Health Care. Jama-J Am Med Assoc. Apr 3 2018;319(13):1317-1318.
18. Parsons DF. Possible Medical and Biomedical Uses of Quantum Computing. Neuroquantology. 2011;9(3):596-600.
19. Pariente P. Quantum computing set to revolutionise the health sector. L'Aterlier BNP Paribas; 2015.
20. A R. Quantum Computing and Health Care. Vol 2018: BMJ Technology Blog; 2017.
21. Gulshan V, Peng L, Coram M, et al. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. Jama-J Am Med Assoc. Dec 13 2016;316(22):2402-2410.

Disclosure

None reported.

MM

Giant Cell Arteritis: 2018 Review

by Anne Winkler MD & David True, DO

Giant cell arteritis is the most common large vessel vasculitis. When suspected, patients should be urgently treated.



Anne Winkler, MD, PhD, MACP, FACR, MSMA member since 2003, on the Editorial Board for Rheumatology for *Missouri Medicine*. She is on the clinical faculty of Missouri State University in Southwest Missouri and has been principal investigator in multiple clinical trials. David True, DO, FACR, practices rheumatology in Southwest Missouri and has been principal investigator in multiple clinical trials.
Contact: aew33@att.net

Abstract

Giant cell arteritis is the most common large vessel vasculitis. Classic symptoms include headaches, scalp tenderness, visual loss and muscle stiffness and pain. First line treatment is with high dose steroids but methotrexate may be of some help in decreasing steroid use. Tocilizumab has been shown to significantly decrease relapse rate and lower steroid cumulative dose.

Introduction

Giant cell arteritis (GCA) (previously called temporal arteritis) is a large vessel vasculitis usually seen in older adults over the age of 50. It is the most common vasculitis in North America and Western Europe. GCA classically targets large vessels with predominance for the aorta and its Branches.[1] Arterial inflammation may lead to vascular damage which can result in stenosis, occlusions and even aneurysms. Additionally, the arterial inflammation may lead to serious loss of function including visual loss, limb anoxia and stroke. Suspicion of giant cell arteritis is a medical emergency and patients need to be quickly diagnosed and treated to prevent irreversible consequences of vessel inflammation.

Clinical Features

Giant cell arteritis (GCA) typically occurs in individuals over the age of 50. Mean age is approximately 70.[2] GCA is 2 .5 more likely to occur in women than men with lifetime risk at 1% for women and 0.5% for men.[3] It is also more likely to occur in Northern Europe countries and those of northern Europe ancestry with incidence rate of 20 per 100 ,000. The incidence of GCA is much lower in southern Europe and Mediterranean and quite rare in patients of African and Asian descent. [4,5,6]

HLA genes that have been identified through GWAS (genome wide association studies) that are associated with the development of GCA as well as increased complications. The HLA gene most commonly associated with GCA in Caucasians is HLA Br1*04. Those with this gene are at higher risk for developing GCA and also at higher risk for complications of GCA such as visual loss and also at higher risk of resistance to glucocorticoids. [7,8,9] There are also non-HLA genes associated with GCA – including PTPN22, LRRC32, IL17A, IL33. Most of the genes that have been identified are involved in endothelial function, innate immunity system, cytokines and cytokine receptors. [10]

2GCA

The onset of GCA may be acute or insidious. Typical symptoms of giant cell arteritis (Table 1) include headaches, scalp tenderness and jaw claudication but constitutional symptoms are common including malaise, fatigue, weight loss and anorexia and low-grade fever. Eighty to 90% of individuals have symptoms involving the extracranial arteries of the aorta, including headaches and scalp tenderness and jaw claudication and visual loss. Headaches occur at least 70-80% of the time, but not universally, and are typically severe and

may be unilateral or bilateral and are usually located in the temporal area.[1] Patients usually describe the pain as sharp and burning and severe. Scalp tenderness usually presages the headaches by a few weeks. Headaches and scalp tenderness tend to occur prior to the onset of visual loss. The visual loss occurs in about 30% of patients and is permanent in about 10-15%. [11] This is considered a medical emergency and patients need to be treated with high dose prednisone or pulse solumedrol as quickly as possible. More than 50% of patients will present with polymyalgia rheumatic which is usually manifested with significant muscle and morning stiffness classically in the proximal girdle locations. Jaw claudication occurs in about 40% of patients and again is usually early finding but tongue claudication is rare. Temporal artery tenderness or bulging of the artery may occur and on physical exam one may find the artery to be nodular or indurated. Aortic arch syndrome is not common nor is lower or upper extremity claudication but may be present due to involvement of the large arteries such as the femoral or brachial arteries. Fever of unknown origin or failure to thrive is a rare but possible presentation of quite elderly patients.

Table 1. Clinical Features of Giant Cell Arteritis

FREQUENT
- Headaches
- Scalp tenderness
- Polymyalgia rheumatic
- Elevated ESR/ CRP
- Anemia

COMMON
- Ocular symptoms
- Jaw claudication
- Malaise
- Weight loss
- Anorexia

UNCOMMON
- Cerebrovascular accidents
- Myocardial infarctions
- Limb claudication
- High fever

Comorbid conditions include myocardial infarctions and patients with GCA are at 4 times more risk of MI than age matched controls.[12] Cerebrovascular accidents are usually a later phenomenon and are increased 2.5 times compared to those without GCA.[13] Other vascular conditions including aneurysms and dissections are also 2.5 times more common to happen in patients with GCA.[14]

Pathogenesis

Immunopathology is not clearly understood as yet but it appears that dendrocytes within the adventitial layer activate T cells – Th1 which produce gamma interferon and Th17 which produce IL (interleukin) 17 and Th21 which produce IL21. Interestingly, Th1 and gamma interferon (IFN) seem to persist throughout the disease process and do not decrease with steroid treatment but Th17 and IL17 does. Other major cytokines detected include IL2, IL17, IL9, IL21, gamma IFN as well as cytokines related to th17 development – il6, il1 and il23. The presence of HLA DR4-01 suggests that antigen selection and presentation play a role in the pathogenesis.[15,16,17]

Diagnosis

The diagnosis of GCA is usually suspected in patients with new onset of severe headache. Workup includes ESR and CRP measurements which are typically elevated with ESR above 50. Anemia and mildly elevated liver enzymes may also occur. Temporal artery biopsy is the gold standard for diagnosis but can be negative in 30% of patients with GCA. [18,19] Data has been shown that the temporal artery biopsy needs to be done within two weeks of starting steroids or other treatment. Skip areas are not uncommon which is why a large sample size is recommended when obtaining a temporal artery biopsy. Classic pathology finding is giant cell granuloma formation often near to a disrupted internal elastic lamina. However multinucleated cells are not required for diagnosis. Evidence of arteritis involves all three layers of the artery – adventitia, media and lamina.

Imaging studies also may be used to determine the presence of GCA. These include MRI, ultrasound, CT and pet scan.[19] These techniques have both positive and negative concerns. MRI/MR angiography is very helpful for identifying edema of the vessel wall with wide vascular areas able to be screened. This is minimally invasive but is expensive and has some contraindications (implanted medical devices, contrast allergy). Ultrasonography can assess involvement of temporal arteries and large vessels but is operator dependent and difficult to assess involvement of the thoracic aorta. CT angiography is very good at looking for large vessel involvement and is rapid and not as expensive as MRI but has limited resolution of small vessels and requires radiation. PET with flurodeoxyglucose is also good at looking at large vessels and evaluating the extent of disease in aorta and its branches it is sensitive and reproducible but is expensive and is limited in evaluating cranial vessels.

Treatment

Treatment has been classically with steroids – these were first used in 1955 and still what is recommended initially due to the quick onset of response as well as the risk of irreversible visual loss often within weeks of the onset of symptoms. Generally, 40-60 mg daily for the first month is recommended with taper not faster than 10% per week or per month. Pulse solumedrol has been used in those with impending visual loss with trials showing equivocal results. Other agents have been looked at either in small case reports or in small clinical trials but so far only tocilizumab which

has been shown to be quite effective to decrease relapses and decrease steroid use has been FDA approved for use in GCA.

Methotrexate was used in three randomized trials [20,21,22]– the first randomized controlled trial used low dose methotrexate (10mg weekly) with 21 patients with newly diagnosed disease. This failed to show a decrease in disease flare or prednisone cumulative dose. The second trial included 42 patients and did show fewer relapses (46.6% vs 83.3%) and steroid sparing effects (1302 mg less steroids in methotrexate treated group.) The third study also done with only newly diagnosed GCA was the largest (92 patients) and with higher dose of methotrexate - 15mg weekly maximum dose but no difference in relapse or median dose of steroids was seen in this trial. A meta- analysis was done suggesting methotrexate decrease relapse by 35% and second relapse by 51%. Hydroxychroloquine and azathioprine have been used by rheumatologists as steroid sparing agents Both have been studied in small group of patients with GCA and did not show any benefit.

Biologic agents including TNF blockers, abatacept, rituximab, ustekinimab, rituximab and anakinra as well as tocilizumab have been looked at in GCA. The TNF blocker trials have been unsuccessful in demonstrating efficacy in GCA.[23,24,25] A randomized controlled trial with abatacept was done with a small number of patients which included new and relapsing patients. The results showed definite improvement in relapse rate with 48% participants relapse free versus only 31% on placebo.[26] Ustekinumab was used in a very small open design study in only 14 patients – this did show marked decrease in steroid use – from 20mg to 5mg daily in patients treated with ustekinimab.[27]There was one report with IL 1 receptor inhibitor (anakinra) used in 3 patients with refractory GCA – all three treated with anakinra showed rapid improvement with a decrease in steroids as well as resolution of imaging abnormalities.[28] Rituxamab was used in 2 refractory GCA patients with some improvement in vasculitic manifestations but with limited followup.[29] Tocilizumab was studied in a fairly large randomized placebo-controlled trial.[30] This included both newly diagnosed patients as well as those with relapsing disease. There was a fixed prednisone taper either 26 or 52 weeks depending on the trial arm in the placebo group. The results in the 52-week period showed 60% of patients on weekly tocilizumab and 58% of patients on every other week dosing were relapse free while on 22% of patients on prednisone alone (either the 26 or 52-week taper) were relapse free at 52 weeks. In patients with relapsing disease at the beginning of the trial 52% on weekly TCZ and 48% on every other week TCZ were relapse free while only 7% and 14% in prednisone 26 and 52-week taper arms respectively. The cumulative dose of prednisone in the placebo arms were over 3800 mg in one year but were decreased significantly in those treated with TCZ - 1887 in weekly and 2207 in every other week.

Summary

Giant cell arteritis is the most common large vessel vasculitis - it is classically seen in patients over the age of 50 presenting with headaches, scalp tenderness and jaw claudication. When suspected patients should be treated urgently with high dose steroids until diagnosis is clearly established or ruled out. Temporal artery biopsy is still recommended in making the diagnosis although imaging studies may also be helpful where available. Steroid- sparing agents including methotrexate may be helpful to decrease cumulative doses of steroids and steroid resistant including methotrexate. Tocilizumab is the first agent to demonstrate increased remission rate in both new and relapsing patients as well as significantly total lower doses of glucocorticoids over one year in a large randomized controlled trial.

References

1. Lee JT. Semin Arthritis Rheum 1995; 26(6): 422-431.
2. Smetana GW et al. JAMA 2002; 2817 (1): 92-101.
3. Borchers AT et al. Autoimmune Rev 2012; 11 (6-7): A544-A554.
4. Pamuk ON et al. Clin Exp Rheumatol 2009; 27(5): 830-833.
5. Bas-Lando M et al. CLin Esp Rheumatol 2007; 25 (suppl 44): 515-517.
6. Ninan J et al. Best Pract res Clin Rheumatol 2016; 30 (1): 169-188.
7. Camona FD et al. Rheumatology 2014; 53(1): 6-18.
8. Rauzy O et al. Ann Rheum Dis 1998; 61(10): 1454-1461.
9. Camona FD et al. Am J Hum Genet 2015; 96(4): 565-580.
10. Camona FD et al. Expert Rev CLin Immunol 2016; 12(1): 57-66.
11. Gonzalez-Gay MT et al. Medicine (Baltimore) 2000; 79(5): 283-292.
12. Amur N et al. Rheumatology 2016; 55(1): 33-40.
13. Gonzalez-Gay MA et al. Arthritis Rheumatol 2009; 61(10): 1454-1461.
14. Nuenninghoff DM et al. Arthritis Rheumatol 2003; 48(12): 3522-3531.
15. Wyand CM et al. J Neuroophthmal 2012; 32(3): 259-265.
16. Ly KH et al. Autoimmune Rev 2010; 9(10): 635-645.
17. Camona FD et al. Am J Hum Genet 2015; 96(4): 565-580.
18. Borchers AT et al. Autoimmune Rev 2012; 11(6-7): A 544-A554.
19. Ninan J et al. Best Pract Res CLin Rheumatol 2016; 30(1): 169-188.
20. Spiera R et al. Clin Exp Rheumatol 201; 19: 495-501.
21. Jover J et al. Ann Intern Med 2001; 134: 106-114.
22. Hoffman G et al. Arthritis Rheumatol 2002; 45: 1309-1318.
23. Hoffman G et al. Ann Intern Med 2009; 146: 621-630.
24. Martinez-Taboada V et al. Ann Rheum Dis 2008; 67: 625-630.
25. Seror R et al. Ann Rheum Dis 2014; 73: 2074-2081.
26. Langford C et al. Arthritis Rheumatol 2015; 67 (suppl 10).
27. Conway R et al. Ann Rheum Dis 2016; 75: 1578-1579.
28. Shepard S et al. Circulation 2005; 111: 3135-3140.
29. Bhaha A et al. Ann Rheum Dis 2005; 64: 1090-1100.
30. Stone JH et al. NEJM 2017; 377: 317-328.

Disclosure

AW is on the speaker's bureau for Celegene, Abbvie, Pfizer, Genentech, Regeneron, Sanofi, Bristol Meyers, Squib, and Janssen, and is involved in clinical trials for Abbvie, Amgen, Novartis, Pfizer, Biohaven, Allergan, Theranica, Electrocore, Teva, ATI, Avanir, Ionis, Lilly, Scion, TX-360, and Zosano. DT is on the speaker's bureau for Celgene, and is involved in clinical trials for Abbvie, Amgen, Novartis, Pfizer, Biohaven, Allergan, Theranica, Electrocore, Teva, ATI, Avanir, Ionis, Lilly, Scion, TX-360, and Zosano. **MM**

Member Services Information

Go to www.msma.org/membership-perks or call 800-869-6762.

MSMA Insurance Agency, Inc.
www.msma.biz
866-676-2467

MSMA Physicians Health Program
www.themphp.org
800-274-0933

Center for Patient Safety
www.cps.org
573-636-1014

Primaris
www.primaris.org
800-735-6776

MO Association of Osteopathic Physicians & Surgeons
www.maops.org
573-634-3415

American Medical Association
www.ama-assn.org
312-464-5000

Centers for Medicare & Medicaid
www.cms.hhs.gov
816-426-5033

MO Dept of Health & Senior Services
www.dhss.mo.gov
573-751-6400

MO Dept of Social Services
www.dss.mo.gov
573-751-2086

MO Dept of Insurance
www.insurance.mo.gov
573-751-4126

MO Board of Registration
www.pr.mo.gov/healingarts.asp
573-751-0098

MO Bureau of Narcotics & Dangerous drugs
www.dhss.mo.gov/bndd
573-751-6321

MO HealthNet
www.dhss.mo.gov/mhd
573-751-3425

Medicare Part B/MO Medicare
www.momedicare.com
866-736-0799



National Medicare Helpline
800-633-4227

CLAIM Helpline
800-390-3330

Provider Hotline
800-735-6776

MO Hospital Association
web.mhanet.com
573-893-3700

CCPA Purchasing Partners, LP
www.ccpapp.org
312-227-7436

DocbookMD
www.docbookmd.com
888-930-2048

GoNext - Travel
www.gonext.com
800-842-9023

I.C. System, Inc.
Collection Service
www.icsystem.com
800-279-3511

Lifelock
www.lifelock.com
800-lifelock

Medical Waste Services
www.medicalwasteservices.org
866-355-7094

Medjet assist
www.medjet.com
800-527-7478

Missouri Drug Card
www.missouridrugcard.com
800-869-6762

Moneta Financial & retirement planning
www.monetagroup.com
800-833-1301

officite
www.officite.com/msma
866-638-6519

Part B News Group
Publication Subscriptions
877-397-1496

Resolve Physician Agency
www.resolvephysicianagency.com
877-758-3318

SHOW ME HEALTH INFORMATION NETWORK
www.shineofmissouri.com
844.424.4370

TSYS Merchant Solutions
www.tsysmerchantinsights.com
888-749-7860

One number accesses
our pediatric specialists.
Any problem, anytime.

Children's
HOSPITAL & MEDICAL CENTER
OMAHA

We know children.

1.855.850.KIDS (5437)

The Physicians' Priority Line is your 24-hour link to pediatric specialists for physician-to-physician consults, referrals, admissions and transport.



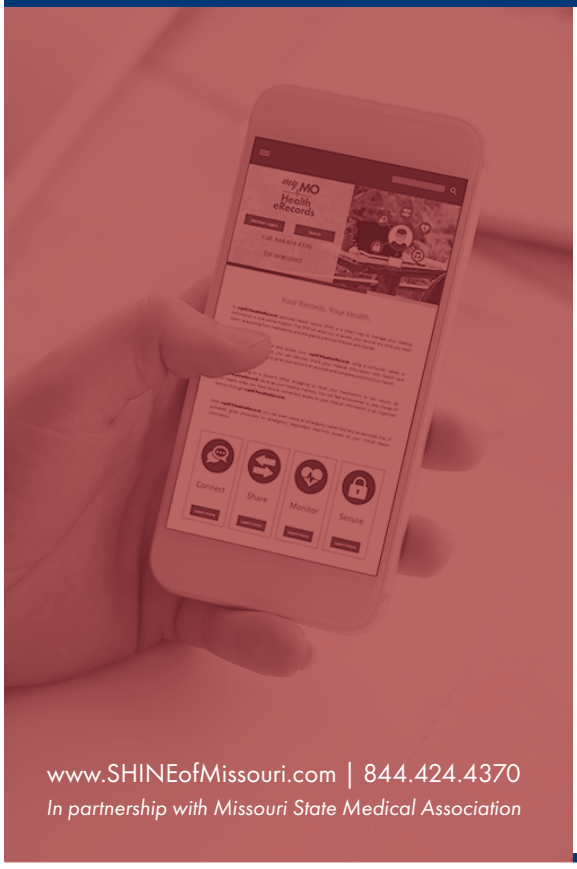
Missouri Physicians Can Access HIE Data To:

- Enhance Patient Encounters
- Effectively Coordinate Care
- Increase Workflow & Productivity
- Realize Cost & Time Savings



Health Information Exchange
The Time Is **NOW**

Join SHINE of Missouri, the physician-led HIE of Missouri.



Missouri Patients Experience:

- Elimination of Duplicate Labs, Testing, & X-rays
- Focus on Patient Safety
- Reduced Readmissions
- Secure Online Access 24/7 to *my*MOHealtheRecords.com

www.SHINEofMissouri.com | 844.424.4370

In partnership with Missouri State Medical Association

SHOW-ME HEALTH INFORMATION NETWORK OF MISSOURI

In partnership with Missouri State Medical Association

A member of the KAMMCO Network



Coverage for Affluent Homes

Experience the peace of mind that comes from working
with an insurance professional who understands your unique needs.

MSMA Insurance cares for physicians and
covers their personal and professional needs.

Contact Ronnie Staggs | 866-676-2467 | www.msma.biz | rstaggs@msma.biz

MSMA
Missouri State Medical Association
Insurance

