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– New Opioid Bill: How Your Practice Will Be Affected
– State of the DCMS 2018: Recharged, Revitalized, and Relevant
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Domestic Violence/intimate partner abuse is prevalent throughout the United States (U.S.), as well as the rest of the world. More than one in three women and one in four men report having experienced some form of rape, physical violence, or stalking by a partner in their lifetime. It is therefore important for healthcare providers to be aware of the prevalence of domestic violence and become familiar with appropriate screening and referral tools in order to identify victims and provide resources.

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From the Editor’s Desk

Northeast Florida Medicine

James St. George, MD
Editor-in-Chief

The 2018 Florida Legislative session recently ended. Did you know or care that in recent years the Florida Legislature considered all of the following bills?

- Assignment of benefits will disappear; checks for your services will now go directly from the insurance company to the patient.
- The lookback period for insurance companies to recoup payments will be 30 months instead of 12 months.
- You will be fingerprinted every two years as the Legislature must believe that our fingerprints change over time.
- Expert witness certificates will no longer be issued. Any physician in any specialty can testify against you in a lawsuit; e.g., a psychiatrist would be able to testify on how a surgeon should have practiced medicine.
- Pharmacists can order and evaluate laboratory and clinical tests, initiate, modify or discontinue medication, and provide treatment of strep or influenza.
- ARNPs can now practice independently.

Did you know or care about how these bills were going to be defeated? Did you know or care that the Florida Medical Association (FMA) worked to defeat these bills through both direct lobbying and supporting the election of physician-friendly candidates?

Physicians often have discussions as to why reform cannot, despite repeated attempts, pass in Congress. They usually agree that changing the current system and malpractice climate makes sense. Major roadblocks to any meaningful reform are the state and federal lobbying efforts of the trial and plaintiff lawyers.

As a group, the lawyers’ effectiveness in blocking common sense legal reforms makes the medical profession look like amateurs in our efforts to exert political influence. The lawyers have gained their influence primarily through large donations, fundraising efforts, being focused on their objectives and the number of legislators who are also lawyers. In contrast, only one percent of congressional leaders over the past 50 years have been physicians. The plaintiffs’ associations have thousands of members who are willing to write checks for the current $1,000 per-individual limit. Congressional campaign contributions by lawyers in the last election cycle far exceeded the total given by physicians. Since 1990, the total amount donated to federal political candidates by lawyers, excluding lobbyists has exceeded $1 billion.

Their funding is also influential in gubernatorial elections, state legislator races, and political appointments.

Consider the Florida Supreme Court. The current Supreme Court is friendly to the plaintiff bar and has struck down most of tort legislative reforms that has taken our profession decades to implement.

In 1986, the Florida Legislature passed a noneconomic damages cap. In 1987, the Florida Supreme Court ruled the noneconomic cap unconstitutional but did provide a legal roadmap on how to institute the cap properly. In response to the malpractice crisis and following the Court’s directions, cap legislation was again passed by the Legislature in 2003 only to again be invalidated by the Florida Supreme Court in 2017.

In 2004, the FMA developed a pretreatment binding arbitration form. In 2013, the Florida Supreme Court invalidated the arbitration agreement in a poorly reasoned decision that ignored Federal law supporting arbitration.

In 2011, after 20 years of effort, the FMA passed legislation that leveled the playing field for defendant physicians in a medical malpractice case by providing them equal access to treating physician witnesses. In 2017, the Supreme Court ruled the legislation unconstitutional.

The Florida Supreme Court has repeatedly discarded the efforts of the Florida Medical Association, our Legislature and Florida voters.

Elections have consequences. The most recent Supreme Court ruling that invalidated malpractice caps was a 4-3 decision. In 2018, Florida will elect a new Governor. The new governor will appoint three new Florida Supreme Court Justices in 2018 and, if re-elected, will replace six of the seven sitting Justices. The average Florida Supreme Court term is 17 years. Obviously, the election of our next governor will have a profound effect on future rulings for many years. If we are to reverse the course of the past, we need to have an equally profound influence on who is elected now and in the future. The trial lawyers and insurance industry will not hesitate in this.

Physicians who engage in political advocacy face many obstacles. The time demands of maintaining a medical practice often prohibit political activity and activism. The medical profession does not have a union to act on important issues. Instead, it relies on the volunteerism of individual physicians to either become politically active themselves or to elect their representatives to contribute to organizations such as the DCMS and FMA that will advocate on their behalf. Unfortunately, most physicians either do not participate in organized medicine or do not contribute to a physician-friendly political candidate or medical society political action committee (PAC). Estimates of physicians contributing to political campaigns vary from only 2 percent to 9 percent.

Elections cost money, lots of money. Influence of those elected (lobbying) costs money, lots and lots more money. If you, as a physician, want to have a physician-friendly governor, and legislature, you should view political contributions as an important and necessary business or professional overhead expense. This is the perspective of most law firms and individual lawyers. They recognize the return on their investment both professional and individually. The easiest and most influential means of contributing is through the FMA PAC.

FMA PAC-endorsed candidates won in 94 percent of their races. Of the 98 candidates in the 2016 Florida election that the FMA supported, 92 were elected.

- Of the Florida Senate races, 22 of 24 FMA supported candidates won – 92 percent.
- Of the Florida House candidates, 70 of 74 won – 95 percent.
- FMA Friend of Medicine Dana Young won a very contentious race in Senate District 18 in the Tampa area.

Your donation ensures that physicians have a voice in the Legislature, which is vital in passing pro-medicine legislation and defeating harmful bills. There are approximately 46,000 licensed practicing physicians in Florida. If just 50 percent made a $250 contribution, the PAC would raise almost $6 million. This would triple the amount of money the PAC currently works very hard to raise and would make Florida physicians a formidable political force. This contribution amounts to only $21/month!

Donations can be made easily through the FMA website, www.flmedical.org/pac.

Physicians may participate in politics and, thus, have some effect on medicine’s political environment, or they may abstain and take the consequences.

“Is it ignorance or apathy? Hey, I don’t know and I don’t care.” – Jimmy Buffett
State of the DCMS 2018: Recharged, Revitalized, and Relevant

As I assume the presidency of the Duval County Medical Society, I am humbled and honored at the opportunity to help our members, patients, and community. The leadership we have in place with our 2018 DCMS Board of Directors is going to be instrumental in promoting the Medical Society, its mission, and our goals of improving physician lives, patient lives, and community health. The groundwork laid by our long and storied history of past presidents and leaders has created a sound foundation for us to grow, be innovative, and evolve the DCMS for 2018 and beyond. I am proud to say the state of the DCMS is strong and better than ever before.

One of the primary goals of my year as president is to help the DCMS grow its physician membership. Working with our Board of Directors, CEO Bryan Campbell, and our all-star administrative team, I hope to expand our membership by 10 percent. Our ability as a medical society to provide more for physicians is truly dependent on our membership growth. I plan on reengaging with as many practices, hospitals, and physicians as I can in the upcoming year and beyond to promote the DCMS. With an expanded membership base, we can have more influence on key healthcare issues at the state and national levels. Growth in membership can also expand the opportunities for partnerships with other businesses and organizations that can help enhance member benefit and value. I encourage all of our members to reach out to at least one other physician who is not a member and share the value and importance of DCMS membership.

The most important program the DCMS has implemented in its 130+ year history is the Physician Wellness Program. Through a 24/7 confidential wellness line, DCMS members can receive six free coaching sessions per year from a certified counselor experienced in working with healthcare professionals. With the demanding and changing lives of physicians, burnout and suicide rates have risen across the country. Unfortunately, in the last several years, our own Northeast Florida physician community has not been immune to this trend with known physician suicides and burnout events. Placing the physical and mental health of DCMS physicians first and foremost is at the core of our DCMS Mission. As physicians, we cannot care for our patients and community if we are unable to care for ourselves. Physician wellness and mental health should no longer be a taboo subject among the physician community. The DCMS will continue to advocate for this vital benefit for all members.

In the last several years, the DCMS has played a larger and vital role in our community. We now are the official and recognized experts for nearly every media outlet in the area for medical, legislative, and patient issues. We have DCMS members writing articles for The Florida Times-Union and Beaches Leader publications. Part of my goal is to expand our community education and outreach through other publications and even alternative media outlets. As a member, the benefit of having your name in the community not only helps patients, it also adds to your ability to reach out to new patients.

The DCMS Foundation and the DCMS will be hosting the 2nd Annual Future of Healthcare Conference on May 21-22, 2018. This is a unique program where physicians, community leaders, politicians, and key stakeholders come together to focus on addressing healthcare issues that are specific to Northeast Florida and working towards unified solutions. Following last year’s conference, a task force began to tackle the issue of local food deserts. The DCMS Foundation and DCMS took the lead to bring together stakeholders to analyze the data, and begin research on solutions and execution. This work will be presented on the second day of the 2018 Future of Healthcare Conference. The Conference will also be tackling the local impact of the ongoing opioid crisis, gun violence as a healthcare problem, and the resurgence of HIV/AIDS in our community. The Future of Healthcare Conference is a unique, innovative, and physician driven initiative. We need input from all of our DCMS members, so please consider registering for this year’s event at dcmsonline.org/futureofhealthcare.

Finally, our strength as the largest medical society in the state helps drive strong and influential legislative advocacy. Starting at the Florida Medical Association (FMA) level, more members leads to a stronger FMA delegation and more influence to drive FMA policy. This in turn helps drive the political activity, lobbying, and advocacy in Jacksonville, Tallahassee, and Washington, DC. As physicians, the political issues that matter to us the most are patient centered as well.

As you can hopefully see, the DCMS has become a significantly recharged, revitalized, and relevant organization for our members, patients, and community. We are grateful to have you as a member.

Ruple Galani, MD
2018 DCMS President

From the President’s Desk
Intensive care medicine or critical care medicine is a branch of medicine concerned with the diagnosis and management of life-threatening conditions that often require sophisticated organ support and invasive monitoring. In general, it is the most expensive, technologically advanced and resource-intensive area of medical care. Over the last several decades, the field has steadily evolved as to whom and how care is delivered.

With respect to major advancements, few have proven to be “game changers.” Rather, advancements of intensive care unit (ICU) delivery has focused on a few key issues:

**Multi-disciplinary team approach:** In most ICUs, care is provided in a multidisciplinary team approach. Teams typically are composed of physicians, nurse practitioners, pharmacists, nurses, nutritionists, physical therapists, respiratory therapists, dieticians, and case managers. Communication and interaction amongst the team members is key to ensuring good outcomes and short ICU stays.

**Electronic medical record (EMR), less invasive procedures, and monitoring:** Technology has allowed ICU care to be delivered with an effort at minimizing risk to patient. EMRs, ultrasound, and modern ventilators are just a few of the items at our disposal to ensure the delivery of high quality care. Another such example is that of Tele-ICU, which allows for a high level of clinical support to be available from a remote site.

**Intensivist Involvement:** In most modern ICU’s, a critical care specialist is involved in the care of all ICU patients. Resources typically do not allow for 24/7 staffing in all units, but daily involvement has been associated with shorter ICU stays and improved outcomes.

Critical care and its location on the patient trajectory:
A primary requisite for admission to an ICU is that the underlying condition can be overcome. This is a concept that I suspect often gets over looked in the U.S. healthcare system. As healthcare costs continue to rise, it remains imperative to ensure that the care being provided is in alignment with patient wishes as well as probable outcomes. Some concerning statistics include a steady rise in the number of ICU beds in the United States and the often-cited statistic that a majority of one’s lifetime healthcare costs occur in the final six months of life. A concerning current trend is that more of us each year will spend our final days of life in a hospital bed. A concept often forgotten is that death is an acceptable outcome, especially when it aligns with one’s health and predefined wishes.

Looking to the future, I suspect that ongoing attention will be placed on how ICU care can be delivered in an effective and cost-efficient manner. This will involve changes in processes to ensure high quality evidenced based medicine. In addition, focus will be placed on transitioning from the traditional reactive means of delivering healthcare, to a more proactive/preventative mindset. As this has proven to be invaluable to improved outcomes in the ICU setting, I have no doubt that it is something we should all strive for in our own fields of medicine.

In this edition of *Northeast Florida Medicine (NEFM)*, some of our local experts in critical care medicine highlight many of the challenging topics faced daily in our ICU’s. They also review potential future efforts on how to improve the care provided and outcomes achieved.

With the known poor results following in and out of hospital cardiac arrest, efforts at improving neurologic outcomes remain of utmost importance. *Drs. Philip Lowman, W. David Freeman, and nurse practitioner Amanda Tomlinson* from Mayo Clinic Florida discuss in detail the role of hypothermia/euthermia post cardiac arrest with regards to...
neurologic outcome. In the review, the evidence for targeted temperature management is discussed at length, as are the means and methods for doing so.

Dr. Michael Pizzi of UF Health Jacksonville discusses an aspect of intensive care medicine often overlooked: post-ICU cognitive dysfunction. Measurable cognitive dysfunction may occur in up to half of all patients following ICU admissions. Early identification of those at risk is vital to decreasing the risk of developing dysfunction. Dr. Pizzi comprehensively reviews the epidemiology and pathophysiology of post-ICU cognitive dysfunction, as well as discusses high-risk populations and potential therapies.

As technology has advanced, so has the traditional physical exam. Drs. Carla Venegas-Boresellino and Jose L. Diaz-Gomez of Mayo Clinic Florida and Dr. Maria Elena Venegas of Universidad del Norte in Colombia discuss the role and utility of ultrasound in the evaluation and management of critically ill patients. In many ICUs, a portable ultrasound machine is as commonly used as a stethoscope in delivering high-level resuscitative care. The authors discuss many of the common applications of ultrasound in the ICU setting. Given the role of ultrasound as an invaluable complement to the traditional physical exam, education on its use is becoming a focus at the medical school level of training.

The burden of COPD is well known to most caregivers. This is likely of particular interest to many of you given the severity of our most recent influenza season. Drs. Jose Soto Soto, Abubakr Bajwa, and nurse practitioners Lauren Harrel and Jenny Brooks of Ascension St. Vincent’s provide us a review of the current classification and therapies for COPD, the morbidity and mortality associated with exacerbations, and the multidisciplinary approach necessary to decrease exacerbations. Furthermore, they highlight the importance of the transition of care from hospitalization to the outpatient setting in patients with underlying COPD.

Sepsis is one of the leading causes of death in patients admitted to an ICU. Drs. Pramod Guru, Philip Lowman, Pablo Moreno-Franco and nurse practitioner Ami Grek of Mayo Clinic Florida review this clinical syndrome, the ongoing efforts to reduce high mortality, early recognition, interventions, and outcomes. Also included is an overview of the many challenges faced when implementing sepsis guidelines and possible means for overcoming these.

Drs. Pramod Guru and Robert Ratzlaff from Mayo Clinic Florida review extracorporeal membrane oxygenation (ECMO) and its renewed interest following the 2009 H1N1 Flu pandemic. Advanced support of cardiopulmonary failure remains controversial. Factors such as patient selection and local expertise are important in obtaining optimal outcomes and defining the role of such therapies. Concepts covered include ECMO physiology, circuit types, outcomes, and potential obstacles to providing this complex form of life support.

It is my hope that this edition of NEFM sheds light on the vast field of critical care medicine. As you will see, the scope of ICU care involves numerous issues: before, during, and after the time of critical illness. I am truly grateful to the authors who took the time out of their busy lives to contribute and help educate us all. As a resident of northeast Florida, it is a privilege to have you as dedicated members of the healthcare team.

PHYSICIAN NEEDED:
Immediate opening for supervising MD or DO in a large multi-specialty facility. Daily review of nurse practitioner’s notes and Rx at home electronically and one-half day per week in office to see special needs patients. Participation on Medicaid and Medicare plans preferred.

Contact Becky at (904) 783-3700.
The University of Florida College Of Medicine-Jacksonville Internal Medicine Program is one of the oldest and most dynamic training programs in the region. Our trainees are provided with a three-year internal medicine experience that primarily takes place at the UF Health Jacksonville downtown campus. Currently, Northeast Florida’s only level 1 trauma and primary safety net hospital, the main downtown campus houses 695 beds, totaling more than 34,000 inpatient admissions a year. The campus has a long history of teaching and service, with the first intern class starting in 1913 and the first residents starting in 1927. The Internal Medicine (IM) program has been accredited by the Accreditation Council for Graduate Medical Education since 1961 and has grown from five Internal Medicine trainees annually to 48 trainees currently.

Subspecialty Training

Residents have the opportunity to take part in nine internal medicine fellowship training programs at the hospital. These fellowships include cardiology, electrophysiology, interventional cardiology, endocrinology, gastroenterology, infectious disease, medical oncology, nephrology, and pulmonary/critical care. A rheumatology fellowship has recently been approved for addition and the medical oncology program may soon expand to a hematology oncology program.

Research

There are many opportunities for research and academic activities. A cornerstone of the research experience is a four-week elective dedicated to research. A recent addition to the program has been the Internal Medicine Research Club, which offers a casual environment for residents to present research ideas in front of peers and experienced faculty members. During the spring of each year, a campus wide Research Day provides trainees an opportunity to promote and present their work. Over the past three years, UF Health IM residents have been responsible for 247 conference presentations, 110 published abstracts, 41 published manuscripts, and 3 Dean’s Grants recipients. Among the most impressive recent accomplishments, is the acquisition of a Dean’s Grant by first year resident Dr. Karan Seegobin. His ongoing research is titled Pilot study in the occurrence of multiple cancers following chemotherapy and radiotherapy at University of Florida Jacksonville.

Quality Improvement and Patient Safety Training Rotation

A portion of the four-week PGY-2 research elective is now dedicated to quality improvement and patient safety training curriculum. The rotation is comprised of quality specialist sessions, Institute of Healthcare Improvement modules, and participation in several hospital-based quality committees. This ultimately culminates in a quality improvement initiative designed and driven by the residents.

IM Procedure Service

Recent changes to the structure and curriculum of the Internal Medicine inpatient consult service has provided trainees with more extensive hands on procedure experience. Lead by faculty member Dr. Win M. Aung, residents utilize and develop their procedural skills to provide a variety of services ranging from lumbar punctures to bone marrow biopsy for other inpatient services. Plans to expand the curriculum even further and include a more intensive ultrasound training experience are underway.
Residents Serving Their Communities

Despite busy schedules, our residents continue to contribute to their communities outside of work. Second year resident Dr. Anna McCarthy recently used her Thanksgiving break to take part in a medical mission trip to Haiti. She was part of a small medical team running a four-day clinic in impoverished portions of Port-au-Prince. Over 1,000 patients were provided with free medical care and medications. Third year resident Dr. Julio Perez-Downes has been very active with the American College of Physicians in advocating to improve the practice of internal medicine and representing his colleagues at the Florida State Capitol sessions in Tallahassee. He was the recipient of the Gary F. Izzo Memorial Scholarship for this work. The award was presented at the 49th Annual Scientific Meeting of the Florida Chapter of the American College of Physicians.

Familiar Faces

We are very proud that many of our faculty members are program alums as well.

Dr. Linda Edwards currently serves as the Senior Associate Dean for Educational Affairs and Division Chief of the Division of General Internal Medicine.

Dr. Jeff House currently serves as Program Director of the Internal Medicine Residency, Associate Chair of Education and Quality Improvement, and Performance Improvement Officer. He was promoted to Professor of Medicine this past July.

Professor of Medicine Dr. Carlos Palacio serves as the Associate Program Director and as the Internal Medicine Residency and Clerkship Director.

Drs. Marwan Shaikh, Jason Hew and Dat Pham serve as Assistant Professors in the Division of Hematology and Medical Oncology.

Dr. Vandana Seeram serves as an Assistant Professor in the Division of Pulmonary, Critical Care, and Sleep Medicine and Associate Program Director of Pulmonary and Critical Care.

Dr. Siva Suryadevara, an Interventional Cardiologist, serves as an Assistant Professor in the Division of Cardiology.

Dr. Ravindra Maharaj is a Hospice and Palliative Medicine, Geriatric Medicine trained physician serving as an Assistant Professor in the Division of General Internal Medicine.

Drs. Lauri Ramrattan and Karishma Ramsuibeik are Assistant Professors in the Division of Rheumatology and Clinical Immunology.

Our graduates’ contributions to the Jacksonville community go well beyond those serving in an academic capacity. Over the past decade, nearly 20 graduates have stayed in the Jacksonville area serving in primary care or hospitalist positions.

We are very proud of the contributions our trainees have made and continue to make in the Jacksonville community. We are excited to keep building upon this progress in new and innovative ways for many years to come.
Battling the Opioid Epidemic

There’s a line from the 1997 film Men in Black that I think about quite a bit this time of year.

Men in Black is about a rookie cop named “Jay,” who is being trained by a vet named “Kay” on how to protect the Earth from alien invaders. Jay is played by Will Smith, who at this time was still really known by most as The Fresh Prince. His partner in the Men in Black agency is a stone-cold G-man named Kay, played by the incomparable Tommy Lee Jones.

The conceit of the film is that aliens are living among us, but that the truth is a little too much for people to really handle, so the Men in Black are responsible for maintaining the façade of normalcy and covering up idiosyncrasies. Jay is our view into this crazy world, and when he’s confronted with a potential world-ending threat, he acts as our proxy to save our world. Here’s the exchange:

Kay: We do not discharge our weapons in view of the public!
Jay: Man, we ain’t got time for this cover-up bulls---! I don’t know whether or not you’ve forgotten, but there’s an Arquillian Battle Cruiser that’s about to...

Kay: There’s always an Arquillian Battle Cruiser, or a Corillian Death Ray, or an intergalactic plague that is about to wipe out all life on this miserable little planet, and the only way these people can get on with their happy lives is that they DO NOT KNOW ABOUT IT!

In many ways, when it comes to the Florida Legislative Session every year, I feel like I’m working for the Men in Black, and that an Arquillian Battle Cruiser is parked in the sky over Tallahassee.

Florida’s 2018 Legislative Session

Every Legislative Session begins with a feeling of hope. Despite your personal feelings about the legislative process, or even one party versus the other, my personal experience is that the Florida Legislature is made up of 160 people who want to do something good for their communities and Florida residents.

That hope exists within the context of reality. This year, the opioid crisis nationally became too large to ignore. It was declared a National Public Health Crisis. Florida has been hit especially hard by the epidemic. Something had to be done.

Then came the tragic shooting incident in Parkland. While the debate over whether gun violence is a public health issue is just getting started, lawmakers knew something had to be done. The $400 million legislation signed by Governor Rick Scott imposes new restrictions on gun purchases and allocates $69 million for early mental health screening and services, among other initiatives.

The last important contextual element is that 2018 is an election year. That’s the reason the session was so early in the first place. Every House seat and more than a third of the seats in the Senate are on the ballot. There will also be a new Governor and cabinet. Those elements impact priorities in an election year.

Opioids – A Public Policy Crisis

So, let’s talk first about the biggest healthcare bill and what it really means. This is the one I get calls every day about from physicians both angry and excited about what’s happening. The bill passed by the Florida Legislature will do the following:

• Prescriptions of opioids will be restricted to three days for acute pain
  – Chronic pain, terminal cancer, and palliative care are exempt
  – Surgery is NOT exempt

• Physicians may extend the three-day limit to seven utilizing an “Acute Pain Exemption”

• The Prescription Drug Monitoring Program (PDMP) currently known as E-FORCSE must be checked for each prescription
  – Nearly a million dollars was added to the budget to upgrade the system
  – It will now have access to patient records from other states
• Each physician with a DEA License and a Florida Medical License must complete a two-hour CME course on safe opioid prescribing for each Florida License renewal

• This will go into effect July 1, 2018

The most common criticism I hear from physicians is that three-days isn't enough following surgery, and that this bill won't do anything because people dying from fentanyl overdoses are using heroine, not prescription opioids.

Both of those facts are accurate. But the position is not.

The blame for the opioid crisis is multi-factorial. There's blame to the pharmaceutical companies who did not share addiction data. There is blame on the part of happy faces and satisfaction scores. There's blame on the part of the Florida Legislature for shutting down the pill mills in such a way that it created a robust market for fentanyl-laced heroine… and there's blame for physicians who have not adjusted industry prescribing guidelines on opioids despite evidence of addiction patterns.

In 2016, 3,310 people died from opioid-related overdoses in Florida. While 2017 data is not released, the numbers are estimated to have doubled. Of those deaths, more than 90 percent of these individuals became addicted to opioids through a legal prescription.

Here's an analogy I like to use: the opioid crisis is like a bathtub that's overflowing and there are two faucets still pouring into it. The Legislature’s position to impose CDC guidelines with a three-day limit will not stop the bathtub from overflowing. It does slow down the flow of potential new patients who become addicted, however.

This isn't the end of the fight against opioid-related deaths. It's just the beginning. However, as we move forward to the future and what will undoubtedly be years of new related public policies, we can say that physicians were on the front-lines and there to do their part to improve the health of the community.

The Arquillian Battle Cruiser

The opioid bill was not a silent threat. You could not turn on your television or radio without hearing about the crisis and the impending legislation. What you did not hear about this year were another round of attempts to increase the Scope of Practice for non-physicians.

• **Pharmacists Scope of Practice** – One of the bills that had a lot of steam in this Legislative Session would have allowed pharmacists to diagnose and treat the flu and Strep Throat.

• **Physician Assistants and ARNPs Signing Orders** – This is a nose-under-the-tent bill. For four consecutive years, there have been bills introduced and sometimes even passed by the Florida House to expand the Scope of Practice for ARNPs and to allow them to practice without the supervision of a physician. Thankfully, the Senate has not supported those bills and they failed. The bill introduced this year would have allowed PAs and ARNPs to sign orders and documents that must currently only be signed by a physician.

These are the bills that make me feel a bit like a member of the Men in Black. These types of measures are introduced every year, and the County Medical Society works very closely with the Florida Medical Association (FMA) to defeat these measures, and to protect what it means to be a physician in Florida.

Your membership in both organizations helps to strengthen our resolve and influence in Tallahassee. Additionally, great thanks go out to the members of the FMA Political Action Committee and to those who contribute to that organization. Through the efforts of the FMA PAC to support physician-friendly candidates, together we have been able to beat back the Arquillian Battle Cruisers virtually every year.

It’s difficult to articulate how frequently inaction is a positive result. Whether it’s the last-minute budget agreement that allowed the existing formula for reimbursement of Medicaid patients at UF Health-Jacksonville or shutting down the latest attempt to expand the Scope of Practice, these efforts are just as hard and sometimes harder than trying to get something new passed. It's our commitment to our members every year… even if I don’t look as good in sunglasses as Will Smith and Tommy Lee Jones. ✧
It Began

INDICATIONS

Adult Ulcerative Colitis (UC)
ENTYVIO (vedolizumab) is indicated in adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for inducing and maintaining clinical response, inducing and maintaining clinical remission, improving endoscopic appearance of the mucosa, and achieving corticosteroid-free remission.

Adult Crohn’s Disease (CD)
ENTYVIO (vedolizumab) is indicated in adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for achieving clinical response, achieving clinical remission, and achieving corticosteroid-free remission.

IMPORTANT SAFETY INFORMATION

- ENTYVIO (vedolizumab) for injection is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.
- Infusion-related reactions and hypersensitivity reactions including anaphylaxis have occurred. Allergic reactions including dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate have also been observed. If anaphylaxis or other serious allergic reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.
- Patients treated with ENTYVIO are at increased risk for developing infections. Serious infections have been reported in patients treated with ENTYVIO, including anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis. ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding ENTYVIO in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution in patients with a history of recurring severe infections. Consider screening for tuberculosis (TB) according to the local practice.
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WITH

REMISSION ACHIEVED
UC and CD patients achieved remission at 52 weeks vs placebo. Studies included bio-naïve and anti-TNF-α-experienced patients.

AND

5-YEAR INTEGRATED SAFETY
A 5-year analysis, including an open-label continuation study, demonstrated consistent results with clinical trials across safety parameters.

Individual results may vary.

Begin the Change

IMPORTANT SAFETY INFORMATION (continued)

- Although no cases of PML have been observed in Entyvio clinical trials, JC virus infection resulting in progressive multifocal leukoencephalopathy (PML) and death has occurred in patients treated with another integrin receptor antagonist. A risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms. Typical signs and symptoms associated with PML are diverse, progressing over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. If PML is suspected, withhold dosing with Entyvio and refer to a neurologist; if confirmed, discontinue Entyvio dosing permanently.

- Prior to initiating treatment with Entyvio, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving Entyvio may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.

- Most common adverse reactions (incidence ≥3% and ≥1% higher than placebo): nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities.

Please see brief summary of Prescribing Information on adjacent pages.


Learn how you can help your patients reach remission—visit EntyvioHCP.com
BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

ENTYVIO (vedolizumab) for injection, for intravenous use

INDICATIONS AND USAGE

Adult Ulcerative Colitis

ENTYVIO (vedolizumab) is indicated for:

- inducing and maintaining clinical response,
- inducing and maintaining clinical remission,
- improving the endoscopic appearance of the mucosa, and
- achieving corticosteroid-free remission

In adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

Adult Crohn’s Disease

ENTYVIO (vedolizumab) is indicated for:

- achieving clinical response,
- achieving clinical remission, and
- achieving corticosteroid-free remission

In adult patients with moderately to severely active Crohn’s disease who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

CONTRAINDICATIONS

ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients (such as dsphyme, bronchospasm, urtica, flushing, rash and increased heart rate) [see Warnings and Precautions and Adverse Reactions].

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions and Hypersensitivity Reactions

In UC Trials I and II and CD Trials I and III, hypersensitivity reactions occurred including a case of anaphylaxis (one out of 1,434 patients [0.07%]) [see Adverse Reactions]. Allergic reactions including dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate have also been observed. The majority were mild to moderate in severity as assessed by the investigator. Experience with other biologic medications suggests that hypersensitivity reactions and anaphylaxis to ENTYVIO may vary in their time of onset from during infusion or immediately post-infusion to occurring up to several hours post-infusion.

If anaphylaxis or other serious allergic reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment (e.g., epinephrine and antihistamines).

Infections

Patients treated with ENTYVIO are at increased risk for developing infections [see Adverse Reactions]. The most commonly reported infections in clinical trials occurring at a rate greater on ENTYVIO than placebo involved the upper respiratory and nasal mucosa (e.g., nasopharyngitis, upper respiratory tract infection). Serious infections have also been reported in patients treated with ENTYVIO, including anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis and cytomegaloviral colitis.

ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding treatment in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution when considering the use of ENTYVIO in patients with a history of recurring severe infections. Consider screening for tuberculosis (TB) according to the local practice. For progressive multifocal leukoencephalopathy (PML), see Warnings and Precautions.

Progressive Multifocal Leukoencephalopathy

Another integrin receptor antagonist has been associated with progressive multifocal leukoencephalopathy (PML), a rare and often fatal opportunistic infection of the central nervous system (CNS). PML is caused by the John Cunningham (JC) virus and typically only occurs in patients who are immunocompromised.

In ENTYVIO clinical trials, patients were actively monitored for PML with frequent and regular screenings, and evaluations of any new, unexplained neurological symptoms, as necessary. While zero cases of PML were identified among patients with at least 24 months of exposure, a risk of PML cannot be ruled out. No claims of comparative safety to other integrin receptor antagonists can be made based on this data.

Monitor patients on ENTYVIO for any new onset, or worsening, of neurological signs and symptoms. Typical signs and symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. The progression of deficits usually leads to death or severe disability over weeks or months. If PML is suspected, withhold dosing with ENTYVIO and refer to a neurologist; if confirmed, discontinue dosing permanently.

Liver Injury

There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. In general, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury [see Adverse Reactions].

Live and Oral Vaccines

Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines (e.g., influenza vaccine injection) and may receive live vaccines if the benefits outweigh the risks. There are no data on the secondary transmission of infection by live vaccines in patients receiving ENTYVIO [see Adverse Reactions].

ADVERSE REACTIONS

The following topics are also discussed in detail in the Warnings and Precautions section:

- Infusion-Related Reactions and Hypersensitivity Reactions [see Warnings and Precautions]
- Infections [see Warnings and Precautions]
- Progressive Multifocal Leukoencephalopathy [see Warnings and Precautions]
- Liver Injury [see Warnings and Precautions]

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to ENTYVIO in 3,326 patients and healthy volunteers in clinical trials, including 1,396 exposed for greater than one year, and 955 exposed for greater than two years.

The safety data described in Table 2 are derived from four controlled Phase 3 trials (UC Trials I and II, and CD Trials I and III); data from patients receiving open-label ENTYVIO treatment at Weeks 0 and 2 (prior to entry into UC Trial II and CD Trial III) and from Weeks 6 to 52 (non-responders at Week 6 of UC Trial I and CD Trial I) are included.

In these trials, 1,434 patients received ENTYVIO 300 mg for up to 52 weeks, and 257 patients received placebo for up to 52 weeks. Of these, 769 patients had ulcerative colitis and 962 patients had Crohn’s disease. Patients were exposed for a median duration of 259 days (UC Trials I and II) and 247 days (CD Trials I and III).

Adverse reactions were reported in 52% of patients treated with ENTYVIO and 45% of patients treated with placebo (UC Trials I and II: 49% with ENTYVIO and 37% with placebo; CD Trials I and III: 55% with ENTYVIO and 47% with placebo). Serious adverse reactions were reported in 7% of patients treated with ENTYVIO compared to 4% of patients treated with placebo (UC Trials I and II: 8% with ENTYVIO and 7% with placebo; CD Trials I and III: 12% with ENTYVIO and 9%, with placebo).

The most common adverse reactions (reported by ≥3% of patients treated with ENTYVIO in the UC Trials I and II and CD Trials I and III combined group and ≥1% higher than in combined placebo group) were nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain and pain in extremities (Table 2).
Table 2. Adverse Reactions in ≥3% of ENTYVIO-treated Patients and ≥1% Higher than in Placebo (UC Trials I and II* and CD Trials I and III*)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ENTYVIO1 (N=1434)</th>
<th>Placebo1 (N=297)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>13%</td>
<td>7%</td>
</tr>
<tr>
<td>Headache</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Nausea</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Cough</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Influenza</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Back pain</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Rash</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Oropharyngeal pain</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Pain in extremities</td>
<td>3%</td>
<td>1%</td>
</tr>
</tbody>
</table>

1* Data from patients receiving open-label ENTYVIO treatment at Weeks 0 and 2 (prior to entry into UC Trials II and CD Trial III) and from Weeks 6 to 52 (non-responders at Week 6 of UC Trial I and CD Trial I) are included.

2 Patients who received ENTYVIO for up to 52 weeks.

In controlled- and open-label long-term extension trials in adults treated with ENTYVIO, serious infections have been reported, including anal abscesses, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis.

In UC Trials I and II and CD Trials I and III, patients, including bacterial sepsis and septic shock, was reported in four of 1434 (0.3%) patients treated with ENTYVIO and in two of 297 (0.7%) patients treated with placebo. During these trials, two Crohn’s disease patients treated with ENTYVIO died due to reported sepsis or septic shock; both of these patients had significant comorbidities and a complicated hospital course that contributed to the deaths. In an open label long-term extension trial, additional cases of sepsis (some fatal), including bacterial sepsis and septic shock, were reported. The rate of sepsis in patients with ulcerative colitis or Crohn’s disease receiving ENTYVIO was two per 1000 patient-years.

In clinical trials, all patients were screened for tuberculosis. One case of latent, pulmonary tuberculosis was diagnosed during the controlled trials with ENTYVIO. Additional cases of pulmonary tuberculosis were diagnosed during the open-label trial. All of these observed cases occurred outside the United States, and none of the patients had extrapulmonary manifestations.

Liver Injury

There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO (see Warnings and Precautions). In UC Trials I and II and CD Trials I and III, three patients reported serious adverse reactions of hepatitis, manifested as elevated transaminases with or without elevated bilirubin and symptoms consistent with hepatitis (e.g., malaise, jaundice, nausea, vomiting, abdominal pain, anorexia). These adverse reactions occurred following two to five ENTYVIO doses; however, based on case report information it is unclear if the reactions indicated drug-induced or autoimmune etiology. All patients recovered following discontinuation of therapy with some requiring corticosteroid treatment. In controlled trials, the incidence of ALT and AST elevations ≥3 x ULN was <2% in patients treated with ENTYVIO and in patients treated with placebo. In the open-label trial, one additional case of serious hepatitis was observed.

Malignancies

In UC Trials I and II and CD Trials I and III, malignancies (excluding dysplasia and basal cell carcinoma) were reported in six of 1434 (0.4%) patients treated with ENTYVIO, including colon cancer (n=2), transitional cell carcinoma (n=1), breast cancer (n=1), carcinoid tumor of the appendix (n=1) and squamous cell carcinoma (n=1). Malignancy was reported in one of 297 (0.3%) patients treated with placebo (squamous cell carcinoma).

Malignancies (excluding dysplasia and basal cell carcinoma) observed during the ongoing open label long-term extension trial included B-cell lymphoma, breast cancer, colon cancer, malignant hepatic neoplasm, malignant lung neoplasm, malignant melanoma, lung cancer of primary neuroendocrine carcinoma, renal cancer and squamous cell carcinoma. Overall, the number of malignancies in the clinical trials was small; however, long-term exposure was limited.

Live and Oral Vaccines

There are no data on the secondary transmission of infection by live vaccines in patients receiving ENTYVIO.

In a placebo-controlled study of healthy volunteers, 61 subjects were given a single ENTYVIO 750 mg dose (2.5 times the recommended dose), and 62 subjects received placebo followed by intramuscular vaccination with Hepatitis B surface antigen and oral cholera vaccine. After intramuscular vaccination with three doses of recombinant Hepatitis B surface antigen, those treated with ENTYVIO did not have lower rates of protective immunity to Hepatitis B virus. However, those exposed to ENTYVIO did have lower seroconversion rates and anti-cholera antibodies relative to placebo after receiving the two doses of a killed, oral cholera vaccine. The impact on other oral vaccines and on nasal vaccines in patients is unknown.

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, and the basis of the test. For these reasons, comparison of the incidence of antibodies to vedolizumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In UC Trials I and II and CD Trials I and III, in patients who received ENTYVIO, the frequency of antibodies detected in patients was 13% at 24 weeks after the last dose of study drug (greater than five half-lives after last dose). During treatment of 16 of 1434 (4%) patients treated with ENTYVIO, 16 of 297 (5%) patients treated with placebo, anti-vedolizumab antibody at any time during the 52 weeks of continuous treatment. Nine of 56 patients were consistently positive (at two or more study visits) for anti-vedolizumab antibody and 33 of 56 patients developed neutralizing antibodies to vedolizumab. Among eight of these nine subjects
with persistently positive anti-vedolizumab antibody and available vedolizumab concentration data, six had undetectable and two had reduced vedolizumab concentrations. None of the nine subjects with persistently positive anti-vedolizumab antibody achieved clinical remission at Weeks 6 or 52 in the controlled trials.

**DRUG INTERACTIONS**

**Natalizumab**

Because of the potential for increased risk of PML and other infections, avoid the concomitant use of ENTYVIO with natalizumab.

**TNF Blockers**

Because of the potential for increased risk of infections, avoid the concomitant use of ENTYVIO with TNF blockers.

**Live Vaccines**

Live vaccines may be administered concurrently with ENTYVIO only if the benefits outweigh the risks. [see Warnings and Precautions].

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

**Pregnancy Exposure Registry**

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ENTYVIO during pregnancy. Information about the registry can be obtained by calling 1-877-TAKEDAY (1-877-825-3327).

*Pregnancy Category B:*

**Risk Summary**

There are no studies with ENTYVIO in pregnant women. No fetal harm was observed in animal reproduction studies with intravenous administration of vedolizumab to rabbits and monkeys at dose levels 20 times the recommended human dosage. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the benefits to the mother outweigh the risk to the unborn child.

**Clinical Considerations**

Any adverse pregnancy effect from ENTYVIO would likely be greater during the second and third trimesters of pregnancy. Monoclonal antibodies are transported across the placenta in a linear fashion as pregnancy progresses, with the largest amount transferred during the third trimester.

**Animal Data**

A reproduction study has been performed in pregnant rabbits at single intravenous doses up to 100 mg/kg administered on gestation Day 7 (about 20 times the recommended human dosage) and has revealed no evidence of impaired fertility or harm to the fetus due to vedolizumab. A pre- and post-natal development study in monkeys showed no evidence of any adverse effect on pre- and post-natal development at intravenous doses up to 100 mg/kg (about 20 times the recommended human dosage).

**Nursing Mothers**

It is unknown whether vedolizumab is present in human milk. Vedolizumab was detected in the milk of lactating monkeys. Exercise caution when administering vedolizumab to a nursing woman.

**Pediatric Use**

Safety and effectiveness of ENTYVIO in pediatric patients have not been established.

**Geriatric Use**

Clinical trials of ENTYVIO did not include sufficient numbers of subjects aged 65 and over (46 Crohn’s and ulcerative colitis patients aged 65 and over were treated with ENTYVIO during controlled Phase 3 trials) to determine whether they respond differently from younger subjects. However, no overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Manufactured by:

Takeda Pharmaceuticals America, Inc.
Deerfield, IL 60015

U.S. License No. 1898

For more information, go to www.ENTYVIO.com or call 1-877-825-3327

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VM8245 R2_Brf. L-8ZV-0218-4
Introduction

Each year in the United States, approximately 400,000 people suffer out-of-hospital cardiac arrest (OHCA), with another nearly 200,000 people experiencing cardiac arrest while hospitalized. Of these, the survival to hospital discharge is only 10.6 percent and 23.8 percent, respectively. While improvements in resuscitative efforts such as effective bystander CPR, public access to automated external defibrillators, and early EMS response have increased rates of return of spontaneous circulation (ROSC), many patients still suffer secondary injury or death in the post-resuscitation phase. Emphasis on enhanced post-resuscitation care, including early coronary revascularization, comprehensive critical care, and targeted temperature management can improve patient outcomes. International guidelines on resuscitation have changed to reflect the recent advances in knowledge surrounding the role of patient temperature on neurologic outcomes of cardiac arrest.

Background

Hypothermia has been used in the treatment of various ailments for centuries, with the earliest usage recorded in the Edwin Smith Papyrus, dated 3500 B.C. Through the centuries, there have been reports of the use of body cooling as treatment for diseases such as tetanus, renal colic, mental illness and malignant pain. The first reports of inducing hypothermia after cardiac arrest began to appear in the second half of the twentieth century. Interest in hypothermia declined thereafter, likely due in large part to complications from cooling to temperatures below 32°C. More recently the term “targeted temperature management” (TTM) has evolved to reflect both induced hypothermia and controlled normothermia. Normothermia is defined as 37°C (98.6°F), whereas most define mild-moderate hypothermia as 32-34°C.

Pathophysiology and Proposed Mechanisms of Neuroprotection

Approximately 80 percent of patients who survive out-of-hospital cardiac arrest have some form of neurologic injury. When cardiac arrest occurs, there is cessation of blood flow which causes ischemia to the brain, as well as lack of oxygen exchange (hypoxia). The term hypoxic-ischemic brain injury (HIBI) is well described in the literature and causes significant and widespread brain injury in a length dependent fashion during cardiac arrest. Further complicating the clinical picture is secondary neuronal death which can be delayed for up to several days following the cerebral reperfusion event. HIBI encompasses a range of pathophysiologic mechanisms from cortical and subcortical neuronal injury. A cascade of intracellular and molecular excitotoxicity is initiated that leads to further neuronal injury and apoptosis. Clinically, HIBI may manifest in a mild form as short-term memory loss given the oxygen sensitive hippocampal regions, or in combination with myoclonus (quick motor movements) and ataxia from hypoxic injury to cortical grey matters and cerebellar Purkinje cells. Severe forms of HIBI affect the more oxygen-sensitive regions such as the basal ganglia and subcortical structures, which manifests as akinetic mutism, Parkinsonism, and persistent coma with preservation of brainstem reflexes of pupillary, corneal, gag and cough reflexes. In severe forms of HIBI after cardiac arrest, higher cortical regions, deeper nuclei, and brainstem are affected, which can result in brain death or
loss of all brainstem reflexes. Also, moderate forms of HIBI can cause global cerebral edema (GCE). As GCE progresses, it can lead to global swelling and secondarily raised intracranial pressure and compression of deeper brainstem structures (i.e. herniation) and, subsequently, brain death.

Supporting Evidence

In 2002, two seminal studies utilizing mild-moderate hypothermia (32–34°C) were simultaneously published and served to revitalize interest in temperature management following cardiac arrest.9,10 Bernard et al evaluated the effects of mild hypothermia compared to normothermia (37°C) in survivors of OHCA. This multicenter Australian study included comatose adult patients in whom the initial cardiac rhythm was ventricular fibrillation (VF). Patients were randomized, and cooling of selected patients was begun prior to hospital arrival by removal of patient clothing and application of cold packs. After hospitalization, these patients were cooled with ice packs to a goal core temperature of 33°C and maintained at this temperature for 12 hours before being actively rewarmed. Twenty-one of 43 patients (49 percent) treated with hypothermia survived to be discharged to home or to a rehabilitation facility compared to only 9 of 34 (26 percent) in the normothermia group (p = 0.046), with odds ratio (O.R.) = 5.25, favoring hypothermia. There was not a significant increase in adverse effects noted in the hypothermia group when compared to the normothermia group.10

The second of these two prospective randomized controlled trials of hypothermia in comatose survivors of cardiac arrest was conducted by the Hypothermia After Cardiac Arrest (HACA) Study Group.9 Eligible patients had suffered a witnessed cardiac arrest due to either VF or pulseless ventricular tachycardia (pVT), with ROSC obtained < 60 minutes from the onset of arrest. Patients randomized to the hypothermia group were cooled to a target temperature of 32°C to 34°C using cold air and ice packs as needed. This temperature was maintained for 24 hours, followed by eight hours of passive rewarming. The HACA trial exhibited reduced six-month mortality (41 percent vs. 55 percent) as well as more favorable neurologic outcomes (55 percent vs. 39 percent) in the hypothermia group when compared to the control group. While both of these two practice-changing studies have been criticized for including significant numbers of febrile patients in the control arms, having no specific protocol for management of patients in the control arm, and restricting inclusion to only ventricular fibrillation and ventricular tachycardia, they still had a large effect on post-resuscitation care and lead to changes in the International Liaison Committee on Resuscitation (ILCOR) guidelines (Table 1).11

Patients suffering OHCA with nonshockable rhythms (nonVF/pVT) have not yet been as well studied and there are no randomized data available. There have been mixed results from observational studies of patients presenting with asystole or pulseless electrical activity (PEA). Dumas et al compared registry data for comatose survivors of OHCA and found that compared to control, hypothermia was associated with better outcome in patients presenting with VF/pVT (44 percent vs. 29 percent), but not in patients presenting in asystole/PEA (15 percent vs. 17 percent).12 By contrast, Testori et al retrospectively evaluated a cohort of 375 OHCA whose first documented rhythm was asystole/PEA, of whom 135 patients underwent mild hypothermia (32°C–34°C) for 24 hours with findings of a significantly lower mortality (O.R. = 0.56) and better neurologic outcome (O.R. = 1.84) in the therapeutic hypothermia group.13

The most recent major change in post-arrest management came in 2013 with the publication of the Targeted Temperature Management (TTM) trial in which Nielsen et al compared TTM at either 33°C (intervention group) or 36°C (control group).14 Patients in the intervention arm were comatose survivors of cardiac arrest. This study differs from those of HACA and Bernard et al in that 939 patients were studied in 36 centers across Europe and Australia. While approximately 80 percent of the episodes of cardiac arrest were due to VF/pVT, the TTM group also included asystole/PEA, potentially making this study more generalizable. Within this study, 950 unconscious adults were randomly assigned after out-of-

### Table 1. ILCOR 2015 Recommendations Summary16

- TTM as opposed to no TTM for adults with OHCA with an initial shockable rhythm who remain unresponsive after ROSC (strong recommendation, low-quality evidence).
- TTM as opposed to no TTM for adults with OHCA with an initial nonshockable rhythm (weak recommendation, very low-quality evidence) who remain unresponsive after ROSC.
- TTM as opposed to no TTM for adults with IHCA (weak recommendation, very low-quality evidence) with any initial rhythm who remain unresponsive after ROSC.
- Selecting and maintaining a constant, target temperature between 32°C and 36°C for those patients in whom temperature control is used (strong recommendation, moderate-quality evidence).
hospital cardiac arrest to targeted temperature management at either 33°C or 36°C. The objective was to compare if milder hypothermia (36°C) was associated with increase in mortality and a secondary outcome of comparing neurological outcomes at 180 days. It was concluded that hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C.

Critics of this study point out that 36°C is perhaps ‘forced normothermia’ to very mild hypothermia. Further, the study lumped both asystole/PEA patients as well as ventricular fibrillation patients which was different than the 2002 studies. Therefore, some consider the Nielsen study a non-inferiority study of 33° vs. 36°C. This study therefore can provide leeway in terms of clinical management for a broad category of cardiac arrest patients for practitioners who encounter cardiac arrhythmias or instability at 33°C to ‘retreat’ to 36°C. Conversely, some centers chose to treat with TTM at 36°C which is easier and has less rewarming time involved. Finally, 36°C can be considered forced normothermia or preemptive fever prevention, as fever is universally detrimental in all brain-injury patients regardless of cause. Some have also pointed out that on re-analysis of the 2002 HACA trial the placebo arm of patients became febrile which may have led to worse brain and overall outcomes. Therefore, fever should be aggressively treated or prevented after cardiac arrest with medications (i.e. acetaminophen) and other cooling methods, given that fever in brain injury is associated with worse outcomes.

Mechanism of TTM Protection

The mechanism of TTM and hypothermia on outcomes are best considered pleiotropic or multicentered. Hypothermia reduces brain oxygen consumption and metabolism in a linear fashion, which is known as thermocoupling. Therefore, reduction in brain metabolism can help optimize demand in a limited supply situation. Conversely, hypothermia reduces excitotoxic glutamate cascade in animals and other models which leads to secondary neuronal death pathways and apoptosis. Similarly, TTM and controlled normothermia prevent fever, which reduces brain metabolism. An injured brain can also lose its ability to regulate metabolism. This is called metabolic decoupling. In the setting of higher oxygen demand in brain injury, higher metabolism can lead to worsening supply-demand mismatch and neuronal injury. Despite all decades of drug and other research, only TTM/hypothermia has been shown to improve clinical outcomes after cardiac arrest.

Discussion

Contraindications

There are few absolute contraindications to TTM. The patients who demonstrate rapid neurological recovery and patients who are DNR/against family wishes should not be cooled or have an illness that precludes meaningful neurological recovery. For the remaining population, TTM should at least be discussed and considered. Relative contraindications are those who are high risk for bleeding or who are actively bleeding. Benefit has not been shown for continuing TTM beyond 12-24 hours after obtaining ROSC. Minor contraindications included patients with known diagnosis of cold agglutinins; however, they should not be excluded as these proteins generally aggregate at temperatures less than 31°C. Counter warming methods such as warming gloves and mittens could be used in this patient population.

There are many perceived barriers to initiation of and adherence to TTM, most often the concern of hypotension and bradycardia. Hypothermia is not directly associated as a cause of hypotension. It is generally considered safe to use in patients with cardiac shock and could potentially stabilize these patients. In the HACA trial, 33°C cooling actually improved cardiac index. If hypotension occurs during or after TTM is initiated, it is usually a common cause such as recurrent cardiogenic shock, recurrent myocardial ischemia, systemic inflammatory response (SIRS) vasodilation response with reperfusion, and sometimes sepsis. Bradycardia is common and occurs in depth-dependent fashion that reverses with rewarming. Also, low dose dopamine infusion or other chronotropic support can be effective.

Prehospital TTM

There is considerable debate about the utility and safety of initiating TTM in the prehospital setting. ILCOR does not endorse prehospital TTM: “We recommend against routine use of prehospital cooling with rapid infusion of large volumes of cold intravenous fluid immediately after ROSC due to pulmonary edema (strong recommendation, moderate-quality evidence).” Other TTM strategies during cardiopulmonary resuscitation in the prehospital setting are inadequately studied, with further research into this area being needed. However, if prehospital cooling was initiated, even with mere icepacks, then the receiving facility could continue TTM therapy. The Canadian TTM guidelines, for example, strongly recommend...
the initiation of TTM in any setting in which the necessary support is present, including the prehospital setting.21

Methods and Duration of Cooling:

The methods of cooling vary depending on the availability of equipment and other supplies. There are three general phases of TTM to consider. The first is an “induction” phase of cooling to a certain temperature. The fastest method of inducing cooling is cold ice bath immersion which is an uncommon method. The Thermocool device was used in the HACA study for induction which was an inflatable ice bath-like device. The Bernard 2002 study, by comparison, used ice packs in the prehospital induction phase. The second phase is the maintenance phase, which involves holding a patient at a given temperature. The third phase is rewarming. Figure 1 shows different methods for TTM and hypothermia.

Based on the 2002 randomized trials offering either 12 hours or 24 hours and the recent Nielsen study, the authors recommend choosing either 12 hours or 24 hours based on the time the patient achieved the desired TTM range. For example, if a ventricular fibrillation cardiac arrest patient arrived spontaneously cool from an out-of-hospital cardiac arrest at 7am in the emergency department at 34°C and achieves ROSC, the authors would continue TTM 24 hours and start slow rewarming at 0.25°C per hour the following morning until the patient reaches normothermia 36.5-37°C. The authors would recommend maintaining that while prognosticating outcome. If, however, such a patient arrives at 5pm or achieves TTM between 33-36°C, the authors would continue it overnight for 12 hours and slow rewarm in the morning. The practical side of this recommendation comes from a systems-of-care issue in rewarming in which there are less resources in hospitals at night. Additionally, during the rewarming phase, often patients can overshoot and become febrile, have severe myoclonus with weaning of propofol and other sedation which can go less noticed or attended to in the middle of the night. Also, severe anoxic myoclonus can cause ventilator asynchrony and emotional distress on the family when there are less medical team members to console the family or caregivers. Each center should adopt their own policies and procedures based on all evidence and individualize the recommendation for each patient. The aforementioned recommendations are based on the authors’ clinical experience and evidence.

Prognostication

As described, hypothermia in the immediate ROSC stage has shown benefit; however, prognostication of neurological outcomes remains a struggle. Interestingly, the number one cause of death after ROSC in the setting of cardiac arrest is withdrawal of life-support.8 Imaging and other modalities aid in the clinic exam to guide prognostication. It is important to note that no index or single exam can predict with absolute conviction, rather a multimodal (clinical exam, imagining, electrophysiology etc.) approach should be taken.22 If cooled, the patient needs to be rewarmed and major confounders need to be excluded or corrected. Additionally, prognostic evaluation should not begin sooner than 72 hours post-event as specificity improves.22,23

Figure 1. TTM/Cooling methods. Part A demonstrates ice packs in axilla, which can also be placed topically in other locations. Ice cold cloths can also be used to cool the skin. A gastric lavage can is also shown as a method, as well as an esophageal cooling device (EVD) from Advanced Cooling Therapy. Finally, cooling blankets are commonly employed in hospitals and have different brands (Artic Sun™, Bard Corp., Cincinnati Blanketrol™). Part B shows an intravenous femoral cooling device (e.g., Innercool, Zoll™) which are reported for TTM induction, maintenance and rewarming phases. Figure courtesy Mayo Foundation for Medical Education and Research. All rights reserved.
In the setting of hypothermia, prognostication based on solely the clinical exam may be unreliable due to residua of cardiac arrest medications on the pupil, such as epinephrine and atropine. In particular, within the first 24 hours, absence of pupillary light reflex is associated with false prediction of poor outcome in about one third of patients. An absence of motor response to pain corresponding at ≥ 72 hours from ROSC is a sensitive, but non-specific sign of poor outcome. Similar to corneal reflex, the motor response may be inhibited by the effects of sedating medications and thus caution should be used when relying on these findings. One clinical finding that has been highly associated with poor outcome is the presence of myoclonus lasting greater than 30 minutes as this serves as a sign of damage to the central nervous system.

Computerized tomography (CT) of the head without intravenous contrast is often performed initially to rule out hemorrhagic stroke or other structural abnormalities. Additionally, the head CT allows for evaluation of the densities and interfaces of the grey and white matter. Diffuse brain edema, as seen with post anoxic injury, is shown radiographically as the loss of grey-white matter differentiation. An average global ratio between the densities of the grey matter and the white matter (GWR) <1.14 or a GWR below 1.22 at the level of the basal ganglia seen one hour post ROSC on head CT was shown to predict poor outcomes with 100 percent. MRI is more sensitive to ischemia than CT, generally speaking. However, MRI is not recommended by the American Academy of Neurology (AAN) for routine prognostication due to heterogeneous injury patterns seen that may or may not correlate with final clinical outcomes. Figure 2 shows the AAN algorithm for prognostication.

Somatosensory evoked potentials (SSEP) are among the commonly used electrophysiology tests after cardiac arrest. They have strong prediction potential of poor outcome when the cortical N20 signals are not present and when performed within 24-72 hours post arrest coma setting. Cortical N20 signals are shown in Figure 3. Cortical N20 signals are the
cortical summation of brain signals from the median nerve which is stimulated peripherally. N20 signals typically occur 20 milliseconds after wrist median nerve stimulation, hence the name and similar numeric nomenclature for the other SSEP signals. Absent cortical N20s are strongly predictive of poor outcome, meaning persistent vegetative state or death in longitudinal studies of cardiac arrest patients. However, SSEP has its limitations, including patients with wrist edema which may cause technical difficulties and prevention of this test.

Biomarkers such as the neurospecific enolase (NSE) measured in the blood and S-100 protein can serve as adjuncts in prognostication. There are limitations with their use, including lack of wide availability at all hospitals and some forms of hemolysis causing false positives. If NSE is ordered, the authors recommend testing within 24 hours post-arrest and again within 48-72 hours after initiating cooling or TTM. Given some of the technical issues in hemolysis, comparison and up trending in NSE values can be seen, rather than a single absolute value. Even when two NSE values are obtained, clinical caution is advised given lab heterogeneity in methods, different cut offs in the literature and time points of obtaining NSE values, and elevation in the setting of renal failure. Further studies and analysis are needed, especially in the setting of TTM for NSE, before using this lab test in isolation compared to a comprehensive clinical impression based on all data.

Conclusion

Achieving ROSC is the starting point for caring in survivors of cardiac arrest, as they are still at high risk for further injury. The continued study of these secondary injuries and their prevention may lead to further decreases in patient mortality and disability after cardiac arrest. Interventions to reduce these secondary injuries include early coronary intervention, avoidance of hypocapnea and hyperoxia, and avoidance of hypoglycemia. While questions remain regarding optimum target temperature and timing, post-cardiac arrest temperature management should be an integral component addressed by a dedicated critical care team. Lastly, while no modality of prognostication is 100 percent reliable, the authors support the use of a multimodal approach starting no sooner than 72 hours post cardiac event.

References


Post-Intensive Care Unit Cognitive Dysfunction

By Michael A. Pizzi, DO, PhD

Medical Director, Neuroscience Intensive Care Unit
Assistant Professor, Department of Neurology
University of Florida, Jacksonville, FL

Abstract: In the United States, there are more than five million patients admitted to an intensive care unit (ICU) per year.1 Of the patients that survive to discharge from the hospital, a significant number of these patients will have residual deficits. In particular, cognitive dysfunction can occur months to years after hospital discharge. It is important to understand the various cognitive deficits patients contend with after their ICU admission, proposed pathophysiological mechanisms underlying these cognitive dysfunctions, and possible interventions to mitigate cognitive dysfunction due to critical illness.

Epidemiology

Approximately half of patients admitted to an intensive care unit (ICU) will develop a cognitive dysfunction.1 Half of those patients with cognitive dysfunction will subsequently have persisting symptoms months to years after their ICU admission.2 A meta-analysis of 19 studies evaluating cognitive function after ICU admission showed cognitive dysfunction in 4 to 62 percent of patients with a range of follow up of 2 to 156 months.2 Cognitive dysfunction 12 months after hospital discharge was seen in approximately 25 percent of patients from a cohort of medical and surgical ICU patients.3 In a single center prospective study evaluating medical and surgical ICU patients over 12 months, approximately half of the ICU patients were noted to have cognitive dysfunction at least three months after hospital discharge.4 Furthermore, 55 percent of acute lung injury patients demonstrated cognitive dysfunction on neuropsychological testing at 12 months after discharge.5

Cognitive dysfunction evaluated prior to a critical illness was conducted in two studies. In one study, 2,929 patients had prior neuropsychological testing with 41 of these patients subsequently hospitalized with a critical illness. The patients hospitalized for a critical illness had a greater likelihood of an abrupt cognitive decline.6 That study did not specifically detail if these critically ill patients were admitted to an ICU. In another study with premorbid cognitive assessments on 9,223 patients, 516 of these patients survived severe sepsis. However, just as in the study by Ehlenbach and colleagues,6 not all of these hospitalized patients were admitted to the ICU. Iwashyna et al found only 43 percent of the patients that survived severe sepsis had been admitted to the ICU.7 Furthermore, they found moderate to severe cognitive dysfunction was present in 6.1 percent of patients prior to severe sepsis, and 16.7 percent at follow up of at least one year after severe sepsis.7

Clinical Features of Cognitive Dysfunction

Cognitive dysfunction is often discerned by neuropsychological testing of attention, concentration, executive function, memory, processing speed, visual-spatial functioning, and word-finding capabilities. The most common cognitive dysfunctions after a critical illness are memory and executive function abnormalities. These clinical findings have electrophysiological and radiographic correlations when patients are assessed using electroencephalography (EEG) and magnetic resonance imaging (MRI). Septic (n=25) and nonseptic (n=19) ICU survivors underwent EEG and MRI evaluation, in addition to neuropsychological assessment, at 6 to 24 months after discharge.8 Sepsis survivors demonstrated significantly lower frequency activity on follow up EEG, decreased left hippocampalatrophy, and persistent cognitive dysfunction.8 The increased occurrence of theta and delta frequencies on EEG was seen globally over both cerebral hemispheres. It is hypothesized that the unilateral MRI findings of left hippocampal atrophy could be due to differential hemispheric expression of the neurotransmitter norepinephrine in the right hemisphere.8 Norepinephrine has been demonstrated to exert anti-inflammatory function,10 which coupled with hemispheric asymmetry could explain the previously-mentioned findings.

Pathophysiology

The mechanisms that are involved in cognitive dysfunction after a critical illness are complex and have not been fully

Address correspondence to:
Michael A. Pizzi, DO, PhD
580 West 8th Street, Tower 1, 9th floor
Jacksonville, FL 32209
(904) 244-1022
michael.pizzi@jax.ufl.edu
elucidated thus far. Many theories have been posited involving alterations to baseline neuronal circuitry, neurochemistry, and the neurological sequelae of inflammation after critical illness. Individual variations in connectivity from cortical and subcortical structures may predispose patients to cognitive dysfunctions, such as hallucinations, which may be the result of changes in circuitry of the frontal corticothalamic and limbic areas. Changes in the neurochemistry of an inhibitory neurotransmitter, γ-aminobutyric acid (GABA), and GABA receptors can alter neurotransmission through cortical circuits. This increase in inhibition is further exacerbated with the use of medications that act on GABA receptors, such as benzodiazepines. This increased “inhibitory tone” has been associated with delirium.

Inflammation within the nervous system and systemically has been a well described pathophysiological mechanism associated with cognitive dysfunction after critical illness. Activation of the immune system results in the release of a cascade of pro-inflammatory cytokines, such as interleukin-1β (IL-1β), IL-12, IL-18, and tumor necrosis factor (TNF). These cytokines can activate immune cells such as neutrophils, macrophages and microglia. Furthermore, these cytokines can gain access to the central nervous system (CNS) due to concurrent breakdown of the blood-brain-barrier (BBB). Cytokines in the CNS affect the cardiovascular system, immune system and water balance. There is also evidence that the CNS can be modulated via the vagus nerve. Activation of the vagus nerve can occur by IL-1β as well as pathogenic antigens, thus providing a potential neural pathway for infection and/or inflammation to affect nervous system function. Inflammatory cytokines such as IL-1β, IL-8, as well as soluble TNF receptor-1 and -2, have been associated with delirious ICU patients.

Animal models have demonstrated an increase in inflammatory cytokines IL-1β, IL-6 and TNF after a systemic injury. However, when bone marrow-derived macrophages are depleted, there is a reduction in the pro-inflammatory cytokine IL-6, hippocampal inflammation and memory dysfunction.

Chronic cognitive dysfunction has been noted in patients years after a critical illness due to sepsis. Chronically elevated IL-6 has been associated with cognitive dysfunction in a multi-year longitudinal study. Proinflammatory cytokines TNF, IL-1β, IL-6, nitric oxide (NO), and interferon γ (INFγ) cause increased apoptosis of neurons resulting in reduction or inhibition of long term potentiation, which is required for establishing and maintaining learned behavior. Chronic inflammation in a rodent model was associated with degeneration of basal forebrain cholinergic neurons, which shares histopathology seen in human dementia. The data provides a mechanistic framework implicating chronic neuroinflammation after a critical illness in cognitive dysfunction.

Clinical Factors Affecting Cognitive Dysfunction

The first publication associating critical illness with cognitive dysfunction reported that 100 percent of the patients with acute respiratory distress syndrome (ARDS) had cognitive dysfunction at the time of discharge and 78 percent had cognitive dysfunction one year after ARDS. The authors of that study hypothesized that hypoxia may have resulted in brain injury causing cognitive dysfunction. At least eight subsequent studies have associated survivors of ARDS with cognitive dysfunction six months to two years after discharge. Histopathology of brains from patients noted to have delirium during a critical illness demonstrated hypoxic and ischemic lesions of the hippocampus in 71 percent of analyzed brains.

Glycemic control also plays a role in cognitive dysfunction. In a retrospective review of 74 ARDS survivors, blood glucose levels > 153 mg/dL were associated with a threefold increase in cognitive dysfunction one year after hospital discharge. A retrospective review of surgical ICU patients with at least one episode of hypoglycemia (blood glucose < 40 mg/dL) demonstrated significantly worse cognitive dysfunction one year after ICU discharge.

Sleep architecture of ICU patients is disturbed in patients evaluated by polysomnographic studies in the ICU. Mechanically ventilated patients in the ICU have been found to have atypical sleep patterns using continuous EEG monitoring. Sleep deprivation in the ICU has been associated with delirium. The cause of abnormal and fragmented sleep in the ICU is due to medications, noise, patient-ventilator dysynchrony, light/impaired melatonin secretion, and patient care interactions. Persistent abnormalities in sleep can occur after the patient leaves the ICU. This was demonstrated in a multicenter trial where approximately one-third of post-ICU patients stated sleep disturbances along with cognitive dysfunction and psychological distress at six-month follow up. Sleep deprivation is also associated with immunosuppression and increased incidence of sepsis. Rats that are sleep deprived have leukocytosis, increased catabolic state, and septicemia due to translocation of intestinal bacteria as a result of cellular damage of bowel epithelia.
Sedating medications can have acute and chronic changes in neurophysiology and various neurotransmitter levels, which are associated with critical illness cognitive dysfunction. When mechanically ventilated patients were randomized to a no sedation protocol versus standard treatment of sedation with daily interruptions, there was no increase in long-term neuropsychological morbidity with the no sedation group.

**Treatment Modalities**

**Minimize sedating medications**

Increasing doses of benzodiazepines is independently associated with the risk of delirium across multiple ICU patient populations, and not surprisingly, when benzodiazepine dosages are minimized, the incidence of delirium also decreases. The implementation of scheduled daily interruptions of sedating medications (“sedation vacations”) has shown benefit in ventilated critically ill patients. The use of less sedating medications such as dexmedetomidine, an α2-adrenergic agonist, reduces delirium in ICU patients. Interestingly, dexmedetomidine decreased lung inflammation in septic mice. Surgical patients that received dexmedetomidine, in addition to standard anesthesia of fentanyl and midazolam, had significantly lower levels of IL-1β, IL-6, and C-reactive protein and cognitive dysfunction compared to controls receiving only fentanyl and midazolam.

**Sleep enhancement**

When patients are given earplugs and sleep enhancement protocols are in place, the incidence of delirium decreases. The hope is that by enacting sleep enhancement protocols the patient will maintain an appropriate circadian rhythm. However, septic patients in the ICU have abnormal secretion of melatonin that can play a role in circadian dysrhythmia. Lower melatonin levels are associated with delirium in post-operative ICU patients. Melatonin supplementation was administered to patients admitted to the hospital (not to an ICU) to evaluate the incidence of delirium. Patients that received melatonin (0.5 mg between 6:00 pm and midnight) had a 12 percent incidence of delirium compared to 31 percent in patients not receiving melatonin. Among ICU or acute care patients, the melatonin receptor agonist, ramelteon (8 mg nightly), was associated with three percent of patients with delirium versus 32 percent not receiving. Taken together, there is evidence to utilize nonpharmacologic and pharmacologic interventions to improve sleep and cognitive function.

**Physical rehabilitation**

Post-ICU patients receiving more intense rehabilitation had better cognitive function at the end of the three-month rehabilitation protocol compared to control patients. The cognitive benefits have also been demonstrated when rehabilitation is initiated in the ICU, and even while mechanically ventilated.

**Psychological intervention and counseling**

Surprisingly, there is very little data on psychological interventions and counseling of critically ill patients while in the ICU or after discharge. The use of various psychological interventions, such as providing emotional support and coping strategies, for conscious trauma ICU patients (n=123) and their families was compared to controls (n=86) not receiving such psychological interventions. Psychological evaluation of patients 12 months after ICU discharge showed a decreased risk of PTSD, depression and anxiety in patients that received psychological intervention starting in the ICU.

**Conclusions**

Cognitive dysfunction after a critical illness requiring ICU admission is due to multiple mechanisms ranging from the pathogen itself; the inflammatory response elicited by the pathogen, hypoxia, dysglycemia, poor quality/lack of sleep, and sedating medications. Potential interventions to reduce the risk of post-ICU/critical care cognitive dysfunction are to minimize sedating medications, promote sleep enhancement, initiate rehabilitation as soon as possible, and to provide psychological support and counseling to patients and their families beginning during the ICU course.
References


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Applications of Ultrasound in the Initial Evaluation of Critically Ill Patients

By Carla Venegas-Borsellino, MD1,3, Maria Elena Venegas, MD4, and José L. Díaz-Gómez, MD, FCCM, FASE1,2,3

Departments of 1Critical Care Medicine, 2Anesthesiology, and 3Neurosurgery at Mayo Clinic, Jacksonville, FL
Departments of 4Newborn Critical Care Medicine and Pediatric at Universidad del Norte, Barranquilla, Colombia

Abstract: Critical care ultrasonography (CriCUS) has evolved over the last 15 years and has attained a prominent role as a point of care during assessment of the critically ill. Its application is broad and includes the use of needle guidance during invasive procedures and in the evaluation of different organs and body cavities.

There are several important aspects of CriCUS including its role in the development of protocols to guide the characterization and management of patients with respiratory and hemodynamic failure, its expanding real-time use during needle-guided procedures, and its discovery as a valuable tool during cardiac arrest where it can help identify potentially reversible causes.

Clear benefits from CriCUS include being portable, reproducible among various practitioners, and repeatable without radiation exposure, allowing an opportunity for real-time assessment of therapeutic effects, and its immediacy in the analysis of the ultrasound findings to allow for timely appropriate decisions within the clinical context.

History and evolution

The evolution of critical care ultrasonography (CriCUS) has allowed critical care providers to recognize life-threatening conditions during the evaluation of critically ill patients. Applications include its use in evaluating the heart, lungs, abdominal and pleural cavities, and guiding the needle during invasive procedures.1 CriCUS has gained ground as a tool during cardiac arrest where it can help identify potentially reversible causes.2

The learning curve for most non-cardiologist, non-radiologist physicians has been challenging but nonetheless exciting given the benefits this technology brings to patient care. Ultrasoundography’s journey to the bedside as a vital role in the management of the critically-ill has included major benefits but also controversy, like questions regarding cost-effectiveness.3

Protocols to guide the evaluator in the differential diagnosis have enhanced CriCUS’s utility and its reproducibility and repeatability have allowed continuous, real-time assessment of therapeutic effects. Using bedside ultrasonography, the intensivist can analyze findings without delay and understand them dynamically within a clinical context, 24/7. Bedside ultrasonography also eliminates radiation exposure from radiographs which carry their own diagnostic limitations.1

The device

Constant improvement in United States technology has resulted in availability of a wide array of devices featuring various sizes, qualities, capabilities, and prices. This allows for better evaluation of different organs and improvements in the approach of the differential diagnosis. New equipment trends feature portability, making bedside care available virtually anywhere the patient in need is located.

CriCUS uses ultrasonography 2D and M-Mode modalities with phased array and linear probes, facilitating access to different acoustic windows in the chest and abdomen. The application of gel, firm pressure, and precise hand movements (sliding, tilting, rocking, rotation) of the transducer are necessary to obtain high quality views.4

A real challenge in the United States and other countries is in obtaining optimal ultrasound training which improves diagnostic accuracy and reduces interpretation biases. Currently, there are national and local centers offering different courses and the required amount of performed exams to acquire proficiency.5 The appropriate selection of CriCUS training has been complicated by the substantial variation in the quality of teaching delivered, content of topics covered, and lack of standardization in their goals and objectives. Furthermore, an upcoming National Board Certification for intensivists in Critical Care Echocardiography might be the right first step in defining competence in this field. The board certification is expected to begin in January 2019.

Address correspondence to:
José L. Díaz-Gómez, MD
Departments of Anesthesiology, Critical Care, and Neurosurgery
Mayo Clinic
4500 San Pablo Road
Jacksonville, FL 32224
Phone: 904-953-2000
Email: Diazgomez.josc@mayo.edu
Evidence

Point of care ultrasonography is perceived as reasonable, affordable, and risk-free, but the need for clinicians’ interpretations can potentially lead to incorrect diagnoses. In today’s environment, where management guidelines are based on scientific evidence, physicians should analyze the impact of CriCUS from several perspectives. One aspect is its use as an extension of the physical exam, where new findings can enlighten or confuse a physician’s perception. Still, findings derived from a U.S. exam can significantly impact dynamic management strategies such as volume resuscitation. According to Manasia et al, “Focused Critical Care Echocardiography” (FCCE) performed by an intensivist can change the initial management in 37 percent of patients. Other authors have found that additional diagnostic information of cardiac abnormalities obtained with ultrasonography is around 10 percent.

While intensivists appreciate the benefits of CriCUS as a point of care in managing critically-ill patients on a day to day basis, generating evidence of its impact on patient outcomes carries challenges due to the learning curve, bias while acquiring appropriate clinical skills, and subjective interpretation of the clinical scenario. Nonetheless, there is substantive available literature, based mainly on expert consensus, supporting international recommendations that guide the approach and management in critical situations.

Applications

Lung Ultrasonography

Lung Ultrasonography has recently been considered as a helpful tool in differentiating the etiology of respiratory failure. With time and experience, intensivists have learned the value of the information that sonographic artefacts provide has greatly expanded and a new language has been created for it. The International Meeting on Lung Ultrasound Conference standardized this language based on expert consensus.

With a patient in a supine position, the use of linear and phased array probes in the evaluation of the four quadrants of the chest allows the clinician to identify a series of patterns that differentiates the normal performing lung and pleural cavity from several pathologies.

- Lung sliding is caused by the movement between the visceral and parietal pleura and generates the seashore sign (Figure 1). Its presence rules out pneumothorax. Its absence in M-mode has been called the “barcode sign” (Figure 2).
- Lung point is confirmatory of pneumothorax and represents the transition point between the presence and absence of sliding lung.
- Lung pulse represents the absence of ventilation and the transmitting heartbeat, usually seen in atelectasis.
- B-lines and lung rockets, caused by a change in density of the subpleural lung tissue, are a consequence of increased pulmonary edema or other interstitial syndromes (Figure 3).

Other findings include normal A-lines (horizontal artefact) (Figure 4), the bat sign (pleural line), sinusoid sign indicating pleural effusion (Figure 5), and dynamic air bronchogram, which can be useful in differentiating atelectasis from pneumonia.

For evaluating the lung, the BLUE protocol (Bedside Lung Ultrasound in Emergency), is a validated tool that guides
the analysis of a patient with respiratory failure. It is useful in differentiating between pulmonary edema and interstitial lung pathology, pneumonia, pneumothorax, pulmonary embolism, obstructive pulmonary disease, and asthma. Lung ultrasound (US) also has a role in the diagnosis and real-time invasive management of pleural effusions and pneumothorax with good sensitivity and specificity.\(^9\)

A limitation in the sensitivity of lung US is the presence of subcutaneous emphysema which causes significant artifacts. There is yet to be solid validated evidence that lung US can precisely determine the size of a pneumothorax, and lung US has limited value when considering placement of a thoracostomy tube.\(^10\)

**Echocardiography**

There are some protocols designed to evaluate patients with acute circulatory failure. These include the FALLS (Fluid Administration Limited by Lung Sonography) which was adapted from the BLUE protocol,\(^11\) the FUSA (Focused Ultrasonography in Anesthesia),\(^4\) the FATE (Focused Assessed Transthoracic Echocardiography),\(^12\) and the FCCE (Focused Critical Care Echocardiography).\(^13\) These protocols assess and provide information about the etiology of the obstructive, cardiogenic, hypovolemic, and distributive shock, combining information obtained from the heart and lung, vascular structures, and inferior vena cava (IVC) measurements.\(^14\)

Achieving optimal FCCE can be challenging due to the difficulty of obtaining high-quality windows and avoiding potentially misleading interpretation with foreshortened structures. Other limitations include poor imaging generated by lung interference, body habits, positioning limitations, and dynamic findings.\(^13\)

With the patient in a supine position, FCCE views are obtained with the phase array probe by cutting planes perpendicular or along the major axis of the heart. In short, the windows and the visualized structures are:\(^3,4,14\)

- **Parasternal Long-Axis (Figure 6):** Ideal view includes visualization of the aortic and mitral valves, descending aorta, horizontal orientation of the heart, and lack of visualization of the apex.
- **Parasternal Short-Axis (midpapillary) (Figure 7):** It provides a symmetric perpendicular cut of the left ventricle and allows evaluating the LV performance in relationship with the right ventricle.
- **Apical (Figure 8):** Located at the apex, provides a familiar visualization of the four cardiac chambers.
- **Subcostal (Figure 9):** Allows perspective of both atrioventricular valves and four cardiac chambers. This is the only window where visualization of the IVC is possible.

FCCE is becoming more accepted in the evaluation of patients with shock\(^1\) or other situations where transthoracic echocardiography (TTE) is helpful. Bedside US has been shown to improve the management of cases of cardiopulmonary failure in cardiothoracic ICU patients where the differentiation between hemorrhage and tamponade can substantially alter the management.\(^3\)

In cases involving hypovolemic or distributive shock, US can guide targeted volume expansion and help prevent excessive fluid resuscitation which causes interstitial edema. It can alert the physician when the patient reaches the flat portion of the...
Frank–Starling curve and the cardiac output would not respond to further volume expansion. Using M-Mode while assessing the IVC, volume responsiveness can be predicted based on its dynamics: distensibility index (patients receiving mechanical ventilation) or collapsibility index (spontaneously breathing patients). Other important findings involve the evaluation of lung/plural US which evaluate the effectiveness of diuresis by showing the resolution of B lines.

In cardiogenic shock, FCCE provides information regarding the impact of a poorly contracting right or left ventricle (RV/LV) or significant valvulopathy recognized by using color Doppler imaging. Even with little data supporting this practice, it is common to titrate inotropics based on US findings when there is decreased ejection fraction and/or RV failure and hypoperfusion, despite adequate mean arterial pressure.

FCCE is increasingly utilized in life support. Its main contribution is revealing mechanical contractility and possible reversible etiologies during pulseless electrical activity (PEA) cardiac arrest such as a pericardial tamponade, profound hypovolemia, or severe LV or RV dysfunction, as well as guiding the prognosis in these situations. It appears clear that the absence of cardiac activity indicates a poor prognosis independent of the underlying electrical rhythm. However, more data is needed regarding whether discontinuation of resuscitative efforts should be taken based on echocardiographic findings.

Abdominal Ultrasonography

Ultrasound has been utilized for the examination of trauma patients since the 1990s. Focused Assessment with Sonography for Trauma (FAST) has attained an important diagnostic value in patients with blunt abdominal trauma (BAT) where a wide range of potential intra-abdominal damage can be present and carry significant mortality risk.

It is crucial that emergency physicians treating BAT accurately assess patients and promptly determine the need for surgical management. Using FAST as a bedside alternative offers advantages over the gold standard abdominal computed tomography (CT). For instance, CT utilization implies the following: higher cost, equipment availability, need for radiology consult, time consumption transferring to patient radiology suit, and radiation exposure. FAST is preferred over diagnostic peritoneal lavage (DPL) which is invasive, poses difficulties in some patients (obese or pregnant), and is not easily or frequently repeated.

The FAST exam goal is to identify free intraperitoneal or pericardial fluid which, in the context of traumatic injury, indicates hemorrhage. It examines four areas for presence of free fluid: the perihilar and hepatorenal spaces, the perisplenic space, the pelvis, and the pericardium (Figure 10). FAST is an adjunct to the ATLS primary survey and can be completed by emergency physicians with high sensitivity and specificity.

Acute Neurology

Application of ultrasonography in acute neurology includes monitoring the intracranial pressure (ICP) with transcranial color-coded Doppler (TCCD) and optic nerve sheath diameter (ONSD), which represent non-invasive alternatives in managing patients with acute brain injury. Recording of pupillary light reflex (PLR) when visual access is obscured was recently added as surrogate measure of ICP. Although the efficiency of these ultrasound alternatives is yet to be scientifically established, they have been gradually integrated as acceptable, even preferable neuro-monitoring modalities.

Information regarding intracranial flow direction and distribution can be obtained by studying the flow velocity in the medial, anterior and posterior cerebral arteries by TCCD, to evaluate the collateral capacity of the circle of Willis, and help detect vasospasms following subarachnoid hemorrhage. However, the operator-dependent nature and the frequent presence of inadequate acoustic windows still pose significant limitations.
Vascular Access

Since 1978, US has been used to guide anatomically central venous catheterization. This is a technique utilized by Ullman and Stoelting but its use was first described as a real-time tool in 1986 by Yonei et al. We now have efficacy studies demonstrating real-time ultrasound guidance in reducing associated complications of central venous catheterization. When compared with conventional anatomical (blind) insertion, ultrasound guided insertion can reduce the rates of incorrect catheter placement, the number of failed attempts, and costs. Novel studies support this practice for catheterization of the internal jugular and subclavian veins.

Ultrasound guidance for vascular access also includes arterial cannulation for diagnostic and therapeutic interventions, which can reduce the risk of insertion failure and complications, especially in cases of shock or for extracorporeal membrane oxygenation placement.

CriCUS in Pediatrics

There is actively evolving literature related to the potential benefits of using CriCUS in the characterization of hemodynamic compromise in the neonatal and pediatric population. For these patients, CriCUS can aid in the diagnosis of structural and functional cardiac abnormalities and guide clinical management. It has elevated the routine practice by allowing the neonatologist/pediatrician to perform a more rigorous evaluation.

Functional echocardiography (fECHO), when performed at bedside by the neonatologist, allows an early identification of congenital anatomical anomalies and individualization of the appropriate therapy by providing immediate hemodynamic information required to understand the critically-ill newborn during the stressful transition from intra-uterine to external life. fECHO is useful in evaluating the influence of the patent ductus arteriosus (PDA) and patent foramen ovale in the patient’s hemodynamic status. Persistent pulmonary hypertension, anoxic-ischemic encephalopathy requiring high oxygen levels, and the presence of other congenital cardiomyopathies, among others, can also be more thoroughly evaluated.

Currently, two updated guidelines are available for pediatric intensivists on appropriate training in fECHO and practice recommendations: Targeted Neonatal Echocardiography (TNE) and Expert Consensus Statement on Neonatologist Performed Echocardiography (NoPE). However, the neonatologist still needs close collaboration with the pediatric cardiologist during the initial training and for the management of patients with congenital cardiomyopathies.

Limitations

As mentioned, CriCUS is a highly operator-dependent procedure susceptible to poor quality views and misinterpretation when affected by variables like patient’s position, body habits and chronic diseases. These can greatly impact its utility.

CriCUS is different from a comprehensive ultrasonography performed by fully trained, experienced, and certified sonographers. In order to perform bedside ultrasonography, all physicians independent from their diverse backgrounds and clinical experiences should be trained in the acquisition and interpretation of findings.

With CriCUS, it is necessary to learn how to use the ultrasound artifacts in the differentiation of normal or abnormal tissues and make them meaningful during a dynamic evaluation. As mentioned previously, this task has required the creation of a new language in order to facilitate communication between different providers.

The combination of the array of available equipment with unique qualities and characteristics, and individual operators using different techniques can generate variable interpretations.

Conclusion

Managing critically-ill patients is challenging, requiring rapid accurate assessment and quick decision-making in order to effectively stabilize patients. CriCUS performed by bedside intensivists can have a positive impact in this challenging task, and its use is rapidly spreading. This technology is now accepted as a useful modality in the diagnosis, monitoring and treatment of patients with potentially life-threatening conditions. In order to maintain the values and quality of CriCUS, it is necessary to familiarize operators with the device and provide appropriate training.

Recognizing the significant value of point of care ultrasonography in the critical care arena, it is necessary that all performers maintain the highest level of quality and accuracy in their procedures and interpretations. All clinicians should acquire the needed technical skills to obtain the maximum benefit that ultrasound can provide.

v
References


Introduction

COPD is a chronic obstructive lung disease that is defined as airflow limitation caused by long term exposure to noxious particles or gases such as those from cigarette smoking. It is diagnosed by spirometry when the forced expiratory volume in one second (FEV1) to the forced vital capacity (FVC) ratio is < 70 percent. COPD exacerbations (AECOPD) are an acute worsening of the chronic respiratory symptoms that result in a change in the patient’s regular medications. Patients with AECOPD have an increase in dyspnea, sputum production, and wheezing. Mild to moderate exacerbations are typically treated with outpatient care using steroids and antibiotics, while severe exacerbations typically require hospitalization and lead to increased risk of morbidity and mortality.

The leading risk factor associated with the development of COPD is smoking. During 2007–2012, 46.2 percent of adults aged 40–79 with COPD smoked cigarettes. Approximately 40 million U.S. adults still smoke cigarettes and 4.7 million middle and high school students have used at least one tobacco product. Other factors that contribute to the development of COPD are family history, frequent respiratory tract infections, second hand smoke exposure and long term inhalational injury from environmental exposure.

COPD-Related Morbidity and Mortality

Multiple studies have identified that male gender, emphysema on CT scan, low BMI, functional dyspnea and decreased exercise capacity also contribute to COPD-related morbidity and mortality. A prospective cohort study of 1,016 patients admitted for AECOPD with an elevated PCO2 of 50mmHg or more were found to have a higher mortality than those patients without hypercapnia. During the hospitalization for AECOPD, the mortality rate was 11 percent higher than patients without hypercapnia. Following hospitalization, 33 percent died within six months and 43 percent died within one year. The COPD patients who requiring mechanical ventilation also had a significantly higher in-hospital mortality of 25 percent and up to 50 percent at one year following discharge.

Pneumonia is a major factor causing exacerbations leading to hospitalizations in COPD patients. Pneumonia patients with associated AECOPD have been directly correlated to worse outcomes, increased length of hospital stay, and increased readmissions. Furthermore, these patients are admitted to the intensive care unit more often than patients with non-infectious COPD exacerbations and their mortality risk is higher. Factors that predispose COPD patients to acquire pneumonia include advanced age, severity of COPD, long term use of inhaled or systemic corticosteroids, immunosuppression, and dysphagia.

Patients with COPD and other comorbid conditions such as heart disease have a higher risk of mortality than patients with COPD and no other associated conditions. COPD patients with heart disease have a higher risk of mortality from heart failure, myocardial infarction or arrhythmia.

Treatment

The treatment for COPD exacerbations should be standardized with a multidisciplinary approach that must include clear criteria...
for early non-invasive ventilation and up-to-date medication management according to guidelines. Treatment should include short acting bronchodilators, systemic steroids, treating infection when appropriate, and providing adequate oxygenation and ventilation. Historically, high dose steroids were used for patients with acute bronchospasm in the hospital. However, more recent guidelines emphasize that the efficacy of oral versus intravenous steroids is equivocal and should be no longer than five days in duration and no higher than a dose of 40-60 mg of Prednisone daily. Antibiotic treatment during hospitalizations of AECOPD has been found to decrease treatment failure as most exacerbations are due to respiratory infections. Current consensus is that empiric antibiotics are appropriate for patients with increased dyspnea, increased sputum volume or purulence, or patients requiring hospitalization. Procalcitonin and C-reactive protein (CRP) are being investigated as biomarkers of bacterial infection in patients with suspected pneumonia with COPD exacerbations. Currently, guidelines recommend these biomarkers to be used with clinical judgment in decisions with antibiotic use in AECOPD.

Patients with AECOPD complicated by hypercapnia (pCO2 > 45mmHg) are candidates for non-invasive ventilation (NIV) in addition to the standard treatment. It has been found that NIV decreased mortality from 21 percent to 11 percent, intubation rates from 33 percent to 16 percent, and treatment failure from 42 percent to 20 percent. The length of stay and hospital complications for AECOPD were also reduced by NIV. However, not all patients with AECOPD are candidates for NIV. Patients with cardiac or respiratory arrest, upper airway obstruction, risk for aspiration and inability to clear secretions, severe hemodynamic instability, severe encephalopathy, facial trauma or surgery, and severe gastrointestinal bleeding are contraindicated or partially contraindicated for NIV and invasive ventilation should be the initial treatment of choice. It is also important to note that a step-up medication approach to treating patients with AECOPD requiring hospitalizations is important to reduce morbidity and mortality. The GOLD guidelines (Figure 1) were recently changed from treating patients based on their FEV1 to treating based on the number of exacerbations and symptoms. Additional bronchodilators or other medications to reduce exacerbations should be added based on the control of symptoms and frequency of exacerbations. Another useful and easy diagnostic tool to analyze the severity of dyspnea a patient experiences is the Modified Medical Research Council (mMRC) Dyspnea Scale (Table 1). Once the mMRC

<table>
<thead>
<tr>
<th>Score</th>
<th>Description of Breathlessness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I get breathless only with strenuous exercise.</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on level ground or walking up a slight hill.</td>
</tr>
<tr>
<td>2</td>
<td>On level ground, I walk slower than other people my age because of breathlessness, or I have to stop for breath when talking at my own pace.</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 yards or after a few minutes on level ground.</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house, or I am breathless when dressing.</td>
</tr>
</tbody>
</table>
score is calculated, the provider can calculate the frequency of exacerbations to categorize the severity of disease into categories A, B, C, or D.

Once the severity of disease is calculated based on the above GOLD and mMRC tables, the provider can ensure the patient is on appropriate therapy. Based on the 2017 GOLD guidelines (Figure 1), the first line treatment is a long acting antimuscarinic and beta agonist combination (LABA/LAMA). The reason for this treatment change is that regular treatment with inhaled steroids (ICS) increases the risk of pneumonia, especially in those with severe disease (Evidence A). The studies have shown that long acting muscarinic agents (LAMA) have a greater effect on exacerbation reduction than long acting bronchodilators (LABA) (Evidence A) and can decrease the hospitalization rate (Evidence B). With the exception of patients with a history of asthma or peripheral eosinophilia, the mainstay of therapy of patients with COPD is a LABA or LAMA. Roflumilast or Daliresp, a selective inhibitor of phosphodiesterase-4 (PDE4), was approved to reduce the frequency of exacerbations in patients with severe COPD once the bronchodilator therapy is maximized. Patients who do not meet criteria for roflumilast, specifically chronic bronchitis, and are former smokers may be candidates for the addition of azithromycin three times a week to reduce airway inflammation. N-acetylcysteine (NAC) has recently been shown to reduce the frequency of AECOPD. Eosinophilia in patients with COPD is becoming an important biomarker and will potentially emphasize customized treatment recommendations in the future. Patients who have a peripheral eosinophil count greater than 2 percent have shown a marked reduction in the annual rate of decline in FEV1 (from 74.5 mL to 40.6 mL) with the use of inhaled corticosteroids. Figure 2 includes recommendations for medications based on the GOLD guideline criteria.

There are multiple non-pharmacological interventions that have been studied to reduce COPD exacerbations, but only a few have been shown to be successful in the reduction of COPD

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**Figure 2. Recommendations for medications based on GOLD guidelines criteria.**

**Group C**

- LAMA+LABA
- LAMA+ICS
- LAMA

Further exacerbation(s)

**Group D**

- Consider roflumilast if FEV1 <50% pred and patient has chronic bronchitis
- Consider macrolide (in former smokers)
- Persistent symptoms/ further exacerbation(s)

**Group A**

- A bronchodilator
- Evaluate effect
- Continue, stop or try alternative class of bronchodilator

**Group B**

- A long-acting bronchodilator (LABA OR LAMA)
- Persistent symptoms
- LAMA+LABA
exacerbations. There is strong evidence to support that pulmonary rehabilitation is beneficial for patients with severe COPD. Smoking cessation counseling is critical during any encounter with a COPD patient, especially post hospitalization. Behavioral interventions and approved pharmacotherapy (like bupropion and varenicline) for smoking cessation are recommended. Pneumococcal and annual influenza vaccination is recommended for all patients with COPD to reduce exacerbations. Correcting hypoxemia by providing supplemental oxygen when oxygen saturation is 88 percent or less or pH < 5.5 at rest is also important, although the use of oxygen for exertional or nocturnal hypoxemia in uncomplicated COPD is now controversial. Nutritional support for patients with COPD, such as dietary counseling and supplements, have been found to improve clinical outcomes (such as six-minute walk test), quality of life, and muscle strength but not mortality.

There has been much debate about using home NIV nocturnally with patients with severe COPD and chronic hypercapnia to improve mortality and decrease exacerbations. Based on clinical practice, it is important to note that not all COPD patients will benefit from this therapy. If underlying sleep apnea is suspected to be contributing to hypercapnia, then the patient should be referred for a polysomnography and titration study if indicated. In a randomized trial of 195 patients with severe disease and a baseline pCO2 of > or equal to 52mmHg, the group using NIV had a lower mortality rate of 12 percent compared to those not using NIV of 33 percent at one year. For patients with recurrent exacerbations due to acute on chronic hypercapnic respiratory failure, starting NIV during the hospitalization where serial arterial blood gases and hemodynamics can be monitored may assist with the reduction in the frequency of exacerbations and improve quality of life. There is no data on initiating this therapy for patients with stable COPD.

### Transition of Care

It is well established that the absence of careful planning for the transition of care from hospitalization is linked to an increased likelihood of readmissions, repeat exacerbations, and mortality. In a study, 50 percent of patients readmitted to the hospital had not had a follow-up since prior discharge. Follow-up within 14 days of discharge in patients with multiple comorbidities has shown to prevent one readmission out of every five discharges after an AECOPD hospitalization. Another study concluded that close outpatient follow-up within a month of hospital discharge with a pulmonologist showed a significant reduction in readmission for patients with COPD.

There are a number of barriers and limitations to access for outpatient pulmonary follow-up. These barriers include financial and transportation related issues, insurance authorization, poor discharge recommendations, anxiety about follow up and test results, and need for child or dependent care. Patient dependent factors such as a lack of understanding of their disease process, lack of participation in physical therapy, and ongoing smoking are also contributing factors to difficulty with follow-up.

Despite maximizing pharmacological and non-pharmacological treatments for COPD patients, it is known that the disease progresses. The severity of disease and frequency of exacerbations proportionally increase morbidity and mortality rates. Palliative care should be discussed with these patients transitioning towards the end of life. Factors such as hypoxemia while on supplemental oxygen, weight loss, poor functional status, frequent exacerbations, and progression of the disease should prompt providers to discuss end of life care with these patients. Palliative care and hospice care can provide additional medical equipment, medications, and emotional support for caregivers that are essential in facilitating this process.

### Conclusion

A patient centered multidisciplinary approach is the key to reducing COPD exacerbations and readmissions. Interventions such as evidence-based order sets, streamlining transition of care, and patient education should become a standardized approach to this difficult population. Investments need to be made in dedicated case managers or transition coordinators who play a key role in facilitating the care of these patients from the hospital to an outpatient setting. By providing an action plan to outline appropriate interventions for worsening symptoms, the clinician will hopefully reduce hospitalizations. Additionally, smoking cessation and outpatient pulmonary rehabilitation programs are also beneficial tools to decrease the likelihood of exacerbations of COPD. The mortality and cost of COPD exacerbations on the healthcare system is staggering and increasing annually; therefore, more resources and improved coordination of care should be allocated to this high-risk population.
Critical Care

References


The DCMS Foundation is committed to providing a resource for members that is free and confidential. Our Physician Wellness Program provides three certified counselors who are experienced in coaching health care professionals. Call 904-631-1446 for help!

Online resources available: dcmsonline.org/Physician_Wellness
Domestic Violence/Intimate Partner Violence: Screening, Detection and Intervention

Background:
The Duval County Medical Society (DCMS) is proud to provide its members with free continuing medical education (CME) opportunities in subject areas mandated and suggested by the State of Florida Board of Medicine to obtain and retain medical licensure. The DCMS would like to thank the St. Vincent’s Healthcare Committee on CME for reviewing and accrediting this activity in compliance with the Accreditation Council on Continuing Medical Education (ACCME).

This issue of Northeast Florida Medicine includes an article, “Domestic Violence/Intimate Partner Violence: Screening, Detection and Intervention” authored by Linda Edwards, MD, Jeffrey Winder, DO, Brittany Lyons, DO, and Francys Calle Martin, Esq., LHRM, which has been approved for 2 AMA PRA Category 1 credits.™ For a full description of CME requirements for Florida physicians, please visit www.dcmsonline.org.

Faculty/Credentials:
Linda Edwards, MD is the Senior Associate Dean for Educational Affairs and Associate Professor for the Department of Medicine, University of Florida College of Medicine, Jacksonville, FL. Francys Calle Martin, Esq., LHRM is the Senior Loss Prevention Attorney for the Florida Board of Governors’ Healthcare Education Insurance Company. Jeffrey Winder, DO is Chief Resident, Department of Medicine, for the University of Florida College of Medicine, Jacksonville, FL. Brittany Lyons, DO is a Resident in the Department of Medicine, University of Florida College of Medicine, Jacksonville, FL.

Objectives:
1. Become familiar with the number of patients within a physician’s practice who are likely to be victims of domestic violence.
2. Learn screening procedures for detecting whether a patient has any history of being a victim or perpetrator of domestic violence.
3. Be able to provide patients with information on resources in the local community, such as domestic violence centers and other advocacy groups that provide legal aid, shelter, victim counseling, or child protection services.

Date of release: March 1, 2018 Date Credit Expires: March 1, 2020 Estimated Completion Time: 2 hours

How to Earn this CME Credit:
1) Read the “Domestic Violence/Intimate Partner Violence: Screening, Detection and Intervention” article.
2) Complete the posttest. Scan and email your test to Kristy Williford at kristy@dcmsonline.org or mail it to 1301 Riverplace Blvd., Suite 1638, Jacksonville, FL 32207.
3) You can also go to www.dcmsonline.org/NEFMCME to read the article and take the CME test online.
4) All non-members must submit payment for their CME before their test can be graded.

CME Credit Eligibility:
A minimum passing grade of 70% must be achieved. Only one re-take opportunity will be granted. If you take your test online, a certificate of credit/completion will be automatically downloaded to your DCMS member profile. If you submit your test by mail, a certificate of credit/completion will be emailed within four weeks of submission. If you have any questions, please contact Kristy Williford at 904.355.6561 or kristy@dcmsonline.org.

Faculty Disclosure:
Linda Edwards, MD, Jeffrey Winder, DO, Brittany Lyons, DO, and Francys Calle Martin, Esq., LHRM report no significant relations to disclose, financial or otherwise, with any commercial supporter or product manufacturer associated with this activity.

Disclosure of Conflicts of Interest:
St. Vincent’s Healthcare (SVHC) requires speakers, faculty, CME Committee and other individuals who are in a position to control the content of this educations activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly evaluated by SVHC for fair balance, scientific objectivity of studies mentioned in the presentation and educational materials used as basis for content, and appropriateness of patient care recommendations.

Joint Sponsorship Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of St. Vincent’s Healthcare and the Duval County Medical Society. St. Vincent’s Healthcare designates this educational activity for a maximum of 2 AMA PRA Category 1 credits.™ Physicians should only claim credit commensurate with the extent of their participation in the activity.
Domestic Violence/Intimate Partner Violence: Screening, Detection and Intervention

By Brittany Lyons, DO, Jeffrey Winder, DO, Francys C. Martin, Esq., and Linda R. Edwards, MD

Department of Medicine, University of Florida College of Medicine-Jacksonville

Abstract: Domestic Violence/intimate partner abuse is prevalent throughout the United States (U.S.), as well as the rest of the world. More than one in three women and one in four men report having experienced some form of rape, physical violence, or stalking by a partner in their lifetime. It is therefore important for healthcare providers to be aware of the prevalence of domestic violence and become familiar with appropriate screening and referral tools in order to identify victims and provide resources.

Introduction

News feeds and newspapers seem to be filled with tragic stories of children and women who have lost their lives because of an abusive partner who then turns the gun on themselves. The media draws our attention to the issue of domestic violence/intimate partner violence (IPV), but it is not a recent societal phenomenon. In the U.S., assault did not become a legally recognized reason for divorce until the late 1800’s, and as late as the 1980’s many states carried an exception to the rape statute that exempted from prosecution a man who raped his legally married spouse. Today, every state holds a partner legally liable for marital rape. IPV has been identified and studied as a social problem with serious consequences to individual health and well-being. Healthcare providers should be aware of the issues of domestic violence, including elder abuse, and the risk of abuse to the children in homes where domestic violence occurs.

Definition of Domestic Violence or Intimate Partner Violence

Florida statutes (741.28-741.31) define domestic violence as any assault, aggravated assault, battery, aggravated battery, sexual assault, sexual battery, stalking, aggravated stalking, kidnapping, false imprisonment, or any criminal offense resulting in physical injury or death of one “family or household member” by another who is or was residing in the same single dwelling unit. A family or household member includes spouses, former spouses, persons related by blood or marriage, persons who are presently residing together as if a family, or who have a child in common regardless of whether they have been married or have resided together at any time. The American Medical Association defines domestic violence as the abuse of power or the domination and victimization of a physically less powerful person by a physically more powerful person.

Epidemiology

Intimate partner violence is disturbingly prevalent throughout the United States and the world. More than one in three women (35.6 percent) and one in four men (28.5 percent) report having been the victim of rape, physical violence or stalking by a partner. Although both men and women can experience IPV, women are far more likely to experience severe sexual and physical violence from a partner or to be killed by one. According to the World Health Organization’s report on Violence by Intimate Partners, between 10 and 69 percent of women were physically assaulted by an intimate male partner at some point in their lives. Most assaults are minor and include pushing, grabbing, slapping, and hitting; however, intimate partner violence can lead to death. Sixty-four percent of women who experience domestic violence have an intimate relationship with the perpetrator; however, only 16.2 percent of men have an intimate relationship with their perpetrator. It is difficult to estimate the percentage of perpetrators because victims historically underreport given the consequences of admitting to such actions. These statistics are alarming since most acts of domestic violence are not reported, likely making the actual numbers much higher. In Florida alone in 2016, 105,640 incidents were reported. The majority of those, specifically 84,382 incidents, were simple assault, followed by aggravated assault, rape and threat/intimidation. There were 179 murders and 14 cases of manslaughter related to domestic violence. Researchers in one major metropolitan city examined
murder/suicide by cop and found that 39 percent of incidents involved domestic violence.

Intimate partner abuse often starts or escalates during pregnancy or the postpartum period. Physical abuse is estimated to occur in approximately 7 to 20 percent of pregnancies, making it more prevalent than preeclampsia or gestational diabetes. Pregnancy may lead the woman to focus her attention on her unborn child and thus less attention may be given to her partner. When the pregnancy is unintended the risk of domestic violence is three times greater. Even more alarming is that abused pregnant women have a threefold higher risk of becoming a victim of homicide or attempted homicide.

Pathophysiology of IPV-Power and Control

To better understand the relationship between a victim and his or her abuser, it is important to understand the pathophysiology of IPV. Abusive relationships develop because one individual in the relationship exerts his or her power over the other. The Duluth Wheel of Power and Control exhibits the methods of abuse used by an abusive individual (Figure 1). The use of these methods of power and control by the abuser are unpredictable.

Figure 1. The Duluth Wheel of Power and Control

A tension building phase may begin with threats, intimidation, fear and guilt (described in the wheel), followed by physical or sexual abuse. The abuser may blame their abusive behavior on the victim and the victim may ignore or deny the abuse until it recurs. Because the abusive behavior is unpredictable, women may feel as though they are “walking on eggshells.”

The Affected Individuals

I. Elders:

Elder abuse is included in domestic violence and is prevalent world-wide. Often overlooked, it does not receive the same prevention and screening awareness as intimate partner abuse. The prevalence of elder abuse ranges from 10 percent of cognitively-intact elders to 45-50 percent of those elders who suffer from dementia. Per the National Elder Abuse Incidence Study, 19 percent of the population in the U.S. is over the age of 80, and over half of all reports of abuse are within this age range. Elder abuse includes physical, mental, emotional/psychological and sexual abuse, neglect, abandonment, poor and improper medical care, and financial exploitation. Risk factors that can predispose an elderly individual to abuse include disability, depression, dementia, social isolation, poor socioeconomic status, external family stressors and substance abuse.

Elder abuse can occur in any setting. In the home, usually a daughter or son becomes progressively more frustrated “parenting their parent.” In a nursing home, it could be caused by burnout among the nursing or ancillary staff. A European study published in September 2017 looked at several hundred nursing staff employees, and analyzed three facets: emotional exhaustion, depersonalization, and personal accomplishment. Emotional exhaustion was observed in almost 50 percent of nurses, depersonalization in over 20 percent, and a feeling of low personal accomplishment in almost 40 percent. These numbers are a cause for concern, particularly if these numbers were to remain similar in larger scale studies. Recognition and prevention of burnout in both caregivers and nurses can reduce elder abuse.

The American Medical Association and the American Academy of Neurology specifically advise screening individuals age 65 years and older for abuse. One approach is to utilize the Abbreviated Screening Method, which recommends...
asking your elderly patients three questions:

1. Do you feel safe where you live?
2. Who prepares your meals?
3. Who handles your checkbook?

It is critical that elderly patients be screened alone to eliminate possible intimidation. If any of the above questions raise suspicion for elder abuse, one of the more detailed questionnaires should be performed such as the Brief Abuse Screen for the Elderly (BASE) or The Elder Assessment Instrument (EAI). Elder abuse or suspected abuse should be reported to the physician’s local elder abuse hotline.

Another approach used by law enforcement in field, the elder abuse suspicion index (EASI), is described in a recent publication in September 2017. Data was collected by officers in Connecticut to help better identify their perceptions and knowledge of elder abuse, barriers of detecting elder abuse in the field, characteristics officers deem most valuable as a detection tool, and the potential to use the EASI score in the field. Eighty percent of officers reported they will use the index score long term as it was shown to more easily and reliably help discern unknowing victims of elder abuse.17

II. Adult Victims

Anyone is a potential victim; however, victims of IPV are predominantly women less than 35 years of age, with many having had prior exposure to IPV. Additional risk factors for IPV can be found in Table 1.

Certain groups have a higher prevalence of IPV including trauma victims, emergency room patients, patients with chronic abdominal pain, patients with chronic headaches, pregnant patients with injuries, patients with sexually transmitted diseases, and elderly individuals with injuries. Women living in non-industrialized countries have higher incidence of IPV than those living in industrialized countries.25

Table 1. Risk Factors for Domestic Violence
Adapted from references 19-24

<table>
<thead>
<tr>
<th>Risk Factors for Domestic Violence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior exposure to intimate partner violence</td>
</tr>
<tr>
<td>History of heavy alcohol or drug use</td>
</tr>
<tr>
<td>Female sex</td>
</tr>
<tr>
<td>Young age (&lt; 24 years of age)</td>
</tr>
<tr>
<td>History of depression or chronic mental illness</td>
</tr>
<tr>
<td>Lower level of education</td>
</tr>
<tr>
<td>Residence in lower socioeconomic neighborhood</td>
</tr>
</tbody>
</table>

III. The Littlest Victims – Children

Nationwide, more than three million children are living in homes where IPV occurs. Among these children, studies estimate that the prevalence of child abuse may be as high as 60 percent.27,28 The U.S. Department of Health & Human Services reported that in 2013 alone 678,932 children were victims of child abuse and neglect, signifying that 9.1 in 1,000 children are affected.29

The long-term effects of a child witnessing or being a victim of domestic violence are numerous. They include increased risk for perpetuation of domestic violence in their future relationships along with psychological effects such as depression and vague somatic complaints.30,31 These children may also display increased rebellious behavior with an increased tendency for truancy, dropping out of school, drug and alcohol use and episodes of running away.

IV. The Batterer:

An abuser may lead what appears to be a “normal” life outside the home. The violent behavior may only occur behind closed doors. The abuser may have been a victim of abuse as a child. Men who lived in violent homes as children are more likely to be violent with their adult partners than men who were reared in non-violent homes. For the batterer, casting blame and guilt on the victim can elevate their own sense of worth. Batterers are often abusers of alcohol and drugs.

Clinical Presentation

A patient experiencing intimate partner violence may present in a variety of manners. Often, they present with inconsistent injuries or vague explanations of injuries. Victims may also have poor follow-up, frequently miss appointments, be non-compliant with treatments or may be reluctant to comply with a physical examination. Their partner may be present and reluctant to leave the room during history or examination. It is estimated that between two and seven percent of acute emergency room visits are from IPV.32 Victims will seek care in the emergency department because they are likely to see different healthcare providers each time and there is less follow-up. The patient’s social history may include substance abuse disorders, tobacco abuse, anxiety and depression. Higher rates of previous abuse as a child and suicide attempts are also observed.32,33,34 According to Medical and Psychosocial Diagnoses in Women with a History of Intimate Partner Violence, published in 2009, several signs and symptoms are associated with intimate partner violence and are
noted in Figure 2. Signs and symptoms with the highest relative risk include anxiety, substance abuse, tobacco abuse, depression, headache, sexually transmitted infections, contusions/abrasions, low back pain and lacerations (Figure 2). Persons suffering from IPV and/or sexual/physical abuse also have a 1.5 to 2 times greater risk of having functional gastrointestinal symptoms. Victims of intimate partner violence also reported worse physical and mental health and increased chronic pain and disability preventing employment or absence from work. Physical examination is often unremarkable. However, the physician may discover old fractures, cigarette burns or bites in areas that are not readily visible.

The Role of the Healthcare Provider

Screening

All healthcare providers should remain alert for the presence of IPV, even in asymptomatic patients. The United States Preventive Services Task Force states that screening asymptomatic females for IPV may provide benefits with minimal adverse effects. As of 2013, the U.S. Preventive Services Task Force had a grade B recommendation for the screening of IPV and current recommendations are being updated. The Affordable Care Act passed in August 2012 required insurance companies to cover IPV screening and counseling as part of eight essential health services for women at no additional cost to the patient. Based on this information, all primary care providers should screen females 12 years of age and older for IPV. Additional red flags that suggest screening is necessary include but are not limited to: trauma, chronic or recurrent sexually transmitted disease infections and injuries in the elderly. In a 2014 meta-analysis looking at screening for IPV in the healthcare setting, moderate evidence was found that screening led to an increase in identification of IPV, particularly in the antenatal setting; however, there was no evidence that identification led to more referrals to support services.

Primary care providers can include screening questions in their initial assessment. Asking questions in a non-threatening and non-judgmental manner is imperative. Using phrases such as, ‘I ask all of my patients about violence in the home’ allows the provider to ask the necessary questions without singling out the patient. The healthcare provider should never ask the patient why they have allowed the abuse to happen or why they have not left the situation as this re-victimizes the patient. Raising questions about potential abuse should occur only if the patient is alone. If the questions are asked when the partner is present, the patient may deny that abuse occurs and the potential for escalation of violence at home is increased. Victims should be assured that information will be kept confidential unless there is a lethal weapon involved. Providing resources in restrooms or other private areas of the clinical setting allows women to obtain

<table>
<thead>
<tr>
<th>Signs/symptoms associated with IPV</th>
<th>Relative Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance abuse</td>
<td>6.33</td>
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<tr>
<td>STDs</td>
<td>3.30</td>
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<tr>
<td>Depression</td>
<td>3.24</td>
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<td>Anxiety</td>
<td>2.73</td>
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<tr>
<td>Tobacco abuse</td>
<td>2.34</td>
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<tr>
<td>Lacerations</td>
<td>2.15</td>
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<tr>
<td>Contusions/abrasions</td>
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<tr>
<td>Low back pain</td>
<td>1.58</td>
</tr>
<tr>
<td>Headache</td>
<td>1.56</td>
</tr>
</tbody>
</table>

Table 2. The HITS Screening Tool for Domestic Violence

<table>
<thead>
<tr>
<th>How Often Does Your Partner</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Fairly Often</th>
<th>Frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physically hurt you</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Insult or talk down to you</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Threaten you with harm</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Scream or curse at you</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

A total score of more than 10 is suggestive of intimate partner violence.

The HITS Tool is a first screen and not a diagnostic test. A score of > 10 is strongly suggestive of domestic violence and requires more in depth diagnostic assessment and a safety profile and plan. See Florida domestic violence CME training requirements for safety and referral protocols from the Florida Medical Association. Experts suggest providing the patient with partner violence safety and referral information and knowledge of local shelters and contacts and documenting the patient education. For immediate risk, help arrange for an advocate to assist the patient immediately. The HITS Tool is reprinted with permission from Kevin Sherin, MD, MPH, MBA and is copyright protected.
information without directly speaking to someone. Reasons cited for the lack of routine screening for IPV by healthcare providers include physician comfort levels, awareness of the various techniques, fear of offending the patient and perceived lack of effective interventions.40

Several effective screening tools for intimate partner violence have been developed. A widely utilized screening tool is the HITS (Hurt, Insult, Threaten, Scream) Screening Tool for Domestic Violence (Table 2). HITS consists of four questions scored on a 5 point scale ranging from never to frequently.41 This test has a 30-100 percent sensitivity and 55-99 percent specificity. Physicians may also consider simply asking the patient if he/she is afraid of their partner or anyone else. A positive response can lead to further questioning.

Secondary and Tertiary Prevention: Four Steps to Take Once Intimate Partner Violence is Detected

**Step 1:** Be supportive. Physicians can best support their patients by acknowledging the patient’s admission of abuse and the difficulty the patient must have faced in disclosing this information. In addition, the physician can also ask the victim how they can best support them.

**Step 2:** Assess the patient’s safety. Clinicians should employ open-ended questions to ask victims of IPV about their concerns and fears.42 A validated 20-Item Danger Assessment Tool (Figure 3) is also available to predict the likelihood of lethality or near-lethality in a relationship afflicted by domestic violence.43 Although the majority of patients are not in imminent danger and are not planning to leave their current abusive relationship, clinicians should not lose sight of the fact that IPV can result in death. Physicians should work closely with the patient to formulate a safety plan. A Safety Packing List (Figure 4) highlights items that should be included in the safety plan. Essential items include a set of keys, important

**Figure 3.** The Danger Assessment is an instrument that helps to determine the level of danger an abused woman has of being killed by her intimate partner.43

Reprinted with permission:
documents such as birth certificate(s), additional cash and clothes, as well as the emergency numbers and the number of someone that the victim trusts and can call in an emergency. Patients should be educated on the course of domestic violence and the potential for escalation of violence if the victim chooses to leave the relationship.

Step 3: Know onsite, local and national resources. The best resource for IPV victims is IPV advocacy services as they are well trained in IPV intervention and can most adequately assist the patient in dealing with IPV. Additionally, the National Domestic Violence Hotline is a valuable resource as are others listed in Table 3. Physicians and patients should ensure that any provided resources are hidden or concealed from the abuser. References can be small (thereby easily concealed in a shoe, etc.), obscure (hidden on the back of the physician’s card along with other useful numbers), or even technologically savvy. The ASPIRE News App appears to be a news website but actually offers a discrete way to call for help and can be downloaded onto a phone or other electronic device.

Step 4: Determine whether or not Child Protective Services should be involved. If any child is thought to be unsafe in the home, it is mandatory for the clinician to report this. However, the IPV victim and parent of the child should be encouraged to report on his or her own as this may assist in custody decision making.

Documentation

Careful documentation is imperative in cases of domestic violence, especially when the patient is contemplating pursuing legal intervention. Documentation should include direct quotes from the patient regarding time, nature and other details regarding the abuse; physical exam findings; photography or sketches of the sustained injuries (photographs to include the patient’s face in case of necessity for evidence); and comments on comorbidities and degree of disability. If necessary, rape kits should be obtained, completed and documented. Physicians should not use words such as “denies” or “claims” as this may suggest disbelief in the patient especially in a court of law. More appropriate language includes “patient reports” rather than “patient denies or claims.”

Mandatory Reporting

In the state of Florida, physicians are not required to report domestic abuse unless serious injury or gunshot wounds were inflicted. Similarly, Florida Statute § 877.155 requires any person who treats for second or third-degree burns affecting
10 percent or more of the body to report such treatment to the authorities if they determine the burns were caused by a flammable substance and if they suspect the injury is a result of violence or other unlawful activity. Reporting of domestic abuse without the informed consent of the patient is illegal even if the patient admits to the violence.46

If there is a suspicion of child abuse or an admission of such, the child abuse must be reported to the Department of Children and Families.

As of 2012, only a minority of states had mandatory reporting of IPV which is largely due to the concern that mandatory reporting requirements threaten patient-physician confidentiality and may deter women from seeking needed medical attention or discussing abuse.47,48 In surveys of victims presenting to emergency departments, most victims do not support mandatory reporting.49 This is likely due to the fact that these women recognize that the reporting may lead to an escalation of the violence by their abuser. Nonetheless, it is important that healthcare providers be familiar with their state requirements for mandatory reporting of IPV.

**Intervention**

Randomized control trials studying IPV are not feasible because of the nature of the “disease.” However, in recent years, many meta-analyses have been performed to further investigate the effectiveness of intervention in IPV. In 2013, the World Health Organization issued guidelines stating that, except for women who have spent one or more nights in a shelter or pregnant women, there was insufficient evidence that interventions for IPV improved health outcomes.50,51 Since that time, one large meta-analysis was published suggesting that women-centered advocacy and home-visitation programs reduce a woman’s risk of further violent abuse.52

The effectiveness of batterer’s intervention is also not completely understood. Therapy for batterers includes counseling and group therapy. The duration of treatment in the state of Florida is 26 weeks. In this setting, men with previous abusive behavior challenge other men about their unacceptable behavior. Many men are court ordered into these intervention programs and for those men who do complete at least a six-month program, there is some data to show that the recidivism rate is low.

**Experiencing the Legal System**

Matters involving abuse and IPV fall under the jurisdiction of the Family Court within each legal jurisdiction in Florida. The Family Court has the authority to review those matters that deal with civil domestic, repeat violence, dating violence, stalking, and sexual violence injunctions. These same matters may also result in or stem from criminal actions which would be reviewed by the Criminal Court, usually within the same legal jurisdiction.

If the alleged IPV does not meet the requirements for mandatory reporting referenced above, the patient may also petition the court to provide a temporary injunction if there is an immediate and

### Table 3. Local, State and National Resources

<table>
<thead>
<tr>
<th>Local Hotlines</th>
<th>1-800-500-1119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hubbard House, Inc. (Duval, Baker and Nassau Counties)</td>
<td></td>
</tr>
<tr>
<td>Quigley House (Clay County)</td>
<td>1-800-339-5017</td>
</tr>
<tr>
<td>Betty Griffin House (St. John's County)</td>
<td>1-800-500-1119</td>
</tr>
<tr>
<td>Florida Coalition Against Domestic Violence</td>
<td>1-850-671-3998</td>
</tr>
<tr>
<td>First Step (Batterer’s Intervention Program)</td>
<td>1-904-354-0076 ext. 201</td>
</tr>
<tr>
<td>National Hotlines</td>
<td></td>
</tr>
<tr>
<td>National Domestic Violence Hotline</td>
<td>1-800-799-SAFE (7233)</td>
</tr>
<tr>
<td>National Sexual Assault Hotline</td>
<td>1-800-656-4673</td>
</tr>
<tr>
<td>Child and Elder Abuse Hotline</td>
<td>1-800-96-ABUSE</td>
</tr>
<tr>
<td>The National Teen Dating Abuse Helpline</td>
<td>1-866-331-9474</td>
</tr>
<tr>
<td>Online Resources</td>
<td></td>
</tr>
<tr>
<td>Futures Without Violence</td>
<td><a href="http://www.futureswithoutviolence.org">www.futureswithoutviolence.org</a></td>
</tr>
<tr>
<td>National Coalition Against Domestic Violence</td>
<td><a href="http://www.ncadv.org">www.ncadv.org</a></td>
</tr>
</tbody>
</table>
present danger of domestic violence. The petition for temporary injunction can be filed where the patient currently or temporarily resides, as well as where the abuser resides, or where the domestic violence occurred. The court may consider a number of factors when determining whether to grant the temporary injunction, including the abuser’s past history of violence against the patient and others.

These proceedings are usually first filed as an ex parte temporary injunction, meaning that the other party, or the abuser, is not present. If the ex parte temporary injunction is granted, it is effective for 15 days, and the court must set a full hearing to take place no later than the 15-day period to determine whether it will grant a permanent injunction. During this temporary injunction period, the court may restrain the abuser from contact with the patient, provide the patient exclusive occupancy of any shared dwelling, or specify places that the abuser must stay away from, like places of employment, children’s schools, or other family homes. The court may also order the abuser to surrender any firearms to the Sheriff’s Office, as well as any other relief the court believes is necessary.

At the hearing for final injunction, both the patient and the abuser are permitted to have advocates present from the State Attorney’s Office, law enforcement, or a domestic violence center. The court may also consider relevant evidence of abuse and violence from the patient’s medical records. If the court approves a final injunction, it may also order temporary support of any minor children, temporary alimony, and refer the patient to a domestic violence center. Though the patient cannot be ordered to attend counseling, the abuser can be ordered to undergo a substance abuse or mental health evaluation and any treatment that is recommended. The abuser may also be ordered to enroll in and complete a certified batterer intervention program. Any violations of these injunctions are treated as criminal matters, and the Florida Department of Law Enforcement maintains a Domestic, Dating, Sexual and Repeat Violence Injunction Statewide Verification System that will communicate these injunctions between state criminal agencies. Violation of a final injunction may result in arrest and charge of a first-degree misdemeanor for each violation with a maximum sentence of one year. The Domestic Violence Case Flow in Table 4 provides an example of the possible course of a case.53

**Conclusion**

Domestic violence is prevalent and impacts the psychological and physical well-being of the victims, as well as the children in the homes where the abuse occurs. It is associated with financial and societal ramifications. Health care providers should pursue a better understanding of victims and their perpetrators, the clinical presentation, who and how to screen for IPV and the resources that are available to victims. Be your patient’s advocate! ✧

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Table 4. Domestic Violence Case Flow created by the Florida Courts53

<table>
<thead>
<tr>
<th>Petitioner completes and files petition with clerk or designee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petition § 741.30(1)1 and Supporting Documents2 reviewed by Judge, ex parte issues order § 741.30(4), earliest time possible</td>
</tr>
<tr>
<td>Injunction Denied3 - written reasons required § 741.30(5)(b)</td>
</tr>
<tr>
<td>Temporary Injunction Issued; Return Hearing Set</td>
</tr>
<tr>
<td>Extension § 741.30(5)(c)</td>
</tr>
<tr>
<td>Service on Respondent § 741.30(8)(b)(1)</td>
</tr>
<tr>
<td>Hearing within 15 days of filing petition § 741.30(5)(c)</td>
</tr>
<tr>
<td>Alleged Violation § 741.30(9)(a)</td>
</tr>
<tr>
<td>Motion for Modification/Dissolution § 741.30(6)(c) § 741.30(10)</td>
</tr>
<tr>
<td>Final Injunction Issued § 741.30(6)(a-c) Provisions; Injunctions set until specified date or until further order of the court</td>
</tr>
<tr>
<td>Final Injunction Denied</td>
</tr>
<tr>
<td>Service on Respondent § 741.30(8)(c)</td>
</tr>
</tbody>
</table>

1Statutory citations are from 2016 Florida Statutes.
2Supporting documents - UCCJA, Affidavit, Confidential Address, Child Support Guidelines, Worksheet, Case Sheet for Family Law Cases.
3Petitioner may file/submit supplemental affidavit.
References


12. Williamson G, Shaffer D. Relationship quality and potentially harmful behaviors by spousal caregivers: How we were then, how we are now. The family relationships in late life project. *Psychol Aging*. 2001 Jun;16(2):217-26.


**Domestic Violence/Intimate Partner Violence: Screening, Detection and Intervention**

**CME Questions & Answers** (circle one answer)/Free to DCMS Members/$55.00 charge non-members*

(Return by March 1, 2020 BY MAIL: 1301 Riverplace Boulevard, Suite #1638, Jacksonville, FL 32207 or ONLINE: www.dcmsonline.org/NEFMCME)

1. Approximately how many women will experience domestic violence at some point in their lifetime?
   a. 1 in 1,000
   b. 1 in 100
   c. 1 in 10
   d. 1 in 5

2. Approximately how many men will experience domestic violence at some point in their lifetime?
   a. 1 in 1,000
   b. 1 in 100
   c. 1 in 10
   d. 1 in 4

3. Which of the following recommendations regarding IPV screening are true:
   a. The Affordable Care Act of 2012 required insurance companies to cover IPV screening at no additional cost to the patient
   b. Additional ‘red flags’ that suggest screening is necessary include, but are not limited to, trauma, chronic or recurrent sexually transmitted disease infections, and injuries in the elderly
   c. All primary care physicians should screen females 12 years of age and older for IPV
   d. All of the above

4. During a patient encounter, which of the following is not a ‘red flag’ that would make a physician consider IPV?
   a. A partner who is reluctant to leave the room
   b. A patient who has repeated unexplained injuries
   c. A patient with poor follow up
   d. A patient who appears anxious or depressed
   e. A patient with consistent follow up

5. Children who witness or are the victims of domestic violence are at increased risk for perpetuating domestic violence in their future relationships.
   a. True
   b. False

6. During pregnancy, domestic violence:
   a. Stays the same
   b. Decreases
   c. Increases
   d. C and/or D

7. Violence may escalate when the victim attempts to leave the abusive relationship.
   a. True
   b. False

8. Victims of domestic violence who have been surveyed prefer that violent crimes perpetrated against them be reported to authorities.
   a. True
   b. False

9. In the state of Florida, the physician is required to report:
   a. All cases of suspected domestic violence
   b. No cases of suspected domestic violence
   c. Cases of suspected domestic violence where serious injury occurs
   d. Cases of suspected domestic violence where gunshot wounds are inflicted
   e. Both C and D

10. Which of the following is not part of adequate documentation of domestic violence?
    a. Direct quotes from the patient
    b. Physical exam findings
    c. Photographs or sketches of injury
    d. Using language such as ‘patient denies’ or ‘patient claims’

11. Which of the following is true regarding offering a patient information on resources?
    a. Physicians should provide a patient experiencing intimate partner violence with a local or national Help Hotline phone number and encourage the patient to leave their spouse.
    b. Physicians should provide a patient experiencing intimate partner violence with a local or national Help Hotline phone number and encourage the patient to leave their spouse.
    c. Physicians should provide a patient experiencing intimate partner violence with a local or national Help Hotline phone number and encourage the patient to leave their spouse.
    d. Physicians should provide a patient experiencing intimate partner violence with a local or national Help Hotline phone number and encourage the patient to leave their spouse.

12. If the Court grants an ex parte temporary injunction, it is effective for:
    a. 1 year
    b. 30 days
    c. 15 days
    d. None of the above

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**Evaluation questions & CME Credit Information**

(Please evaluate this article. Circle one number using this scale: 1= Strongly Agree to 5= Strongly Disagree)

| The article met the stated objectives: | 1 | 2 | 3 | 4 | 5 |
| The article was appropriate to my practice: | 1 | 2 | 3 | 4 | 5 |
| The topic was current and well presented: | 1 | 2 | 3 | 4 | 5 |

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Account # ___________________________ Expiration date ___________ Security Code ___________

Signature ___________________________
Sepsis: Past, Present and Future

By Pramod K. Guru, MBBS,1 Ami A. Grek, ARNP,1 Philip Lowman, MD,1 Pablo Moreno Franco, MD1,2

1Department of Critical Care Medicine, Mayo Clinic, Jacksonville, FL
2Division of Transplant Medicine, Mayo Clinic, Jacksonville, FL

Abstract: Sepsis is a clinical syndrome characterized by life-threatening multi-organ dysfunction due to an unbalanced host response to infection. It remains an important global health challenge, despite significant advancements in medical sciences. More than one-third of hospitalized patients with sepsis succumb to their illness even after receiving the best available, evidenced-based care.1 Many factors related to patient, provider, and place of care are responsible for this dismal outcome. The biggest challenge is the absence of pharmacologic therapy to reverse the disrupted host response in sepsis. However, there has been a paradigm shift in the management of sepsis patients over the past couple decades. International and national collaborative efforts for standardized care, and focused research on pathophysiology, early detection, and treatment of sepsis have resulted in improved outcomes. Among the various interventions and bundled therapy proposed for care of sepsis patients, source identification and timely initiation of appropriate antimicrobial therapy and hemodynamic interventions are primarily responsible for the observed downward trend in mortality.

Introduction

Sepsis is not a disease, but rather a heterogeneous clinical syndrome. The life-threatening organ injuries encountered at bedside are not necessarily due to causative infectious agents; they may be due to unchecked and unbalanced host immune response directed to contain the infection. These responses are primarily responsible for the multi-organ abnormalities.1 Though physicians have been aware of sepsis as a lethal condition and have been trying to mitigate its consequences for hundreds of years, no attempts were made to define sepsis until the latter part of the 20th century.2 Since the first publication of Surviving Sepsis Campaign Guidelines (SSCG) in 1992, there have been three revisions, the most recent in 2016.1,3,5 Under the auspicious umbrella of the Surviving Sepsis campaign, remarkable progress in sepsis care has been achieved throughout the world. Increased awareness and adherences to bundled care, with primary focus on early goal-directed therapy (EGDT), despite the critique to the elements of this bundle, are the backbone of the progress. The latest ‘Sepsis-3’ consensus definition has reiterated the importance of aberrant immune response and acknowledged that host damage can continue even after successful treatment of the triggering infection. Still, there are multiple challenges to overcome to achieve optimal desired goals in the quest to conquer the devastating sepsis syndrome.6-8 It is important for physicians to look at the current status of sepsis care at local and international levels. It is also critical to understand the epidemiology of sepsis, the evolution of bundle therapy, current screening criteria, including benefits and limitations, and the hurdles in implementation of the guidelines.

Sepsis Burden, Causes, and Pathogenesis

Disease Burden:

Sepsis is a major public health burden similar to cardiovascular disease and stroke. Assessment of the global burden of sepsis has been hampered by lack of a uniform definition, proper documentation, and access to health care facilities.6,8 Epidemiologic data from low and middle-income countries are scarce to nonexistent. In the latest report from the United States, the incidence of sepsis varies between 300-1,031 cases per 100,000 populations and is rising.9 The reported case fatality remains high at 14.7-29.9 percent.9 Another recent study of seven high-income countries estimated the incidence rate for hospital-treated sepsis at 437 and for hospital-treated severe sepsis at 270 cases per 100,000 person-years.10 Case fatality rates were 17 percent and 26 percent for sepsis and severe sepsis, respectively, from 1979-2015.10 Extrapolation of data to the entire world gives an estimate of 31.5 million sepsis cases, 19.4 million severe sepsis cases, and up to 5.3 million deaths annually.10 However, there is a silver lining as the mortality rate has been reduced to 20 percent in recent years, improving overall sepsis burden.11

Causes of Sepsis:

In high income countries, including the United States, bacterial pathogens are primarily responsible for sepsis. Patients acquire the infections both from the hospital and community. The primary
source of infection leading to sepsis and intensive care unit (ICU) admission is pneumonia (more than half of patients), followed by infection from abdominal and genitourinary sites. In the past, gram-positive bacteria were mostly responsible for sepsis; however, recent studies have reported predominance of gram-negative bacteria as the leading cause of severe sepsis. Viral, protozoal, and fungal infection can progress to sepsis, though there are fewer incidences compared to bacterial infection. Underlying co-morbidities and virulence of the pathogen play important roles in the risk of progression to sepsis after initial infection.12

Pathophysiology of Sepsis:

As emphasized in the Sepsis-3 report, the current understanding of sepsis pathophysiology is primarily based on abnormal host response to the infection. Excessive innate host inflammatory response to the inciting pathogen and consequent collateral tissue damage are primarily responsible for sepsis-associated organ dysfunctions. Down-regulation of adaptive immune function also plays a significant role in pathogenesis. The theory of dysregulated host response to the infection does not take into consideration the importance of direct injury to the organs inflicted by the inciting pathogens and/or their virulent products. This limits the generalizability of case definitions and management guidelines. An in-depth discussion of the pathophysiology of sepsis is beyond the scope of this article, but can be found in reviews.

Sepsis Definitions and Care Plans:

Sepsis Definitions: Past and New Changes

To speak the same language, understand the disease burden, and improve care, there was a movement to focus on research to develop universal care guidelines for better outcome efforts. Initial efforts were made in 1992 to develop sepsis definitions, with subsequent efforts in 2003 and 2016 (Table 1).

The non-specific nature of systemic inflammatory response syndrome (SIRS) criteria outlined in Sepsis-1 led to the development of Sepsis-2 in 2003. Sepsis-2 was more complex, but still lacked specific diagnostic criteria. With the aim of more universal definitions, Sepsis-3 was developed in 2016.
Critical Care

The aim of this constantly changing process is for early and accurate diagnosis of sepsis. This highlights the complexity of the sepsis syndrome and the challenges it brings to the medical community.6

Major changes from previous iterations found in Sepsis-3 include the removal of the term “severe sepsis,” as all sepsis is considered to be life-threatening organ dysfunction. The term “septic shock” includes that subset of patients with both serum lactate >2 mmol/L and the requirement for vasopressors to maintain their mean arterial pressure >65 mm Hg in the absence of hypovolemia. A new diagnostic tool to screen for sepsis, termed qSOFA (quick Sequential Organ Failure Algorithm) was also introduced by the task force. This scoring system, which evaluates for altered mentation, respiratory rate ≥ 22, and systolic blood pressure ≤ 100 mm Hg, was found to be as predictive as SOFA score for in-hospital mortality.16 Hospitalized patients with an acute change in SOFA score ≥ 2 due to infection had an overall mortality risk of 10 percent. The task force emphasized that neither SOFA nor qSOFA are intended to be all inclusive, and a positive score should prompt further investigation by clinicians.1,5,16 Clinical usefulness and how to operationalize the current definition remain unclear.6,7,20

Sepsis Care Plans: Current Status of Bundled Therapy and New Developments:

Attempts to reestablish the immune homeostasis and improve patient outcomes by multiple therapeutic agents and other adjuvant strategies in patients with sepsis have been ineffective so far. The agents include activated protein C, antithrombin III, hydrocortisone, intensive insulin therapy, high-volume renal replacement therapy, tifacogin, starch, and antioxidant therapy.21-27 The SSCG advocates continued education and implementation of the recommendations, not only for early diagnosis, but also timely introduction of a care bundle for better patient outcomes in sepsis. In Sepsis-1 and -2, the focus of care was mainly centered on EGDT.28 However, three recent major trials from three different continents showed that there was no difference in mortality between EGDT care and usual care.29-31 Based on the accumulated data, Sepsis-3 guidelines involve changes in management from past guidelines both in fluid resuscitation and measure of volume responsiveness. As part of the bundled therapy, aiming to avoid under resuscitation, the guideline supports 30 ml/kg of fluids in sepsis patients. However, the significance of both the dose and timing of fluid administration in clinical practice is to be determined.32 Recent updates to these guidelines (available at www.survivingsepsis.org) also move away from central venous pressure and mixed venous oxygen saturation monitoring as measures of resuscitation to a weight-based crystalloid resuscitation followed by frequent reassessment of dynamic physiologic variables used to predict volume responsiveness.

Multiple promising therapy and organ support strategies are on the horizon, but more work needs to be done before we can experience their utility. Examples include the use of ghrelin, innovative blood purification and extracorporeal therapy, pharmaconutrients such as...
as large dose vitamin D therapy and the recent report of using vitamin C and thiamine, mediator modulations by recombinant alkaline phosphatase, cytokine inhibitors, and gene profiling and metabolomics for individualized patient care.\textsuperscript{17,33-36}

**Challenges and New Strategies:**

**Early Diagnosis: Role of Biomarkers and Screening Tools**

Despite the years of research, there is not a single specific test to diagnose sepsis. However, the importance of early diagnosis of sepsis cannot be undermined, given the high mortality and morbidity associated with it. To circumvent this challenge, multiple screening tools (electronic and non-electronic) and biomarkers have been developed and used by providers.\textsuperscript{7}

Available biomarkers are limited by their lack of sensitivity and specificity. Future research and studies should not only focus on biomarkers for early diagnosis and differentiation of infections from colonization, but also individual patient-specific targeted therapy for better outcomes.\textsuperscript{6,20}

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**Figure 2. Sepsis Observed/Expected Mortality Index and Bundle Compliance at Mayo Clinic in Jacksonville, Florida from 2013-2016**

<table>
<thead>
<tr>
<th>Tracking #</th>
<th>Change</th>
<th>Initial Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Surviving Sepsis Campaign 2012 was published</td>
<td>2/15/2013</td>
</tr>
<tr>
<td>2</td>
<td>Quality Improvement Team Formed</td>
<td>3/15/2013</td>
</tr>
<tr>
<td>3</td>
<td>Stakeholders Initial Presentation</td>
<td>7/15/2013</td>
</tr>
<tr>
<td>4</td>
<td>Selected Antibiotics Added to Pixis</td>
<td>8/1/2013</td>
</tr>
<tr>
<td>5</td>
<td>Sepsis Sniffer Testing</td>
<td>8/1/2013</td>
</tr>
<tr>
<td>6</td>
<td>Activation Flow Sheet Posted in ED</td>
<td>9/1/2013</td>
</tr>
<tr>
<td>7</td>
<td>Process of Care Paper Checklist</td>
<td>9/1/2013</td>
</tr>
<tr>
<td>8</td>
<td>SSRT Team Activation</td>
<td>9/1/2013</td>
</tr>
<tr>
<td>9</td>
<td>Internal Website and Suggestion Box</td>
<td>9/9/2013</td>
</tr>
<tr>
<td>10</td>
<td>Monthly Email Feedback to Providers</td>
<td>10/1/2013</td>
</tr>
<tr>
<td>11</td>
<td>Grand Rounds Presentation</td>
<td>10/4/2013</td>
</tr>
<tr>
<td>12</td>
<td>ED Nursing Didactics</td>
<td>10/1/2013</td>
</tr>
<tr>
<td>13</td>
<td>Pocket Cards Distributed to Providers</td>
<td>10/10/2013</td>
</tr>
<tr>
<td>14</td>
<td>Add Medical Record Number to pager info</td>
<td>10/18/2013</td>
</tr>
<tr>
<td>15</td>
<td>Training PCU and ICU Nurses</td>
<td>1/1/2014</td>
</tr>
<tr>
<td>16</td>
<td>ED Nursing Simulation Training</td>
<td>1/7/2014</td>
</tr>
<tr>
<td>17</td>
<td>Central Line and SCVO\textsubscript{2} Focus Group</td>
<td>2/1/2014</td>
</tr>
<tr>
<td>18</td>
<td>Initial Lactate Ordered as Protocol</td>
<td>2/19/2014</td>
</tr>
<tr>
<td>19</td>
<td>ProCESS Trial was Published</td>
<td>3/18/2014</td>
</tr>
<tr>
<td>20</td>
<td>Multidisciplinary Sepsis Orderset</td>
<td>7/1/2014</td>
</tr>
<tr>
<td>21</td>
<td>Tracking of MAP improvement and Lactate percentage clearance started</td>
<td>9/1/2014</td>
</tr>
<tr>
<td>22</td>
<td>Control phase starts</td>
<td>9/1/2014</td>
</tr>
<tr>
<td>23</td>
<td>ARISE Trial was Published</td>
<td>10/1/2014</td>
</tr>
<tr>
<td>24</td>
<td>Tracking of Central line, Central Venous Pressure and SCVO\textsubscript{2} discontinued</td>
<td>12/31/2014</td>
</tr>
<tr>
<td>25</td>
<td>ProMise Trial was Published</td>
<td>3/17/2015</td>
</tr>
<tr>
<td>26</td>
<td>Shock Alert Introduced</td>
<td>8/1/2015</td>
</tr>
<tr>
<td>27</td>
<td>Feedback email to providers within 48hrs</td>
<td>9/1/2015</td>
</tr>
<tr>
<td>28</td>
<td>Bi-weekly feedback introduced</td>
<td>10/1/2015</td>
</tr>
</tbody>
</table>

SSRT: Septic Shock and response team, ICU: Intensive care unit, PCU: Progressive care unit, ED: Emergency department, SCVO\textsubscript{2}: Central venous oxygen saturation

Data Source: Mayo Clinic Florida Sepsis and Shock Response Team Database and University Healthcare Consortium Sepsis Mortality
The current electronic screening tool and scoring system is promising for early detection and management. Sepsis is a dynamic process, and the patient’s clinical condition changes rapidly; therefore, development of a single diagnostic algorithm may not be applicable to all clinical scenarios. Although the alert system seems promising, available evidence for its usefulness is yet to be validated.

Local Initiatives: Sepsis and Shock Alerts at Mayo Clinic in Jacksonville, Florida

At Mayo Clinic Florida, there are electronic screening systems available that alert for both sepsis and shock. The algorithm evaluates each patient admitted to the emergency department (ED) and sends a sepsis alert based on certain criteria. Details on the criteria used in the electronic “sepsis sniffer” algorithm can be found in the supplement to this article. If after receiving a sepsis alert page the ED team feels that the patient is septic, the registered nurse starts the sepsis checklist and asks the clinician to evaluate for signs of severe sepsis or septic shock. If the clinician determines the patient meets one of these two criteria, they will activate the sepsis and shock response team (SSRT). The sepsis sniffer followed by human decision to activate SSRT approach had a sensitivity of 100 percent (95 percent CI 99.1-100 percent) and specificity of 96.3 percent (95 percent CI 96.1-96.6 percent) for patients who had sepsis present as a discharge diagnosis and met Sepsis-2 criteria on manual review between 2013-2014. In comparison, Sepsis-3 definitions have sensitivity of 55-68 percent and specificity of 63.4-84 percent.

After recognizing the value of sepsis alerts, a shock alert was implemented at Mayo Clinic Florida’s ED, ICU, and medical step down unit during 2015. A shock alert was initiated based on the following criteria: the patient was older than 16 years of age and either two consecutive blood pressures were less than 90 mmHg or a lactate greater than 4 mmol/L within the first six hours of admission to a patient care unit. Alongside these shock alerts, physicians were able to track bundle compliance on patients who met severe sepsis or septic shock criteria. These alerts required notification to primary care providers, asking them to confirm the type of shock and to come to the bedside to assess the potentially decompensating patient. During the initial two months, Mayo Clinic Florida experienced 265 shock alerts; 71 percent of those patients required an intervention at the time of alert. Some of the interventions included blood transfusions, medication administration, and escalation of care. Furthermore, 28 percent of these patient alerts had sepsis as the cause and 15 percent.

Figure 3. Centers for Medicare and Medicaid Services Sepsis (Sep-1) Quality Measures- All or Nothing Bundle Compliance at Mayo Clinic in Jacksonville, Florida
percent met criteria for septic shock. During the study period, all-or-none bundle compliance with the three-hour bundle elements was 74 percent.

In the authors’ experience, the screening algorithm is very helpful for triage and increasing the compliance as mandated by the Centers for Medicare and Medicaid Services (CMS) Sepsis Core (SEP-1) Measure. Our compliance with the three-hour bundle elements is depicted in Figure 1. The impact on decreasing the Observe/Expected Sepsis Mortality Index is illustrated in Figure 2 and all-or-none compliance with SEP-1 is shown in Figure 3.

Challenges with Implementation of Clinical Guidelines

The pathogen responsible for the sepsis, their antimicrobial sensitivity, and the practice pattern varies among regions and hospitals. There is no gold standard for sepsis diagnosis, and sepsis physiological deranges in multiple organ systems. Sepsis patients can vary widely on their presentation; definitions have changed frequently, and available evidence is not robust enough to dictate which specific bundle elements will improve patient outcome. Because of these complexities, the guidelines are not routinely followed at bedside. The other issue is knowing all the details of recommendations in order to apply the guidelines in real life situations at the bedside. Practice culture and individual physician beliefs play an important role in sepsis care. However, there are some observational studies that show consistent and reliable implementation of advocated quality metrics by guidelines is feasible, and the institutions that are able to achieve higher bundle compliance have observed better clinical outcomes.

Mandates released in October 2016 that are regulated by CMS pose new challenges to healthcare organizations. Early management bundle metrics for patients presenting with severe sepsis and septic shock are based on initial definitions from 2012. With the announcement of new sepsis definitions (Sepsis-3) and recommendations provided by the SSCG, quality reporting to CMS difficulty has been aggravated. Implementation of these programs requires an enormous amount of resources, manpower, time, money, and commitment to ensure the process is successful and sustainable. Mayo Clinic Florida has overcome some of these challenges with the use of the SSRT team in addition to monthly root cause analysis meetings to evaluate the current CMS SEP-1 compliance and develop processes to continually improve compliance percentages. Despite the successful multidisciplinary collaboration, hospital leaders recognize gaps for continued improvement in our bundle compliance. Staff education regarding SEP-1 metrics is an ongoing effort; training is presented to new residents entering the ICU each month and reiterated during internal medicine rotations with attending staff. A number of technology issues have been resolved over the year working with nursing informatics colleagues, which notably helped with fluid compliance.

Long-Term Burden

The consequences of sepsis are not limited to the ICU or hospital wards. Besides the reported high early mortality after diagnosis, there is also substantial morbidity and late mortality in hospital survivors. Long-term quality of life is substantially worse in patients after they are discharged from the hospital. However, data on this is not commonly available, as primary hospital mortality still remains the outcome of interest in most published research on sepsis. Future work with alternative end point assessment will give ideas about the impact of sepsis on healthcare and society and will open areas for future research and new policy.

Conclusion

Sepsis is the end result of many disease processes, claiming millions of victims. Despite recent progress, there remains much to understand about the pathophysiology of sepsis and effective therapeutic strategies to avoid short- and long-term consequences. Individual and societal efforts are needed to tackle the sepsis menace. Team work, integrated research, innovative quality improvement projects, and leadership commitments are essential to continued success in sepsis care.
Supplement: Sepsis Alerts at Mayo Clinic in Jacksonville, Florida

Mayo Clinic in Jacksonville, Florida has developed a modified Sepsis identification algorithm that is based on a modified version of SIRS/Sepsis criteria. The modification consists of changes to the cut-off values and the addition of certain variables that can be captured by a computerized algorithm without requiring human intervention such as blood culture orders.

Our current identification computerized “sepsis sniffer” algorithm includes the following alerts:

1. SIRS Alert: Any 2 of the following
   - Temp=< 36C (96.8F), =>38.3C (101F) oral,
   - => 39C (102.2F) core
   - SBP <= 90
   - RR >24
   - HR >100
   - MAP <=65

   Action for SIRS alert: this only creates a color change in the electronic medical record without a pager function

2. Sepsis Alert, SIRS alert PLUS one of the following:
   - WBC >=12K or <=4K
   - Blood cultures ordered

   Action for Sepsis Alert: another color change on the medical record screen and trigger a pager alert to the ED team leader RN.

3. Shock Alert:
   - Lactate >= 4
   - 2 consecutive SBP < 90 mmHg

   Action for Shock Alert: a different color change on the medical record screen and trigger a pager alert to the ED team leader RN.

To ensure that all pertinent Labs and vital signs are accounted for, those can be from:

- Up to 8 hrs before ED admissions for lab and BC.
- Up to 2 hrs before ED admission for vital signs.
- Keep alert algorithm active in the EMR for 2 hrs after admission to floor in case more labs/data become available.

If after either one of these alerts the ED team feels that the patient is septic, the RN starts the sepsis checklist and asks clinician to evaluate for signs of severe sepsis and activate the sepsis and shock response team if those signs are present.

References


### Extracorporeal Membrane Oxygenation: Basics and Challenges

By Pramod K. Guru, MBBS¹ and Robert Ratzlaff, DO¹,²

¹Department of Critical Care Medicine, Mayo Clinic, Florida
²Department of Anesthesia, Mayo Clinic, Florida

**Abstract:** Severe cardiorespiratory failure due to myriads of causes remains a daunting medical task to solve. Extracorporeal membrane oxygenation (ECMO) as a form of extracorporeal life support has increasingly been used to ease some of the challenges faced by the intensivist. Scientific advances made over the past couple of decades are primarily responsible for the increased use of ECMO support at the patient bedside. The main advantage of the system is the unique capability to by-pass the heart and lung function simultaneously. While the practice is gaining wide acceptance across the medical subspecialty, there are many unresolved issues and challenges. More research and experiences are required to capitalize the benefits of ECMO while avoiding the iatrogenic harms. To understand ECMO as a whole, it is important to look at the basic physiology and configuration of the ECMO circuit, management principles, and the common difficulties encountered in the practice.

### Introduction

Extracorporeal membrane oxygenation (ECMO) is a form of extracorporeal life support therapy that is increasingly being used in patients with refractory cardiorespiratory failure.¹ The function of the heart and lungs are partially and temporarily bypassed by a miniature version of the cardiopulmonary bypass machine, which are used in the operation theater during coronary artery surgery.¹ Technological advancements in the components of the machine, increased confidence and experience in its application at bedside, and reduction in overall complications are some of the factors attributed to the increased use of ECMO at bedside in the intensive care unit (ICU).³⁴³⁵

### Need for Extracorporeal Therapy

Despite advancements in medical science, the challenges to manage severe cardiac and respiratory failure in the ICU remains extremely high for the critical care medical communities. Acute respiratory distress syndrome (ARDS) caused by a multitude of direct and indirect injuries to the lungs is commonly encountered in ICUs as a cause of acute hypoxemic respiratory failure. Annual incidence of ARDS in the United States is more than 140,000 cases.⁶ There is no pharmacologic therapy available for treatment of ARDS, and mortality remains high at about 22-41 percent.⁶ Around 20 percent of ARDS patients die of refractory hypoxemia despite lung protective ventilatory support and other currently available supportive therapies.⁷ Similarly, cardiogenic shock remains an unresolved medical challenge. About 2-8 percent of patients with acute myocardial infarction present to the hospital with cardiogenic shock. Mortality in these patients remains high, up to 40 percent, even after percutaneous coronary interventions and the use of other extracorporeal devices such as an intra-aortic balloon pump (IABP).³⁴ Annual incidence of cardiac arrest in the United States is more than 250,000.⁸ The morbidity and mortality of cardiac arrest, regardless of location, is enormous. The survival to hospital discharge with a good neurological function remains dismal at less than 20 percent despite the existence of standardized guidelines to rescue these patients.⁸

There is an urgent need to help these groups of patients. In recent years, ECMO has shown some promising results, and has renewed the interest among physicians in this old technique.

### Types of Extracorporeal Support

The ability to support cardiac and pulmonary function simultaneously is the unique characteristic of the ECMO system compared to other available extracorporeal devices. The basic ECMO circuit configuration is comprised of an inflow and outflow cannula, tubings, an oxygenator, a centrifugal pump (integrated or separated from oxygenator), and a heat exchanger.⁹¹⁰ Deoxygenated blood is siphoned to the ECMO oxygenator via the inflow/drainage cannula, and the oxygenated blood from the oxygenator is returned to the patient via the outflow/return cannula. Classification of the ECMO system is based on the supported organ system and the position of the blood drainage and return cannula in the patients’ vascular system. VV–ECMO
stands for veno-venous extracorporeal membrane oxygenation, and it provides only pulmonary support. As the name suggests, in this configuration the patient’s deoxygenated blood is drained from a peripheral vein and the oxygenated blood is then returned to either the same or a separate vein to the right side of the heart. This system takes over partial control of the lung functions, and the native cardiac function is necessary to achieve the desired goal of lung rest. In contrast, VA-ECMO, which stands for veno-arterial extracorporeal membrane oxygenation, needs arterial cannulation to bypass the heart function. It provides both pulmonary and circulatory support. It is classified as either peripheral or central type depending upon the position of the return/outflow cannula either at a peripheral artery or at the aorta respectively. Thoracotomy is needed for central VA-ECMO configuration with the drainage and return cannula in the right atrium and aorta respectively. The femoral artery is most frequently cannulated for peripheral VA-ECMO configuration, though the return arterial cannula can be placed in axillary artery, subclavian artery. Figures 1 and 2 depict these configurations.

The major differences between the VA- and VV-ECMO are outlined in Table 1. The membrane lung, a semipermeable membrane made of polymethylpentene (PMP), is the primary site of gas exchange during extracorporeal support. As shown in Figure 3, a gas mixture (oxygen + air), also called ‘sweep,’ circulates on one side while blood flows on the other side of the membrane. The three main modifiable components of the circuits are: pump speed, which determines the flow of blood, the sweep gas rate, respectively.

<table>
<thead>
<tr>
<th>Organ Support</th>
<th>Venoarterial (VA) ECMO</th>
<th>Venovenous (VV) ECMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circuit Configuration</td>
<td>Arterial and venous cannulation</td>
<td>Venous cannulation</td>
</tr>
<tr>
<td>ECMO Circuit Management</td>
<td>Flow adjusted to preserve tissue perfusion</td>
<td>Sweep gas adjusted for carbon dioxide removal; delivered oxygen adjusted for oxygenation</td>
</tr>
<tr>
<td>Pulmonary Blood Flow</td>
<td>Most native flow is circumvented</td>
<td>Native flow is maintained</td>
</tr>
</tbody>
</table>

Table 1. Major differences between venovenous and venoarterial ECMO.
which determines the level of gas exchange with blood and helps in carbon dioxide removal, and the oxygen setting, which is the amount of oxygen supplementation to the blood passing through the circuit. Oxygenator settings (FIO2 and sweep flow rate) and blood flow rate are adjusted according to the blood gas and other hemodynamic results. Details of the basic physiology are beyond the scope of this article, but can be found in other reviews.9,10 However, it is important to know that ECMO can only support up to 80 percent of the patient’s native cardiac output.9 Limitations are mainly due to the available cannula size to completely drain the venous blood and the presence of anatomic variability. Also, carbon dioxide elimination through the membrane lung is easier to achieve and monitor as compared to the oxygenation.

**Current Status of the ECMO Practice**

The concept of taking over the function of the heart and lung by artificial means and thus allowing the disease process to be controlled or cured is not new. This was envisioned by Dr. John Gibbon as a medical student in 1937, and the heart-lung bypass machine has been in use for various cardiac surgical procedures since the mid-nineteenth century.2 However, the first use of this machine outside the operation theater at the bedside in a young trauma patient was credited to Dr. Donald Hill in 1972.11 Unfortunately, the enthusiasm in ECMO as a salvage therapy for refractory cardiorespiratory failure was abruptly ended after the National Institutes of Health sponsored trial published in 1979.12 In this trial, VA-ECMO for severe ARDS did not provide any mortality benefits; the result was 90 percent mortality in both arms, compared to conventional therapy. However, the work continued mostly in pediatric patients by ECMO believer Dr. Robert Bartlett in the mid 1990’s and established a role in ARDS due to meconium aspiration.13,14

The technological advances in the machine and the cannula, as well as the positive clinical results in ARDS patients experienced via the CESAR trial from UK and H1N1 pandemic in the last decade, renewed the interest in ECMO practice.15,16 The new generation machine, membrane, and cannula simplified management and reduced some of the complications.17,18,19,20 In the CESAR trial, patients with refractory hypoxemia transported to a single ECMO center had 63 percent survival compared to the conventionally managed patients at another site.16 During the H1N1 pandemic, patients supported by ECMO were found to have 78 percent absolute survival benefit compared to those who were not.15 The latest report of the extracorporeal life support organization (ELSO) showed that ECMO has been used in more than 25,000 adult patients, and the survival to discharge rate for respiratory and cardiac failure was 57 percent and 40 percent respectively.1 Over the past few years, multiple reports on the benefits of using ECMO for cardiac arrest, also labelled as extracorporeal resuscitation (ECPR), have been published.8 Survival to discharge in this group as per ELSO data was 28 percent.1 As of now, however, there is not yet a large randomized control trial available to establish the benefits of ECMO in all these conditions. In addition to these circumstances, ECMO is currently being utilized for transportation and retrieval of organs for transplantation.5

**Indications and Contraindications**

There are certain fundamental principles that physicians need to keep in mind before initiating any form of ECMO in patients. First, ECMO is a support system (not a therapy) for the compromised respiratory and cardiac function. Second, since it is temporary in nature, the primary pathology should be either of reversible nature or there should be an exit strategy. Third, anticoagulation is necessary for optimal and proper functioning of the system. Fourth, the practice is resource intensive and demands multidisciplinary coordinated team commitments.

The application of ECMO as a rescue support system is primarily increasing in three main areas of critical care practice. These include severe refractory hypoxemic and hypercapnic respiratory failure, severe cardiogenic shock, and both in-hospital and out-of-hospital cardiac arrest patients.3 As per the ELSO guidelines, VV-ECMO should be considered in ARDS patients if the PaO2/FiO2 is below 150 with a Murray Score of 2-3, and it is indicated if the ratio falls below 80 or for a Murray Score of 3-4. Both as a rescue strategy...
for hypoxemia, and to reduce ventilator induced lung injury in patients with potentially reversible pulmonary disease, ECMO has been used in patients with severe hypoxemia (PaO2/FiO2 <80) with high positive end-expiratory pressure (typically 15-20 cm of H2O), severe hypercapnia with arterial PH <7.15 or plateau airway pressure of 35-40 cm of H2O despite optimal mechanical ventilation. VV-ECMO is also increasingly being used in patients in need of a bridge to lung transplant, primary graft failure during lung transplantation and many other acute hypoxic and hypercapnia respiratory failures.\textsuperscript{21-22} Indications of VA-ECMO include refractory cardiogenic shock due to myocardial infarction, myocarditis, drug overdose and failure to wean from cardiopulmonary bypass after cardiac surgery. Although previously contraindicated, recent data shows a beneficial role of ECMO in suspected septic cardiomyopathy.\textsuperscript{3,4} VA-ECMO indications are also expanded to rescue hemodynamically compromised patients due to pulmonary embolism, recurrent dysrhythmias such as ventricular tachycardia/fibrillation, trauma to major vessels or myocardium, and primary graft failure following heart transplantation. The American Heart Association guidelines recommend considering ECMO as a rescue therapy for both in-hospital and out-hospital cardiac arrest patients in appropriate situation.\textsuperscript{23}

Absolute contraindications for ECMO support are severe neurological injury or intracranial hemorrhage, end-stage non-recoverable disease and organ damages, contraindications to anticoagulation, unwitnessed cardiac arrest or prolonged cardiopulmonary resuscitation (> 60 minutes), unrepaired aortic dissection, severe aortic valve regurgitation and refusal by surrogate decision maker.\textsuperscript{3,4,9,10,22} Some of the relative contraindications include advanced age, active malignancy, morbid obesity and severe peripheral vascular diseases.

**Complications**

Despite significant advancements in technology and experience in the ECMO practice, the complication rates still remain at an unacceptably high level. Major bleeding and thrombosis complications remain the most feared complications during ECMO support.\textsuperscript{9} The incidence rate varies between 5-79 percent depending upon the literature reviewed. Infection and renal failure are two other major complications with reported rates of 17-49 percent and 30-60 percent respectively. Mechanical failures such as pump thrombosis and oxygenator failures are also reported in 4-30 percent patients.\textsuperscript{3,24,25}

**Outcomes**

The clinical outcome of patients supported by ECMO for cardiorespiratory failure depends upon multiple factors. The interplay between the patient and ECMO circuit, as well as the specific attributes of the system, is key to obtaining a good outcome. There are three possible clinical outcomes of the patients once supported by ECMO. First, complete recovery of the cardiac or respiratory dysfunction and weaning from the support (called bridge to recovery). Second, irreversible cardiac and pulmonary failure with ECMO dependence, leading to bridging to transplantation (BT) or bridge to long-term mechanical circulatory devices, such as ventricular assist devices (also called bridge to bridge). Thirdly, irreversible neurologic injury or death may occur.\textsuperscript{4,22}

**Challenges**

The pitfalls of increased use of ECMO techniques are many. Practices vary widely across the continents due to limited experience, lack of guidelines, and absence of adequately powered, randomized control trials. There is a dire need for basic and clinical research on many fronts of the practice.

First, anticoagulation remains the Achilles’ heel of optimal ECMO machine functioning. The current guidelines regarding the anticoagulant selection, timing, dosing, methods of delivery, and monitoring of efficacy are mostly based on either retrospective and small underpowered studies or experiences of the individual centers or persons. No adequately powered research is available to guide the best practice.\textsuperscript{26}

Second, similar to anticoagulation, the data on appropriate analgesics, sedatives, and antimicrobials is also sparse to nonexistent. Extrapolating the experience from general ICU patients, the role of these agents on patient outcomes cannot be completely ignored.

Third, bleeding is one of the major complications of ECMO support, and patients on ECMO support frequently need blood product transfusion. It is a well-known fact that transfusions are not harmless because of the cost, as well as the risks of infection, allosensitization, and additional lung injury. The transfusion thresholds for red blood cell (RBC) and platelets in patients receiving ECMO is unknown at this time.

Fourth, there is very little knowledge and experience regarding the benefits of minimal sedation and early mobilization in patients on ECMO.

Fifth, ECMO support is currently offered to patients as rescue therapy prior to their impending death. It is also a well-known fact that the practice demands substantial financial and manpower commitments.\textsuperscript{16} The best care model, and the appropriate training for maintenance of competence is still unknown.
Sixth, physicians also do not know have answers for the many ethical issues that can arise prior to initiation and during the continuation phase of the ECMO run.27,28

Conclusion

ECMO is a promising rescue therapy for patients with refractory cardiorespiratory failure. Despite the plethora of recent literatures showing the benefits of its application in critically ill patients, there is still an enormous need to evaluate the risk–benefit ratio at the individual patient level. The practice requires sophisticated machines, specialized training, and substantial organizational commitments. Appropriate patient selection remains the key for a good outcome in patients supported by ECMO.  

References

James L. Borland, Jr., MD, MACP
1976 DCMS President

James L. Borland, Jr., MD, MACP (11/20/1932-1/30/2018), died peacefully in Jacksonville surrounded by his loved ones. He graduated from The Bolles School (1950), The University of Florida (1954), and The Johns Hopkins School of Medicine (1958). Jim completed his post-graduate medical training with a fellowship in gastroenterology at Duke University in 1963 and then served as a Lieutenant Commander at NAS Jacksonville from 1963-65. He then joined his father’s gastroenterology private practice in Jacksonville and thus began his 53 years of service to our community.

Dr. Borland was a strong believer of stewardship. Locally, Jim served as president of numerous organizations throughout his career including the Duval County Medical Society (DCMS), the Jacksonville Hospital Education Program, St. Luke’s Hospital Medical Staff, St. Vincent’s Medical Center Medical Staff, the Duval Chapter of the American Cancer Society, the Foundation for Medical Care of Duval County, and The Rotary Club of Jacksonville. On the state level, he served on the Dean’s Advisory Committee of the University of Florida College of Medicine, Committees and Councils of the Florida Medical Association (FMA), President of both the Florida Society of Internal Medicine (FSIM) and Florida Gastroenterologic Society (FGS), and Governor of the Florida Chapter of the American College of Physicians (ACP). Nationally, Jim served as Chairman of the American Medical Association’s (AMA) Council on Medical Education, on the Board of Directors for all three major gastroenterology associations (ACG, AGA, and ASGE), and as President of the ASGE.

Dr. Borland’s commitment to excellence was recognized with such awards as Young Internist of the Year (ASIM), ACP Governor of the Year, ACP Laureate Award, Distinguished Service Award (ASGE), Distinguished Clinician Award (AGA), the James L Borland, Sr., MD Memorial Award (FGS), and the status of Master, ACP. Outside of medicine, he was an All American at the University of Florida for 3-meter diving, an expert downhill skier, and a certified open water diver with over 265 dives.

Jim’s commitment to mentorship was wide ranging and profound. Eight Past Presidents of the DCMS, including three of his former partners, trace their involvement in organized medicine directly to Jim. Five Past Governors of the Florida Chapter of the ACP, three Past Presidents of the FMA, and two Past Presidents of the AMA have cited Jim as one of their most important mentors.

Jim was in private practice (now known as The Borland-Groover Clinic) from 1965-98. From 1999 to 2011, he served in administrative roles with the Outpatient VA Clinics in North Florida and South Georgia. He was honored with the VA Performance Award in 2005 and the VA Exemplary Award in 2010. Jim was beloved by thousands of his former patients. As his partner from 1981, I saw firsthand his hard, selfless work, done behind the scenes, for the benefit of all physicians and patients. Jim sought first to listen and understand, rather than to speak. Repeatedly, he deflected praise intended for himself to the excellent efforts of others. I witnessed his remarkable focus on others’ concerns over his own issues. I also saw the love and attention he showered upon his wife, children, and grandson. It was inspirational.

Jim Borland will always be my role model as leader, gentleman, and the Consummate Physician. ❖

-W. Alan Harmon, MD, FACP
Paul J. Scioscia, MD

Paul J. Scioscia, MD, a plastic surgeon who practiced with Ponte Vedra Plastic Surgery for the past seventeen years, died on December 3, 2017. He was 57.

Dr. Scioscia was born on July 6, 1960, in Oak Park, Illinois. He began his studies at Vanderbilt University where he earned a Bachelor of Science degree, studying molecular biology and chemistry. He received his medical degree from the University of Pittsburgh School of Medicine. Dr. Scioscia then completed an internship and five-year residency in general surgery at the University of Pittsburgh and Pennsylvania State University. Subsequently, he completed a two-year residency in plastic and reconstructive surgery at the Medical University of South Carolina in Charleston. Dr. Scioscia elected to extend his training to sub-specialize in cosmetic surgery by completing a one-year fellowship in aesthetic surgery at New York University's prestigious Manhattan Eye, Ear and Throat Hospital. There he trained with many of the world’s most prominent plastic surgeons.

Following his surgical training, Dr. Scioscia began his practice in Jacksonville, ultimately joining Ponte Vedra Plastic Surgery as a partner in 2001. His professional goal was to always provide his patients with the highest-quality care in both a respectful and discreet manner. In addition to being an esteemed and congenial partner at PVPS, Dr. Scioscia was also highly respected by his peers and, as such, served as President of the Greater Jacksonville Society of Plastic Surgeons. Dr. Scioscia enjoyed traveling, golf, cooking and spending time with friends. But what he enjoyed most was spending time with his four children Jenna, Olivia, Christian and Ava, whom he adored.

David R. Moomaw, MD

David R. Moomaw, MD, an internist and cardiologist who practiced medicine in Jacksonville for over fifty years, died peacefully at home on January 21. He was 93.

David was born in Bulsar, India, where his parents, Ira and Mabel Moomaw, were agricultural missionaries; his father founded the Vocational Training College Ankleshwar in the province of Gujarat. David’s childhood in India inspired his life of service and adventure. He completed his preparatory education at Woodstock International School in Landour, India, a British Raj-era hill station near the Tibetan border.

After moving to the United States at age 16, David attended Manchester College and Northwestern University School of Medicine. He married Jeanne Rutherford Williams and moved to Jacksonville, Florida in 1955, when David established his private practice in internal medicine. During the 1960s, as chairman of the Department of Internal Medicine at St. Vincent’s Medical Center, he helped organize the first coronary and intensive care units in the area. He was active in the development of the Jacksonville Health Education Programs and the Family Medicine Residency Program at St. Vincent’s. David served as a visiting medical consultant in Afghanistan with CARE/Medico in Kabul before the Soviet invasion. His medical career included appointments as assistant medical director of CSX and medical director of Capitus Financial, Inc. Following retirement from active medical practice in 1996, he provided volunteer patient care as director of the Healing Hands Medical Clinic and served on the board of WE CARE Jacksonville into his 80s. ✯
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