

PROGRESSNOTES

MUSC'S MEDICAL MAGAZINE // SUMMER 2019



MUSC Celebrates New Children's "One-Stop" Care and Ambulatory Surgery Facility

Patients can now visit over 27 specialty clinics at the newly opened MUSC Children's Health R. Keith Summey Medical Pavilion.

The MUSC Children's Health R. Keith Summey Medical Pavilion opened to patients and families April 1. Dr. Mark Scheurer, chief medical officer for MUSC Children's Health, spoke about the new pavilion at a ribbon-cutting ceremony in March.

"I get incredibly excited thinking about how this facility is going to transform and grow comprehensive pediatric care for the people in this community and for all those driving from around the state to see our specialists," Scheurer said. "From ear tubes and flu treatments to infusions and specialized outpatient surgeries, it can be done here."

The R. Keith Summey Medical Pavilion is designed around children and their health. "Children are not mini-adults," Scheurer said. "And they deserve a child-focused, convenient and specialized facility to handle any need, regardless of size or scope."

The North Charleston community donated the land necessary for the 100,000-square-foot pavilion. MUSC Health CEO Dr. Patrick J. Cawley said, "This new facility would not have been possible without the vision and commitment of Mayor Summey, the North Charleston City Council and the community at large."

The Summey Medical Pavilion offers pediatric specialty and surgical services in a location with convenient and enhanced access to the children and families living throughout the Tri-county area, as well as families traveling to the clinics from all corners of the state.

Among its many services and amenities, this new facility includes a pediatric ambulatory surgery facility with four operating rooms, nearly 40 medical exam rooms with space for many pediatric specialists and clinics, an after-hours clinic, imaging services (MRI, CT scan and ultrasound), an EKG stress room, infusion services for very difficult and complex patient cases, a pharmacy, a lab, child life play spaces and technology that allows families to register at home or check in at the touch of a screen.



The entire patient experience is delivered in one place, which is a first for the Charleston area in terms of the level of coordinated, comprehensive and specialized pediatric health care available all at one convenient location.

Another first involves the facility's connection to a research collaboration with MUSC and Clemson University. Funded by a four-year, \$4 million grant from the Agency for Healthcare Research and Quality, MUSC and Clemson University will redesign operating room spaces and equipment placement for better, safer and more efficient surgical outcomes.

Early simulations of the operating room designs in the new Summey Medical Pavilion have been part of the testing phase of the project, and as part of the project's fourth year, real-time data will be collected to see how the new operating room designs improve patient care delivery.

MUSC Board of Trustees Chairman Charles Schulze sums it up: "MUSC Children's Health will be providing the highest level of outpatient care in one location. More than 27 specialty clinics, pediatric physicians, nurses and other staff all in one space. Just imagine how that will change the patient experience for children and their families."

PHOTO: BRENNAN WESLEY

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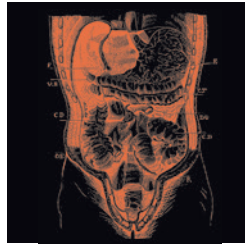
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NEWS

Transformative Teamwork

MUSC and Medtronic partnership aims to enhance care, reduce costs

BY HELEN ADAMS

Just about every week, MUSC Health vascular surgeon **Ravi Veeraswamy, M.D.**, sees a patient with gangrene in the toes due to vascular disease that has cut off the blood supply. Sometimes, it's too late to avoid amputation.

"At that point in the disease, we don't have as many options," he said. "We underestimate how reluctant patients are when it comes to seeking medical care, especially those in rural

or suburban areas. They're waiting until their condition becomes unbearable to seek care."

He's hoping that will change under a new partnership between the Medical University of South Carolina and Medtronic, one of the world's largest medical technology, services, and solutions companies. The five-year deal is aimed at identifying health problems earlier, streamlining and improving care, and simultaneously reducing costs.

It will combine MUSC's clinical and academic expertise with Medtronic's therapies, technology and operational knowledge.

Early areas of focus in the MUSC-Medtronic partnership include:

- Vascular disease
- Tracheostomy procedures
- Respiratory monitoring after surgery.

MUSC President **David J. Cole, M.D.**, calls the agreement transformative. "We believe this partnership will help us find new ways to deliver the best outcomes for patients at the lowest cost possible. That's the true meaning of value-based health care."

Omar Ishrak, Ph.D., chairman and CEO of Medtronic, said health care has to move in this direction. "We recognize that the shift to value-based health care is hard work, but we truly believe this approach offers the best

Omar Ishrak, Ph.D., Chairman and CEO of Medtronic (left), and Patrick Cawley, M.D., CEO of MUSC Health and Vice President for Health Affairs of the Medical University of South Carolina (right), formally acknowledge the MUSC-Medtronic partnership.

pathway to better outcomes and reduced costs. It requires a new way of thinking and the involvement of many stakeholders. It will take time. But we'll get there."

The leaders of both MUSC and Medtronic see the future of health care as a system where payment is based on patient outcomes, not volume. That means catching diseases early, before they escalate, and flagging people at risk for problems so they can get preventive treatment. Both believe that patient outcomes will improve and care will be less expensive as a result.

MUSC Health doctors will continue to make their own decisions about patient care but now will have more data, thanks to Medtronic, to help guide those choices. Both teams hope to develop new delivery and payment systems that can benefit the health care system as a whole, well beyond MUSC.

And since MUSC is an academic medical center, there will be opportunities for joint research and publication as well as an educational focus. The partnership will mean the development of new curricula to educate future health care providers.

Veeraswamy likes the partnership's emphasis on pushing for better results for patients. "This is a data-driven process. We take current patient demographics on things like smoking, obesity, geo-location and build an algorithm that defines their risk profile. We apply this algorithm to other patients, and as we gather more data and more outcomes, our ability to predict who is at risk for the disease will improve. Partnering with Medtronic will allow us to continuously improve the care we provide our patients."

DISCOVERY

Link Between 'Leaky Gut' and Immune Dysfunction in HIV-Positive Patients

Patients with human immunodeficiency virus (HIV) are treated with antiretroviral therapy (ART), which helps the immune system recover but can lead to production of self-destructive autoantibodies. We all produce low levels of autoantibodies, but persistently high levels may cause autoimmunity, as is common in HIV patients.

Wei Jiang, M.D., associate professor in the Department of Microbiology and Immunology at the Medical University of South Carolina (MUSC), researches immune dysfunction in HIV-positive patients. In a recently published article in *Microbiome*, Jiang and her team report that HIV-positive, ART-treated patients with high levels of autoantibodies also have increased levels of *Staphylococcus aureus* products in their blood.

The MUSC study compared autoantibody production in HIV-positive and healthy individuals before and after administration of a seasonal flu vaccine. Patients provided blood samples before vaccination and one and two weeks after, and the samples were tested using a 125-autoantibody array panel. The mechanism of autoantibody generation was examined by determining the plasma levels of microbial products, gene expression profiles of B cells and B cell receptor repertoires.

The autoimmune response in the HIV-positive patients was linked to the presence of *S. aureus* products in the blood. Some people with HIV have a higher baseline level of these bacterial products in their system. The team examined other strains of bacteria but

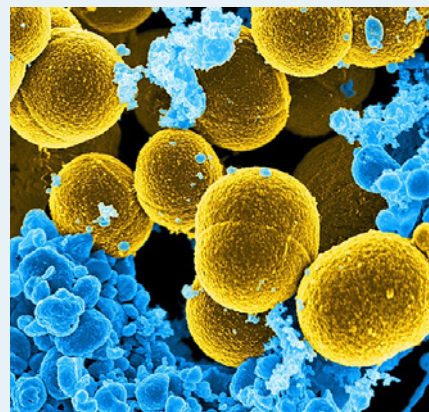


IMAGE: FRANK DELEO, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

linked only *Staphylococcus* to autoantibody production.

The increased level of *Staphylococcus* products may be linked to "leaky gut." Patients with leaky gut have a compromised intestinal lining, which enables toxic products from the gut microbiota to translocate into the blood and become accessible to the immune system. This persistent immune response may stimulate autoantibody production. A leaky gut is associated with several autoimmune diseases, including irritable bowel syndrome, celiac disease and type 1 diabetes.

To verify their findings, Jiang and her team injected heat-killed *Staphylococcus* bacteria into healthy mice and found that it did in fact stimulate autoantibody production.

"We are now studying which specific *Staphylococcus* products are active in autoantibody production in mice," says Jiang. "It may be possible to design an inhibitor to block these bacteria from activating the immune cells."

— MEGHAN GRANDAL



Community-based efforts are critical to increased inclusion of diverse groups in clinical trials.

CLINICAL RESEARCH

Changing the Game

Cancer centers design strategies to include more racial and ethnic minorities in clinical trials

BY DAWN BRAZELL

Not one size fits all, and nowhere does that show up more than in the recruitment of racial and ethnic minorities into clinical trials, says Hollings Cancer Center researcher **Marvella E. Ford, Ph.D.**, associate director of population sciences and cancer disparities at MUSC Hollings Cancer Center. She was part of a study involving eight cancer centers looking at best practices and providing recommendations for

how these populations can best be engaged in clinical trials.

"This is a major focus of the National Cancer Institute, and it's very important because we need to make sure that at the end of the day the research results can be generalized across multiple population groups," she says. "We can't use a one-size-fits-all approach and use the same recruitment strategies in every single group. We

really have to tailor the recruitment strategies to the needs of the group."

The study identified that African Americans, who represent 13% of the general U.S. population, comprise 5% of patients enrolled in clinical trials, with Asian Americans and Hispanics comprising only about 3%.

Ford says researchers must take a different tack with racial and ethnic minority groups. "We can't recruit all groups the same because different groups have different relationships, histories and past abuses with the health care system and with the federal government."

Though minority enrollment in clinical trials tends to be low in general, it's particularly an issue in cancer, where advances in research are driving a paradigm shift in precision medicine. It's important that the development of personalized medicines that account for biologic factors, such as genetics, gender, race and ethnicity, have a diverse pool of participants.

A key component in increased inclusion is the development of trust in the community. One tactic Hollings Cancer Center uses is its MOVENUP Program, which takes a train-the-trainer approach in rural communities that are medically underserved. The program is now being expanded in a new partnership with the Seventh Episcopal District of the African Methodist Episcopal Church, with monthly programs planned, including modules on clinical trials, to reach its more than 400 churches spread across the state.

Though research is about data, the core of it is about people, Ford says.

"We want to bring in community members and talk to them and bring in key people from the community who can advocate for the trials that we're conducting. Communities want a relationship with the people who are conducting the trial. They don't want a nameless, faceless entity. That doesn't mean anything to them," she says.

CLINICAL RESEARCH

The Maria Generation

Hurricane Maria's impact on Puerto Rican children's mental health

BY HELEN ADAMS

Psychologists at MUSC measured the magnitude of Hurricane Maria's impact on the mental health of children in Puerto Rico in one of the largest postdisaster screening projects in U.S. history.

Rosaura Orengo-Aguayo, Ph.D., an assistant professor in the Department of Psychiatry and Behavioral Sciences at MUSC, grew up in Puerto Rico and led the study. "More than 7% of youth, 6,900 of the children surveyed by the Puerto Rico Department of Education, reported clinically significant symptoms of PTSD," she said.

Post-traumatic stress disorder can develop after a traumatic event, such as a natural disaster, and can affect the ability to cope with everyday life. PTSD can cause nightmares, flashbacks, the feeling of being always on guard, trouble sleeping and an inability to remember parts of the traumatic event.

Orengo-Aguayo said the survey also found that more than 6,000 children reported that a family member, friend or neighbor may have died as a result of the hurricane.

While more than 7% of the children surveyed had PTSD symptoms, that's actually lower than anticipated. **Regan Stewart, Ph.D.**, an assistant professor in MUSC's Department of Psychiatry and Behavioral Sciences, is part of the research team. "I expected it to be higher, based on other studies that have been done in the mainland U.S. in which rates are somewhere between 13 and 30%."

Stewart said one potential protective factor for Puerto Rican children may be a concept called "familismo" in Spanish. "It's

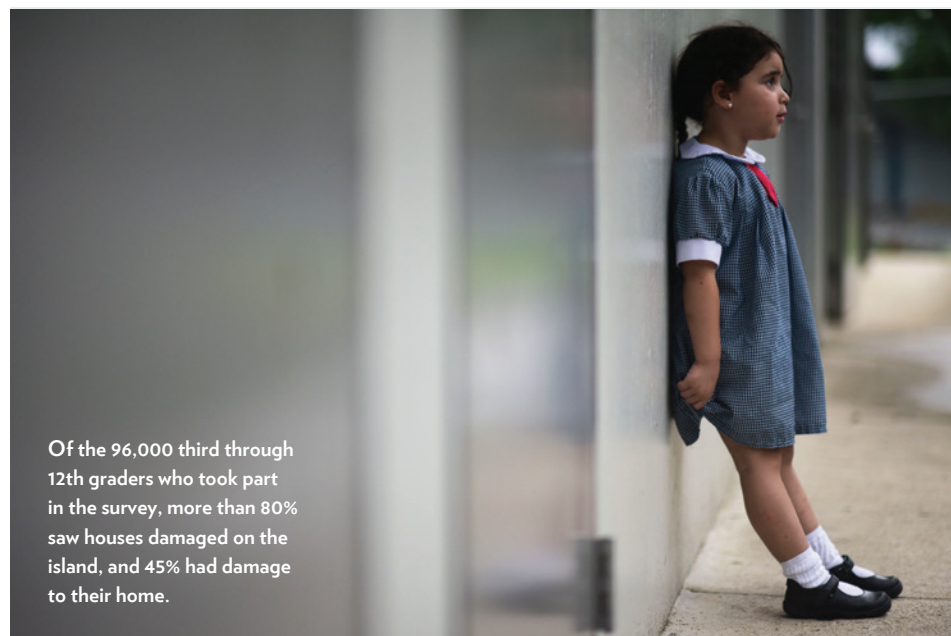
the importance of family and community. Puerto Ricans place a high value on these social connections. We know from the literature that social support may be a protective factor after a traumatic event."

The PTSD rate might also have to do with the timing of when the Puerto Rico Department of Education conducted the survey, she said. "Most surveys have been done at the six- to 12-month mark. In this case, the department administered the surveys at five to nine months. Many of the students were still dealing with losses of basic necessities, such as food and electricity. Their focus could still be on getting these basic needs met, and mental health difficulties may have developed later, at the six- to 12-month mark, which was not captured in this survey."

Soon after the storm hit, Orengo-Aguayo, and Stewart started working with another bilingual mental health expert, **Michael de Arellano, Ph.D.**, a Psychiatry and Behavior Sciences professor at MUSC, and the Puerto Rico Department of Education to train teachers in how to take care of their own mental health while also caring for the kids who weathered the storm. This effort was funded using a grant they already had from the Substance Abuse and Mental Health Services Administration and the National Child Traumatic Stress Network.

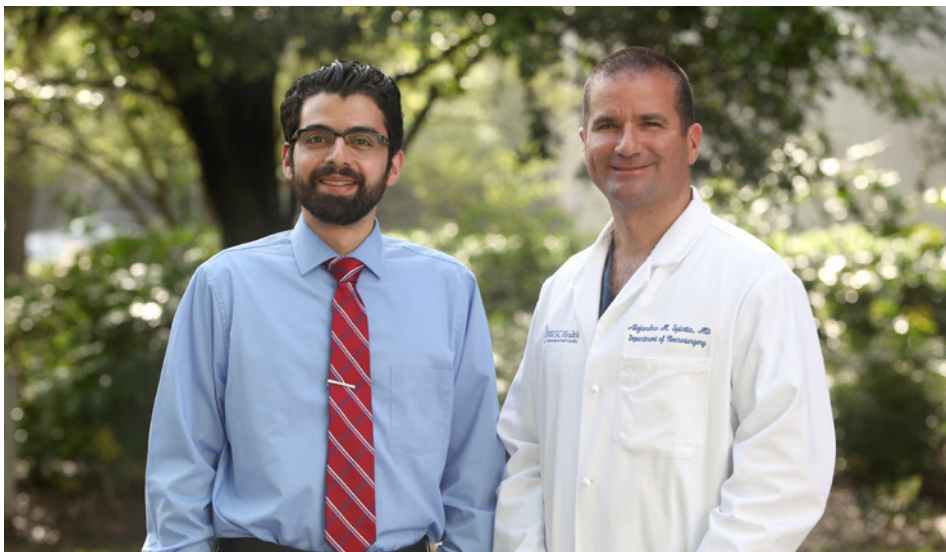
The team emphasizes the importance of asking what people need instead of telling Puerto Ricans what to do during this project. They've also worked closely with Joy Lynn Suarez-Kindy, a clinical psychologist who lives there, to strategize and analyze what is needed.

"Puerto Rican youth experienced significant disaster exposure and reported trauma symptoms that warrant evidence-based services," Orengo-Aguayo said. "Academics partnering with community stakeholders is the way to go to change the world one child at a time. That is our lab's motto."



Of the 96,000 third through 12th graders who took part in the survey, more than 80% saw houses damaged on the island, and 45% had damage to their home.

PHOTO: CARLOS GIUSTI



MUSC research team lead Dr. Spiotta (on right) worked with Dr. Alawieh to study endovascular thrombectomy procedure times both at MUSC and nationally.

TRANSLATIONAL RESEARCH

Procedure Time Vital in Thrombectomy Success

Researchers find diminishing returns in patient outcomes after endovascular thrombectomies pass 60-minute mark

BY CELIA SPELL

The “Stroke Belt” refers to the swath of states in the Southeast where rates of stroke death are high, and according to the Department of Health and Environmental Control, South Carolina comes in at number six for the nation’s highest rates of stroke death.

A stroke occurs when blood flow to a particular area of the brain is cut off, which could be due to a clot, a blood vessel leak or the bursting of a brain aneurysm. Without enough oxygen, the cells in that part of the brain begin to die and can leave behind motor and cognitive deficits.

Timely removal of the blockage is vital when treating a stroke, and while the acceptable time to treatment has slowly lengthened

with more effective thrombectomy techniques, physicians and surgeons must still act within 24 hours of the onset of stroke. Researchers at MUSC report in a recent paper in the *Journal of the American College of Cardiology* that the current standard of care for stroke should also factor in procedure time when considering surgical intervention.

“People will try once to remove the clot,” said **Ali Alawieh, M.D., Ph.D.**, a neurosurgery researcher at MUSC who worked on the study under the direction of MUSC Division of Neuroendovascular Surgery Director **Alejandro Spiotta, M.D.** “They’ll then try two, three and even four times hoping for a successful attempt. The idea of the study is

to look for a limit where you start doing more harm than good.”

By studying the number of attempts and the amount of time spent performing procedures, the team concluded that the likelihood of completing an endovascular thrombectomy without significantly increasing the risk for the patient decreases dramatically after the first 30-60 minutes, depending on the technique used. Complication rates increase by the minute after that.

Endovascular thrombectomies are performed using either stent retrievers (SRs) or aspiration thrombectomy (ADAPT). By comparing both techniques, Alawieh and Spiotta found that the most important detail to consider is the time spent manipulating the vessel. Using SRs, the golden time for the procedure is at the hour mark, and using ADAPT, it is a half-hour.

“We had noticed this trend at MUSC, but we wanted to know if it extended nationally,” said Alawieh. “As it turns out, it does. After that 30- to 60-minute mark, depending on the procedure, surgeons should reassess if the procedure is worth continuing.”

Because they are in the Stroke Belt, physicians at MUSC perform some of the largest numbers of endovascular thrombectomies in the country, totaling over 200 procedures a year. While rates of positive outcomes are highest with successful surgical intervention, patients may still recover some of the deficits with medical management.

This work involved a collaboration between MUSC and other centers across the country who are part of the Stroke Thrombectomy and Aneurysm Registry (STAR), a collaborative effort coordinated and initiated by MUSC to monitor outcomes in stroke patients nationally.

“Stroke intervention procedures are so effective in helping patients that it’s difficult for the physician to give up on a procedure when it’s not successful,” said Spiotta. “This work provides a potential stopping point.”



TRANSLATIONAL RESEARCH

A 'Joint' Problem

Investigating marijuana and tobacco co-use and its impacts on smoking cessation

BY CALLAN FRYE

Tobacco isn't the only thing being smoked in the Deep South, and for many, it's only half of their habit.

Marijuana, long thought to be a gateway to harder substances, turns out to be popular among cigarette smokers, with rates of co-use of the two substances increasing among adults from 2003 to 2012. Researchers don't yet know how much of a problem that poses for people trying to quit tobacco.

To learn more, a team of addiction investigators at the Medical University of South Carolina (MUSC), led by **Erin A. McClure, Ph.D.**, assistant professor in the Department of Psychiatry and Behavioral Sciences, conducted an online survey of smoking habits among individuals who had used both marijuana and tobacco within a 30-day period. The survey results were published in *Addictive Behaviors* in March 2019.

The MUSC team found that more participants used marijuana and tobacco sequentially than simultaneously. For

example, more participants used a tobacco cigarette as a "chaser" to marijuana than smoked joints containing both marijuana and tobacco, called spliffs.

The study also found that the degree to which marijuana and tobacco usage was interrelated differed greatly by user. Twenty-six percent of users reported that they had smoked most of their cigarettes around the time that they were using marijuana or were high. Compared to those who smoked the two substances individually, these co-users were more likely to have a greater tobacco dependence and to smoke more cigarettes per day.

"So if somebody's trying to quit smoking cigarettes but they always use marijuana and tobacco together, it's probably going to be much, much harder for them if they are still using marijuana than for somebody who uses both but their use is not related in any way," says McClure.

The finding also raises the question of whether smoking tobacco after marijuana use enhances its subjective effects. It is possible that co-users of marijuana and tobacco who feel a more intense high because of the tobacco use are more likely to use them together. If this is the case, quitting cigarettes may be more difficult for these individuals, though this requires further study.

What is clear from the researchers' findings is that everyone's habit is a little different, and cessation programs will thus need to be personalized if they are to be effective.

McClure hopes to focus on tobacco cessation as she continues her research but also to identify people likely to struggle with quitting due to their marijuana use. She plans to further tailor treatment to these individuals to improve the success of their smoking cessation efforts.

NEWS

Champion Achievement

Raymond N. DuBois, M.D., Ph.D., dean of the College of Medicine at the Medical University of South Carolina, was recently recognized by the American



PHOTO: SARAH PACK

Association for Cancer Research (AACR) for his global leadership in the early detection, interception and prevention of colorectal cancer. Among his many contributions to cancer research and the cancer community, DuBois discovered the role of prostaglandins (PGs) and cyclooxygenase in the genesis and progression of colon cancer and unraveled the functions of PGs in the tumor microenvironment. He pioneered the concept of targeting these inflammatory pathways for cancer prevention, facilitating the start of clinical trials to examine the use of nonsteroidal anti-inflammatory mediators as preventive therapies.

DuBois received the Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research at the AACR's 2019 annual meeting, held in early April. This award was established in 2007 to recognize a champion of cancer research who has had a major impact on the field.

"Dr. DuBois is a highly distinguished researcher whose innovative work has made him an international leader in the field of early detection and prevention of the disease," said Margaret Foti, Ph.D., M.D. (hc), CEO of the AACR. "I am thrilled that he has been chosen by the selection committee to receive this award."

— SHAWN OBERRATH

Trimming the Fat



MUSC clinical trials hope to identify novel combinatorial therapies for NAFLD and NASH

BY MATTHEW GRESETH

Silence is not always golden

Nonalcoholic fatty liver disease (NAFLD) is an umbrella term that covers a wide spectrum of liver diseases that are serious and often difficult to diagnose. As the name suggests, this condition results in a build-up of extra fat in liver cells that is not caused by alcohol consumption. The diseases involved can range from a simple increase in fat in the liver tissue to fatty tissue accompanied by inflammation. The inflammation, in turn, can cause injury and eventually scarring or fibrosis; this more severe form of fatty liver disease, which includes the inflammatory type, is called nonalcoholic steatohepatitis (NASH) and is now known to lead to cirrhosis in many patients.

“What I think is important is the fibrosis and scarring,” says **Wing-Kin Syn, M.D., Ph.D.**, associate professor and attending physician in the Department of Medicine at MUSC and the Ralph H. Johnson Veterans Affairs (VA) Medical Center. “These are fundamental things that define outcomes, not fat. The fat is just a sign that maybe you’ve been less physically active, maybe you ate too much, or maybe you have other risk factors such as diabetes or hypertension.”

It is normal for the liver to contain some fat, but NAFLD is the diagnosis when more than 5% of liver cells show fat accumulation.

One of the most dangerous aspects of NAFLD is that it is a silent, indolent disease. Most people don’t recognize this disease and often associate it with alcohol consumption. Although NAFLD is the most common liver disease, the vast majority of patients with fatty liver can live years asymptotically. According to The NASH Education Program, 34% of Americans have NAFLD and 12% have the more severe disease, NASH.

NAFLD is becoming increasingly more common, especially as the incidence of metabolic syndrome—type II diabetes, hypertension, centripetal obesity and hypercholesterolemia—is on the rise across the nation, and notably in South Carolina. Relatedly, having NAFLD may enhance the risk of cardiovascular death, developing chronic kidney disease or developing type II diabetes.

“Our westernized diet and lack of exercise are key contributors to the development of fatty liver disease, and we are now in the middle of an epidemic of fatty liver disease leading to inflammation, fibrosis and cirrhosis,” says **Don C. Rockey, M.D.**, professor and chair of the Department of Medicine.

“This is extremely common. People need to really be aware of the risk factors of fatty liver,” adds Syn. “Patients need to be monitored

for these diseases with a view to early treatment through lifestyle changes as well as antifibrotics if they have severe disease.”

Pioneering novel therapy options at MUSC and the Ralph H. Johnson VA Medical Center

While there are currently no FDA-approved medical treatments for NAFLD or NASH, some of the negative effects of NAFLD can be mitigated, and even possibly reversed, by implementing lifestyle changes like eating a healthy diet and exercising regularly.

“There is always a balance of input and output,” says Syn.

“Nutritional diet ties in with physical activity. Exercise has been shown in clinical trials to lower liver fat, mitigating your risk of fibrosis and even reducing some of the symptoms.”

The next phase in treatment for NAFLD aims to supplement lifestyle changes with pharmacotherapy. Currently, there are 55 different drugs in various stages of approval that target comorbid conditions, such as diabetes or cardiovascular disease, or aim to reduce liver fibrosis. However, there are only a few centers around the country that offer these clinical treatments.

“I’m delighted to say that here at MUSC, we have developed a portfolio of studies that will provide novel treatments to patients here that aren’t available anywhere else in South Carolina,” says Rockey. “This provides patients with opportunities that they don’t have at other places and have never had before.”

As one of the only sites offering these clinical trials in the Southeast, MUSC enrolls patients in trials that focus on the most promising therapeutic candidates. MUSC is currently running five active clinical trials, and additional studies should begin soon. Furthermore, the Ralph H. Johnson VA Medical Center, one of the largest centers in the country conducting clinical trials on NAFLD, has three active trials and five more in the pipeline. For more information on clinical trials at MUSC or the VA, please visit scresearch.org.

“We are one of the few centers nationally now recognized to have a framework built to noninvasively diagnose and treat

patients with NAFLD,” says Syn, who is leading the effort at the VA. “We have state-of-the-art elastography machines that quantify the degree of liver fibrosis without the need for a liver biopsy. Eventually, once you develop progressive disease, you may need these new antifibrotic drugs to prevent further disease progression or induce disease regression.”

In addition to pioneering several encouraging clinical trials, researchers at MUSC are also studying the biology of these diseases to better understand them and to develop more targeted therapies.

“We’re also very interested in understanding how the liver responds to injury. In the laboratory, we have identified the key fibrogenic cell,” explains Rockey. “These cells respond to the injury process by producing abundant amounts of scar tissue. As far as we can tell, it doesn’t care too much about fat but does care a great deal about inflammation. By identifying this cell and manipulating its pathways, we believe that we may be able to modify fibrosis.”

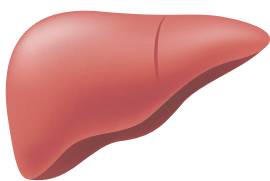
The best way to predict the future is to create it

While diet and exercise can help curtail the pathogenesis of NAFLD, it is becoming clear that there is a need for sustained treatment of this silent class of diseases. Due to the Western diet and lifestyle, the affected population is skewing younger and younger.

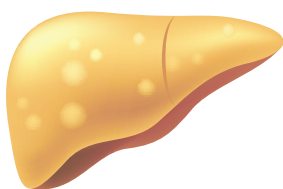
Future work in this field will aim at developing noninvasive diagnostic technology and identifying new pharmacotherapeutic targets and treatments. Currently, the only definitive way to diagnose NAFLD is with a liver biopsy. It is very difficult to identify at-risk patients when the disease is silent. A collaborative research endeavor at MUSC hopes to provide the next step in early detection of NAFLD.

“We are using artificial intelligence to try and refine the way we identify individuals at risk for progressive disease as early as we can,” says Syn, who is developing this technology at the VA with **Lewis J. Frey, Ph.D.**, associate professor in the Department of Public Health Sciences. “Then we can intervene with diet and lifestyle changes, and maybe even drugs.”

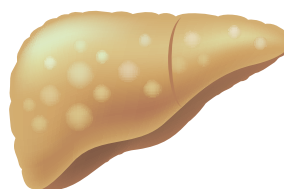
Stages of Liver Damage



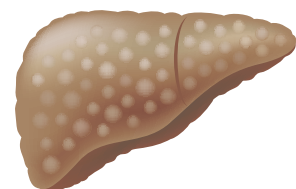
Healthy Liver



Fatty Liver

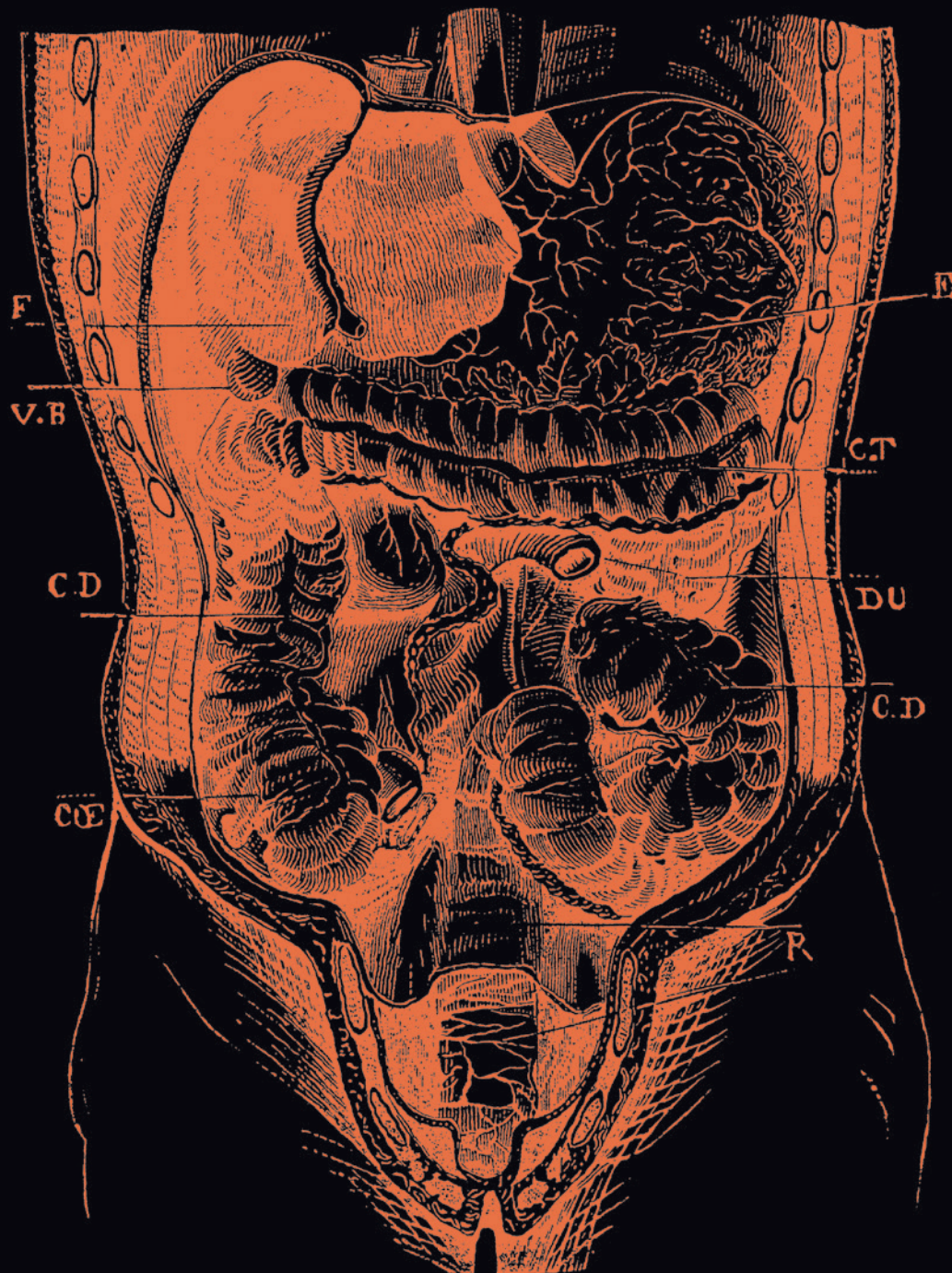


Liver Fibrosis



Cirrhosis

Breaking Through the Barricade



HIPEC gives physicians opportunity to treat hard-to-reach cancers in the abdomen

BY CELIA SPELL

Walls are designed to do one of two things: contain or keep out. And the peritoneum is no exception. As the serous membrane lining the abdominal cavity and covering the organs within, the peritoneum provides protection from infection as well as storing fat.¹ It keeps the organs in place while allowing blood vessels, lymph vessels and nerves to pass through.

It is also extraordinarily effective at keeping everything else out, which makes treating cancer in the abdominal cavity difficult to target with systemic chemotherapy.

This “plasma-peritoneal barrier” isolates the abdomen from the cytotoxic effects of intravenous (IV) treatment. Poor intraperitoneal blood supply then causes poor oxygenation of the cancer cells, which in turn results in hypoxic tumors with low levels of apoptosis, or programmed cell death.² To get around this obstacle, physicians turned to hyperthermic intraperitoneal chemotherapy (HIPEC) to treat cancers within the abdominal cavity.

“Our goal is to surgically remove all of the disease that we can,” said **Ramsay Camp, M.D., FACS**, a surgical oncologist at MUSC who performs these procedures with **Virgilio George, M.D.**, a gastrointestinal surgeon at MUSC. “And then use HIPEC to treat residual cells that we can’t see throughout the whole abdomen.”

HIPEC was developed in the 1990s for patients whose cancer had metastasized to the peritoneum, a progression with a poor prognosis. Researchers studying colorectal cancer found that surgically removing the tumors resulted in a 21-32% 10-year survival rate, with only 3-12% of patients remaining free of disease, but when surgery was combined with HIPEC, the 10-year survival rate climbed to 60-80%, and 55-74% of patients were free of disease.³

Primary colorectal cancer, ovarian cancer, gastric cancer, appendiceal cancer, mesothelioma and peritoneal carcinomatosis can be treated with HIPEC as long as they are contained in the peritoneum.

“The combination approach provides the only chance for long-term survival in patients with these diseases,” said George.

After cytoreductive surgery, the physician team treats the patient with a heated sterile chemotherapy solution, which can be administered via an open or closed technique; Camp and George deliver the solution to their patients by using the closed technique. They place inflow and outflow catheters throughout the abdomen and then temporarily close the incisions around them with a watertight seal that keeps the perfusion inside a closed circuit. The chemotherapy solution is then heated to 41-43 degrees Celsius, as studies have shown that the benefits stem from a solution that is warmer than the patient’s body temperature.³

Once the solution temperature reaches 41 degrees, it activates selective cytotoxicity on the tumor cells, which allows the heated drugs to destroy any remaining microscopic cancer cells. The heat also activates protein degradation in these cells, which stops oxidative metabolism while increasing the cell’s pH levels. These changes activate the lysosomes and encourage apoptosis.⁴ The heat also compounds the cytotoxic effects of the chemotherapy and helps with absorption.

Using a HIPEC perfusion system to maintain a consistent temperature and push three to five liters of the solution through the catheters into the abdomen, chemotherapy is circulated throughout the patient’s peritoneum for 90 minutes.

Physicians monitor the patient’s internal temperature throughout the procedure to ensure that the core does not become too warm with the infusion of heated chemotherapy. Camp said his team generally uses a cooling blanket to avoid overheating, but they have used ice and cool IV fluids as well. After perfusion, the surgical team reopens the sutures and performs any necessary anastomoses.

HIPEC offers a solution for patients with peritoneal metastasis by delivering a higher concentration of the drug while being less toxic due to the same plasma-peritoneal barrier that makes this location hard to treat. The barrier confines chemotherapy exposure locally, allowing HIPEC doses that are 20-50 times more concentrated than those for traditional systemic chemotherapy.³ Side effects from the procedure usually stem from the magnitude of the cytoreductive surgery rather than the exposure to the solution.⁵

HIPEC in conjunction with cytoreductive surgery involves a coordinated effort between multiple teams to remove the tumors and administer the heated chemotherapy. Because of the complex nature of this treatment, HIPEC is usually only performed at tertiary care centers in the U.S. “We are excited to no longer have to send patients outside the state,” said Camp. “We can perform it right here at MUSC.”

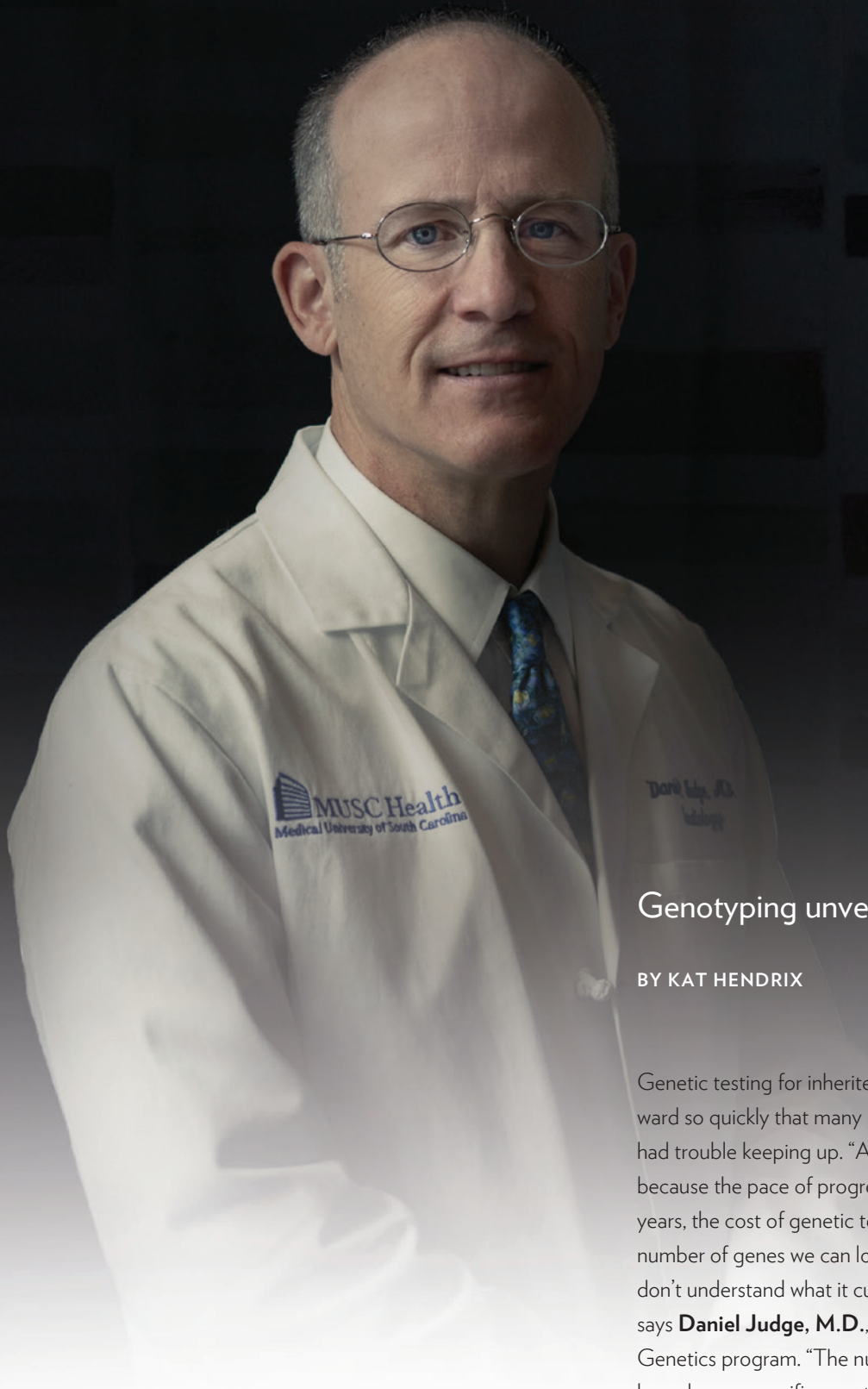
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To view surgical footage of a HIPEC procedure performed by Dr. Camp and Dr. George, see the MUSC Health Medical Video Center (<http://MUSChealth.org/medical-video>).

Precision Prevention



Genotyping unveils hidden cardiac risks

BY KAT HENDRIX

Genetic testing for inherited cardiovascular disease has moved forward so quickly that many physicians, patients and policy makers have had trouble keeping up. “A lot of people have outdated impressions because the pace of progress has been so fast. Over the last few years, the cost of genetic testing has dropped dramatically while the number of genes we can look at has risen just as fast. So most people don’t understand what it currently costs or what it can do for them,” says **Daniel Judge, M.D.**, director of the MUSC Cardiovascular Genetics program. “The number of cardiovascular conditions that we know have a specific genetic basis has grown exponentially, and we’re finding more genes and more contributing factors all the time.”

In fact, the MUSC Cardiovascular Genetics program now provides detailed genetic evaluation for at least 14 different inherited heart conditions, including cardiomyopathies, cardiac syndromes, muscular dystrophies which affect the heart, familial aortic aneurysm, familial hypercholesterolemia, unexplained cardiac arrest, transthyretin amyloidosis and Fabry disease. These evaluations are now considered a vital component of health care for families with inherited cardiovascular disease.

Most genetic heart conditions are inherited in an autosomal dominant pattern, meaning that men and women are equally affected and that just one copy of a mutation can cause the disease. On average, half of those in a family with such a mutation will develop the associated condition.¹ However, genetic testing is underutilized. Leading cardiologists agree that there is a need to raise awareness of inherited cardiovascular disease among community-based cardiologists and primary care physicians.² “It’s challenging,” says Judge. “People are often told that a virus may have caused their heart to weaken. And while this might be true in some cases, genetic conditions are the second leading cause of a weak heart, after coronary artery disease.”

Health care needs may differ between people with inherited heart conditions and those who have the same conditions due to nongenetic factors. Treating inherited heart disease requires screening individuals and their relatives to determine whether other family members also need medical care, even if they have no symptoms. Undetected, genetically linked heart conditions are a major cause of morbidity and mortality in young people.³ When a pathogenic variation is identified, genetic cascade testing is recommended for relatives who might be asymptomatic carriers of the same mutation, which would put them at risk for serious complications, including sudden cardiac death. Importantly, numerous professional organizations recommend genetic cardiovascular testing to improve diagnosis and management in at-risk patients and their relatives.⁴

The MUSC Cardiovascular Genetics program focuses on the patient and their family as a unit. **Kim Foil, MS**, a certified genetic counselor in the MUSC program, explains, “This service is different because we look at the full family history, not just the individual. We look at the whole family to find clues to genetic problems that may have been passed along and to determine the most appropriate tests.” Obtaining a detailed family history helps clinicians determine who will benefit from testing and the best testing strategy to use. Judge says, “We try to figure out why a condition happens. We don’t want to just say, ‘here it is and this is what we’re going to do.’ I listen quite a bit rather than just relying on medical records—they’re

important but they don’t provide the whole story.”

Once a patient who might benefit from genetic testing is identified, specialized counselors explain the disease as well as the process and potential impacts of genetic testing. Counseling is essential because the decision to undergo genetic testing is not a simple one. Patients receive pretest counseling about the abilities, limitations and consequences of genotyping and post-test counseling to discuss the results and their impacts.

Because genotyping results can have a range of medical and psychosocial implications, genotyping should be performed by a specialized cardiovascular genetics program with appropriate counseling.⁵ Foil explains, “It’s our job to explain the pros and the cons. The pros are that a lot of people see knowledge as power. The more we know about what’s driving their condition, the better we can manage it and prevent serious problems. Another advantage is that we may find other relatives who have that gene and may need high-risk care even before any symptoms show up. The cons are that some people find genetic testing to be anxiety provoking. They might feel like they’re living with a ticking time bomb. Also, although genetic test results are very well protected in health care and health insurance systems, that’s not the case for life insurance. Genetic test results can affect someone’s ability to get life insurance or impact their premiums.”

Patients come to the MUSC Cardiovascular Genetics program for a wide variety of reasons. “We see the whole patient spectrum—from very early to very late disease. We’ve also seen people who are completely asymptomatic who come in because they’re worried about developing a heart condition based on their family history. And there have been patients in end-stage heart failure whose final request is that we find the cause and make sure no one else in their family gets caught by surprise,” says Judge.

Cardiovascular genetic testing can improve diagnostic precision and clinical decision-making and provide family members with potentially life-saving information. The challenge is making sure physicians and patients know about this life-changing technology. “I’d like to see more awareness about genetic evaluation in general cardiology practice so that more patients can benefit from it,” says Foil.

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Easing the Withdrawal Burden

BY CELIA SPELL

Treating patients with opioid use disorder has been top of mind for frontline practitioners since the opioid epidemic began, but as it has only gotten worse the last few years, new treatment solutions are being tested.

As a statewide approach to reducing the impact of opioid addiction, physicians have joined SC MAT Access to bring medication-assisted treatment (MAT) to emergency rooms, primary care offices and obstetrician offices.¹

MAT combines behavioral therapy and medication as an evidence-based pharmacotherapy for patients with an opioid addiction. Using methadone, buprenorphine or naltrexone, physicians can target the opioid receptors in the brain to ease the effects of withdrawal, curb cravings and begin the opioid addiction recovery process.

Physicians at MUSC are working with a grant from the South Carolina Department of Health and Human Services in conjunction

with SC MAT Access funding from the SC Department of Alcohol and Other Drugs of Abuse Services (DAODAS) and the Substance Abuse and Mental Health Services Administration (SAMHSA) to increase education and access to MAT throughout the state.

“It’s by no means a one-size-fits-all approach,” said **Carolyn Bogdon, MSN, FNP-BC, CPTC**, a board-certified family nurse practitioner at MUSC who has coordinated the MAT-ED program from its onset. “It’s very individualized to the patient, and this project allows us to treat them as such.”

A patient’s chance of relapse changes based on many factors, including their age, duration of drug use, employment status and marital status,² but it is estimated to be between 40 and 60%, on average.³ By changing how a person’s brain responds to opioids and lessening the burden of withdrawal, physicians can lower this risk. Characterized by nausea, depression, agitation, anxiety and

intense cravings, withdrawal is highly uncomfortable and can be life-threatening.

Methadone is a synthetic opioid agonist that occupies and slowly activates a person's opioid receptors without providing any feelings of euphoria. It is taken in daily doses strictly at methadone clinics and provides relief for four to eight hours per dose. Buprenorphine is the first medication to treat opioid use disorder that can be prescribed in a primary care office or a hospital. It is also a long-acting partial opioid agonist, meaning it activates the same receptors as full agonists but less strongly.⁴

The third medication, naltrexone, is an opioid antagonist that works by blocking activation of the opioid receptors. It prevents the rewarding effects of opioids but does not treat withdrawal or curb cravings. It can be prescribed by a licensed health care provider after a patient has abstained from opioids for seven to ten days and is also used to treat alcohol use disorder.⁴

In the past, patients had to make it at least a week on their own without opioids before they could begin treatment. But now, with SC MAT Access, patients can improve their odds and start treatment immediately in multiple places in the region.

Treatment immediately after overdose

With the help of DAODAS and SAMHSA, MUSC is leading a pilot program to address opioid addiction straight from the emergency room.

"Previously, we would just treat the acute overdose," said **Lindsey Jennings, M.D.**, who is an assistant professor in the Department of Emergency Medicine at MUSC and a physician champion for the program. "And then give them a referral for outpatient treatment and hope they follow through." The next available appointment might not be for a week, and the patient would have to either abstain from opioids or avoid an overdose in that time period. This standard of care is still practiced in many hospitals across the country, but with the new program, MUSC has shown that treating addiction straight from the emergency room has a real impact on helping opioid users recover.

Researchers at Yale School of Medicine published a paper in the *Journal of the American Medical Association* on a similar clinical trial back in 2015, which showed that 78% of patients treated with buprenorphine in the emergency room were still engaged in treatment after 30 days, compared to 37% in the group that received only a referral.

Even with these results, treatment for opioid addiction hasn't changed much in the years since. Many providers don't like the

idea of trading one medication for another, even if the replacement medications are not addictive.

Under the pilot program, patients at risk for addiction are screened for substance use. If the results are positive for substances like methamphetamine, marijuana, cocaine, alcohol or opioids, a recovery coach will come in and speak with the patient.

"Recovery coaches are often in recovery from illicit substances themselves," said Bogdon. "And can bring a different perspective to the conversation, which is by design."

If a patient is interested in overcoming their addiction, physicians will prescribe buprenorphine. After the initial dose, the patient is referred to a fast-track provider who will see them the next day. These providers must have additional training and obtain a DEA number in order to prescribe buprenorphine to these patients.

With buprenorphine administered in the emergency room, patients can avoid painful withdrawal symptoms and get a jump start on their recovery. This program has since expanded from MUSC to Tidelands Waccamaw Community Hospital and the Grand Strand Memorial Hospital as well as Spartanburg. Between these sites, over 7,000 patients have been screened for potential substance abuse across the state. Of those patients, 765 patients screened positive for opioid use disorder, and 80% of inducted patients arrived to their next-day appointments. Over 60% of those patients were still in treatment after 30 days, according to Bogdon.

Using peer recovery coaches in the project has also proven effective in both combatting the stigma around addiction and engaging with high-risk patients, but one of the drawbacks to the pilot is making sure there are enough fast-track providers to treat these patients.

"This project has absolutely changed the culture of how we treat addiction in medical settings," said **Kelly Barth, D.O.**, Department of Psychiatry and Behavioral Sciences associate professor and member of the MUSC-DAODAS team. "Having life-saving medications for opioid use disorder available in the emergency room not only enables patients to get started on the treatment they need when they need it, but it also empowers health care providers to be a positive part of our response to the opioid crisis."

Treatment during pregnancy

The opioid crisis is mirrored in pregnancy according to **Constance Guille, M.D.**, a psychiatrist and associate professor in the Department of Psychiatry and Behavioral Sciences at MUSC and member of the SC MAT Access team.

Guille's current primary clinical research focus is opioid misuse and opioid use disorder in pregnancy. By working with psychiatry

and obstetrics providers at MUSC and after interviewing pregnant women and their providers throughout South Carolina, Guille facilitated the development of a program that is delivered both in person and via telemedicine in obstetric practices across the state and is aimed at reducing opioid misuse in pregnancy.

Women who are both pregnant and misusing opioids present a hard-to-treat crossover. When a woman comes into the emergency room, she leaves a department with more experience handling opioid misuse and is sent to obstetrics, where fewer physicians are trained to treat addiction. People who do have training in treating opioid misuse are also not always comfortable treating pregnant women.

“It’s a group of people who often don’t have a lot of providers willing to take them on and manage them,” said Guille. Which is why the program is so specific to the needs of that population – to provide access to evidence-based treatments that help appropriately manage patients through pregnancy and postpartum.

Buprenorphine and methadone can be used to treat pregnant women with opioid use disorder, but naloxone cannot. Multiple studies show no birth anomalies after treatment with buprenorphine, and some show that buprenorphine may present less risk than methadone.⁵ Infants experiencing withdrawal immediately after birth, referred to as neonatal abstinence syndrome (NAS), also appear to suffer less severely if the mother was treated with buprenorphine during pregnancy.

One way the SC MAT Access team delivers care via telemedicine is through county drug and alcohol treatment centers. Patients with or without insurance can go to these state-funded centers for treatment, but the centers are often not trained or approved for MAT. Members of the SC MAT Access team will then travel to meet these pregnant patients and prescribe buprenorphine and start MAT.

“As one of the strongest departments of addiction sciences in the country, MUSC is a place where we’re going to provide access to evidence-based treatments and implement them,” said Guille. And targeting a population that is often hard to treat allows her to do that.

Treatment in primary care offices

Another part of SC MAT Access is academic detailing, which connects providers with the extra training and certification needed to provide MAT. Clinical pharmacists from MUSC meet with primary care providers in different communities throughout the state to discuss opioid use disorder and the different treatment options.

“We help providers put clinical evidence into daily practice,” said **Sarah Ball, Pharm.D.**, assistant professor in the Department of Medicine at MUSC and member of the SC MAT Access team. “We

“Previously, we would just treat the acute overdose,” said Jennings.

“And then give them a referral for outpatient treatment and hope they follow through.”



are promoting monitoring strategies for safer opioid prescribing as well as expanded access to medication-assisted treatment.” But it’s also more than that. These visits are interactive, where the clinical pharmacists are listening to the providers’ needs and then engaging them in discussions around treatment options for their patients.

These discussions can range from providing resources for a patient referral to discussing that provider’s interest in being trained to prescribe MAT or becoming a fast-track provider with the program.

As many patients interact with their primary care providers more than they interact with the emergency room, it’s important that these providers can help those interested in recovery before a potential overdose happens. “You are not there just to teach,” said Ball. “You’re finding out what barriers exist to treating their patients and supporting ways they can incorporate MAT.”

Academic detailing started out in a few counties in South Carolina and has now expanded to incorporate others and is just another way MUSC is working with other entities to change the way opioid use disorder is treated.

Between projects that address MAT in the emergency room, MAT during pregnancy and MAT in primary care offices, MUSC is expanding access. “We have so many initiatives around this topic here at MUSC,” said Ball. “And this uniquely collaborative team at MUSC has done an effective job of bringing these individual projects together in a way that continues to promote MAT for patients in South Carolina.”

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Long-Distance Medicine

MUSC is a leader in telemedicine, providing important services while also pioneering new, innovative programs to improve health care across the state

BY MATTHEW GRESETH

The future of health care has reached an inflexion point, and there are several problem areas in the health care system that need to be addressed: a shortage of physicians, escalating costs of delivering health care and an increasing elderly population. Telemedicine offers an innovative solution to these problems.

In the beginning, there was light

MUSC's telehealth initiative began with several independent programs, each receiving individual funding. In 2005, a telehealth obstetrics program was started at McLeod hospitals to enhance maternal and fetal care. Then, in 2008, MUSC began to use telehealth to care for stroke patients, and one year later, the psychiatry department started their own program. By 2013, there were 12 different programs at various levels of maturity using telehealth to provide better care for patients.

At this stage, the state was looking to invest in alternative care delivery methods to address the state's health disparities and deliver care across the state. Working with **Raymond S. Greenberg, M.D.**, then MUSC President, MUSC secured funds to form the South Carolina Telehealth Alliance (SCTA).

With new funding in place, MUSC was all-in. The telehealth program began to pick up speed and expand to other program areas.

"It was clear that hospital leadership, university leadership and the president were all fully engaged at a remarkable level," says **James T. McElligott, M.D., MSCR**, Telehealth Executive Medical Director. "Every chair of every department was told they were going to have a telehealth plan. MUSC was jumping at this opportunity."

MUSC has demonstrated continued telehealth success

Growing from 12 telehealth programs to more than 70, the MUSC Health Center for Telehealth also includes partnerships with over 30 SC hospitals, including McLeod Health, Prisma Health, Beaufort Memorial Hospital and Spartanburg Regional Healthcare System.

"There has been a lot of expansion with different services," says **Shawn Valenta, MHA, RRT**, MUSC's Center of Telehealth administrator. "There is also an expansion of infrastructure to support that growth."

For instance, the telehealth stroke program started in 12 hospitals and now exists in 30, with ten more coming on board next year. Additionally, telehealth started in eight non-affiliated primary care clinics and is now found in more than 100.

This success has been recognized on the national level. The Health Resources and Services Administration (HRSA) designated MUSC's Center for Telehealth as one of only two National Telehealth Centers of Excellence. In May of this year, SCTA was also awarded the American Telemedicine Association President's Award, the only one in the country, for their innovations in health care delivery.

The Center for Telehealth has a great team ensuring that SCTA continues to meet and exceed the needs of the state.

"It's hard work but we have a great team," says Valenta. "We are all very fortunate to be doing what we're doing. Everyone who works here is very passionate about what we do."

Bringing health care closer to home

The Center for Telehealth mission statement is "Telehealth for efficient, effective care," and the program has seen exponential growth and has identified several innovative strategies across the state to deliver health care. Below are examples of new and upcoming telehealth initiatives that include utilizing telemedicine to monitor diabetes, perform post-op follow-ups for transplant patients and provide invaluable palliative care.

Diabetes: empowering patients to be involved in their own care

According to the **American Diabetes Association**, there are 576,211 people living with diabetes in South Carolina. Monitoring a patient's glucose level is key to controlling diabetes; however, reliable data is



Telemedicine offers innovative solutions to many pressing health care challenges.

often difficult for doctors to obtain. In the past, doctors have relied on patients to purchase a meter, test their glucose values, and bring either the meter with the recorded values or a written list of values to their next visit. But often, patients forget the meter, fail to record their levels, or never get the meter in the first place. This results in “blind estimation” of their glucose levels and makes controlling their disease difficult.

Remote patient monitoring provides a way to overcome these obstacles.

“It gives reliable data to the providers to have confidence in the decisions they are making,” says **Elizabeth B. Kirkland, M.D., MSCR**, assistant professor and co-medical director of Technology Assisted Case Management for Low Income Adults with Type II Diabetes (TACM2). “Our goal is to improve diabetic control for low income, rural adults in SC with type II diabetes who otherwise have difficulty accessing primary care.”

Participating patients are given a device that allows them to monitor their blood-glucose levels at home. The device has an embedded

SIM card that transmits all measurements to a secure server, where two program nurses, Dawn Dericke and Caroline Wallinger, monitor the data and notify the point person at each individual primary care office to let them know which patients need attention.

“What we found is that there are dramatic improvements in A1C levels in the first six months,” says Kirkland. “The next six months showed, generally, that there was not a lot of change, but it is sustaining at a lower rate. It is encouraging that we’re making changes that are able to hold over time.”

Kirkland attributes this success to patients being able to manage their own disease. Remote monitoring also reduces the barrier of having to continually go to the doctor’s office, saving patients time and money.

In the future, this program will focus on three of the most heavily impacted counties in South Carolina. The goal is to determine if remote monitoring of diabetes and hypertension impacts downstream cardiovascular outcomes. It is expected that results from this work may inform policy making decisions.

Transplant: tapping into a growing network

MUSC's telehealth program continues to grow by tapping into the Center for Telehealth at larger sites for transplant care. MUSC is the only solid organ transplant program in South Carolina and, as of 2017, was the tenth busiest kidney transplant program in the country. Because of this, MUSC provides a service that is not replicated anywhere else in the state.

"We're still in the infancy, but I think that MUSC has a fantastic footprint that we're beginning to utilize," says **Daniel Stanton, MHA, MBA**, transplant administrator at MUSC. "When you're talking about a sub-specialist, it's a really effective way to connect the patient and provider."

Previously, MUSC utilized satellite clinics across the state for follow-up care, where physicians were physically sent to observe patients. Telemedicine has significantly improved this process and allows the team to conduct post-op visits remotely. The post-op care allows physicians to ensure that patients are taking the appropriate medications and that they are working, to check critical lab results and to physically see how the patient is recovering.

So far, the program has seen no-show rates drop dramatically while still providing the same level of care. If patients need further testing or follow-up procedures, they can be scheduled with local clinics, making it more convenient and cost-effective for patients.

One of the biggest beneficiaries of the telehealth transplant program is the living donor population. These donors come into the program healthy and require a different type of post-op follow-up; telehealth provides a convenient method to deliver that care.

"Of all of our patient populations, it's probably the most appreciated, utilized and convenient for healthy donors," says Stanton. "It's fairly unique because it's a healthy individual that has undergone surgery to help someone else out. It really is a perfect match for the patient with our technological capabilities."

The current telehealth transplant program is focused on kidney transplants. Because of the success of this program, the transplant team will be looking to utilize telemedicine for other organ transplants, such as heart, liver and lung transplants. Furthermore, the team is developing a pre-transplant evaluation that can be done remotely to further minimize the number of trips to MUSC for the procedure.

Palliative care: serious care for serious illnesses

Palliative care focuses on relieving symptoms and stress in patients with serious illnesses to improve the quality of life for both the patient and their family. MUSC has a robust palliative care team that is

pioneering a new project with the Center for Telehealth.

"It's a big deal for South Carolina because there is a national shortage of palliative care physicians," says **Patrick J. Coyne, MSN, ACHPN, ACNS-BC, FAAN, FPCN**, program director of the Palliative Care Program at MUSC. "It's a new, exciting program. It will be one of the pioneers in the country."

The palliative care team received a 3-year, \$1.26M grant from the Duke Endowment last summer. This grant provides money to train and educate partner providers, as well as social workers and chaplains, to deliver true interdisciplinary palliative care, rather than strictly medical care. The program hasn't gone live yet but aims to go live in July. Since receiving funding, six sites that lack palliative care teams have been enrolled and are undergoing preparation for care delivery.

One of the steps that the team is working on during this ramp-up phase is credentialing the physicians at each participating site.

"There's a lot of work to do before you go live," says **Lauren Seidenschmidt**, manager of the Palliative Care Program. "You have to get your physicians licensed at each participating site. There isn't an all-encompassing South Carolina credential that covers you at each hospital – you have to get credentials at every single site."

The team is optimistic about the future of this program.

"I envision it going nationwide, being able to provide palliative services to other states that are lacking," says Seidenschmidt.

"We've been contacted by other states in rural areas, like South Dakota, asking when they can sign up for this," adds Coyne. "We're not there yet, but we see an opportunity in the future to be able to meet the needs of people in rural or underserved areas."

The future looks bright

There is still a lot of work to be done as the Center for Telehealth continually strives to meet patients where they are.

"Now we've built it, we've proven that we can do it and do it well," says McElligott. "I think the next five years will be about focus, depth and outcomes. I'm really excited about it."

Using digital tools, the Center for Telehealth is looking to expand several programs, including at-home care for chronic conditions such as congestive heart failure and virtual urgent care for low-acuity conditions such as conjunctivitis and rashes.

Overall, digital engagement of at-risk populations increases patient contact with physicians and engages people with their own health. The data acquisition of these programs allows the Center for Telehealth to continuously improve health care delivery.

Making Sense of It All

Essentials of secondary stroke prevention for primary care providers

Thrombectomy

Lower BP

Manage lipids

Thin the blood

Control blood sugar

DTN goal – 45 minutes



**SUBJECT MATTER EXPERT:
DR. CHIRANTAN BANERJEE**

BY SHAWN OBERRATH

On completion of this article, readers should be able to:

- Summarize the most recent guidelines for acute ischemic stroke management
- Tailor patient care management after stroke based on the state of the art of secondary stroke prevention.

The incidence of stroke in the United States is around 795,000 cases per year, or about the same as the heart attack incidence (790,000 cases per year). Stroke is the fifth leading cause of death and the leading preventable cause of serious long-term disability in the United States. Acute stroke care improved dramatically with advances in tissue plasminogen activator (tPA) treatment and, more recently, mechanical thrombectomy. Unfortunately, stroke recurrence is still a major source of morbidity and mortality—about 25% of all strokes are recurrences. For patients with a history of stroke, the overall risk of another is 6% at 1 year, 16% at 5 years and 25% at 10 years.^{1,2}

Stroke can be caused by ischemia (80% of strokes), intracerebral hemorrhage (15%) or subarachnoid hemorrhage (5%). This article focuses solely on ischemic events, which can be either transient ischemic attacks (TIAs) or ischemic strokes. TIA was traditionally defined in terms of duration, but the contemporary definition of TIA is a “transient episode of neurologic dysfunction caused by focal brain, spinal cord or retinal ischemia without acute infarction.” This definition is based on tissue status, not time, but generally a TIA lasts for less than an hour. In contrast, ischemic stroke is defined as an episode that includes infarction and usually lasts for more than an hour.^{3,4}

In early 2018, the American Heart Association and the American Stroke Association (AHA/ASA) jointly published the *2018 Guidelines for Early Management of Patients with Acute Ischemic Stroke*.⁵ New blood cholesterol management guidelines were released in late 2018, and even more recently, the 2019 guidelines on primary prevention of cardiovascular disease made their debut.^{6,7} Each of these publications is comprehensive and replete with data, graphs and charts, potentially leaving providers overloaded with information. In addition, there have been numerous advances in secondary stroke prevention since the most recent official guidelines, published in 2014.

This CME article curates the state of the art of secondary stroke prevention for primary care providers, beginning with a broad

Date of Release:
July 22, 2019
Date of Expiration:
July 22, 2021

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Dr. Banerjee and Shawn Oberrath have no relevant financial relationships to disclose.

overview of acute care and then focusing on modifiable risk factor management for stroke prevention after TIA or ischemic stroke.

Don't delay, use tPA

Although acute ischemic stroke (AIS) management almost always occurs in the hospital, primary care providers should be familiar with modern best practices. According to the 2018 guidelines for AIS management, the goal door-to-needle time for IV alteplase (a recombinant form of tPA) is 45 minutes. Prior to alteplase administration, all patients suspected of AIS should receive brain imaging evaluation, which should occur without hesitation and without waiting for creatinine levels if there is no history of renal disease. Usually a noncontrast CT scan is the only imaging requirement,

POCKET GUIDE TO SECONDARY STROKE PREVENTION

HYPERTENSION

Goal BP: <130/80 mm Hg
Use any evidence-based treatment

HYPERLIPIDEMIA

Goal LDL-C level: $\geq 50\%$ reduction or <70 mg/dl
Start with high-intensity statin therapy
Add ezetimibe if needed

PREDIABETES/DIABETES MELLITUS

Standard management
Add pioglitazone to reduce risk

ATRIAL FIBRILLATION

NOAC therapy, except with mitral stenosis or mechanical heart valve

PREVIOUS STROKE/TIA

Aspirin at 50–325 mg daily OR
Clopidogrel at 75 mg daily

SMOKING

Strongly support patient efforts to quit

SLEEP APNEA

Perform sleep study
Prescribe CPAP if indicated

OTHER LIFESTYLE FACTORS

Strongly encourage patient to:

- Exercise
- Eat well
- Drink lightly or not at all

and the only result that excludes alteplase treatment is intracerebral hemorrhage. The only lab required prior to alteplase treatment is the blood glucose level to exclude stroke mimicry by hyper- or hypoglycemia.⁵

IV alteplase should be administered to almost all patients with AIS whose onset was less than three hours previous and to eligible patients whose stroke onset was three to four and a half hours previous. This includes patients with sickle cell disease, those already on antiplatelet therapy, and those with end-stage renal disease. IV alteplase administration with telestroke guidance is as safe and beneficial as that at stroke centers.⁵

Mechanical thrombectomy with a stent retriever should be initiated within six hours of symptom onset for patients meeting all eligibility criteria. For carefully selected patients, mechanical thrombectomy can be initiated within 24 hours of stroke onset.⁵

All primary care providers should bear in mind that in cases of stroke, time is equivalent to brain tissue; therefore, it is imperative to act quickly, call 911 and utilize stroke center and telestroke resources.

Mitigate risk

Because of the advanced state of modern acute stroke care, stroke patients should be undergoing appropriate pharmaceutical therapy at the time of discharge from the hospital. The challenge is to ensure

ongoing medication compliance and management of major modifiable risk factors to lower the risk of recurrence. The following sections highlight the most recent advice regarding these factors.

Hypertension

Arguably the most important measure to address is hypertension. Aim for a blood pressure of less than 130/80 mm Hg. Treatment may include any evidence-based pharmacologic intervention and/or lifestyle modifications, such as weight loss, dietary changes, reducing alcohol consumption and finding ways to move the body regularly.⁷

Hyperlipidemia

The 2018 ACC/AHA Multisociety Guideline on the Management of Blood Cholesterol recommends the following for patients with hyperlipidemia. Initiate or maintain high-intensity statin therapy to manage lipid levels, adding ezetimibe or a PCSK9 inhibitor (PCSK9-I) if needed. Begin by aiming for a 50% or more reduction in LDL-C levels by use of a statin; if the level is still more than 70 mg/dl at the maximally tolerated statin level, it may be time to add ezetimibe. For patients with very high risk and multiple high-risk clinical factors, it may be reasonable to add ezetimibe to statin therapy, and then if the LDL-C level is still greater than 70 mg/dl, consider adding a PCSK9-I.⁶

Prediabetes/diabetes mellitus

Diseases of glucose metabolism leave stroke survivors at an almost doubled risk of recurrent stroke. Approximately one third of stroke patients have diabetes, and prediabetes rates in patients with recent stroke or TIA range from 23 to 53%. Clinical outcomes for such patients are poorer after either ischemic or hemorrhagic stroke, with higher mortality rates, poorer functional outcomes and longer hospital stays. Thus, all stroke survivors should be screened for diabetes, and those with prediabetes or diabetes should be treated according to standard practice. In addition, pioglitazone added to standard treatment is associated with a 32% reduction in risk of recurrent stroke and a 25% reduction in risk of major cardiovascular events.^{8–10} Consider adding pioglitazone therapy for supplemental management of stroke patients with prediabetes or diabetes.

Antithrombotic agents

Aspirin is the most well-studied and well-known antithrombotic agent, and it remains an important part of secondary prevention of ischemic stroke because it is very effective and is the most budget-friendly choice. Clopidogrel is also effective and may be used in patients who are allergic to aspirin. The combination of aspirin and clopidogrel for short-term use may prevent recurrent stroke, especially for patients with symptomatic severe intracranial stenosis, but the combination is not appropriate for long-term use because of increased bleeding risk. Finally, aspirin in combination with dipyridamole may provide an even larger risk reduction for stroke, but this combination is expensive and may not be well tolerated, and it should not be used for long-term secondary prevention.^{11,12}

Atrial fibrillation (AFib) is a highly important risk factor for ischemic stroke, as it is associated with a five times greater risk of stroke. For patients with AFib, coronary artery disease, acute coronary syndrome or stent placement, addition of anticoagulant therapy is warranted. According to the most recent update to the guidelines for AFib, non-vitamin K oral anticoagulants (NOACs) are now recommended as the preferred alternative to warfarin. The exceptions to this recommendation are patients with moderate to severe mitral stenosis or a mechanical heart valve. Note that an advantage of some NOACs is that their action may be reversed if needed.¹³

Lifestyle factors

Work with patients and their families to encourage lifestyle improvements. Patients who are capable of exercise should do so regularly, nutritional guidance should be provided, and heavy drinkers should be counseled to reduce or avoid alcohol consumption. A sleep study

and treatment with CPAP should be considered for patients with any symptoms of sleep apnea. It is very important that smokers or those exposed to secondhand smoke find ways to stop smoking or eliminate their exposure: smokers are two to four times likelier to have stroke than their nonsmoking counterparts.¹

Patient compliance

One of the difficult realities for primary care providers is that often patients are placed on an optimized medication regimen in hospital but fail to comply with treatment at home. More than one third of patients stop their medications within two years after stroke. In a recent survey of factors that influence adherence to secondary stroke prevention medications, the major barriers were side effects, negative perceptions about medications, physical difficulty with swallowing pills, and drug costs. On the flip side, there were numerous facilitators of patient adherence: adequate side effect management, a belief that medications are important, use of medication storage devices and routines to help with habit formation, and assistance from caregivers.¹⁴ Consider focusing efforts on some or all of these facilitators, as well as encouraging patients and caregivers to use mobile health applications with calendars and reminders. See the American Stroke Association website (strokeassociation.org) for further excellent resources to guide and encourage patients.

Conclusion

To wrap up, hypertension management, antithrombotic medication and smoking cessation are top priorities for secondary prevention of stroke. It is also imperative to remain current on modern standards for acute stroke care, lipid and glucose management and antithrombotic therapies. Provide the best advice possible to patients, and don't be shy about using known facilitators of patient behavior to assist them.

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Interview

MUSC welcomes Terry Kowalenko, M.D., professor and chairman of the Department of Emergency Medicine



Dr. Kowalenko oversees clinical care, education, research and financial/operational performance of the Department of Emergency Medicine at MUSC. Prior to joining the MUSC Health family, he served as a professor of Emergency Medicine at the Oakland University William Beaumont School of Medicine and as Chairman of Emergency Medicine at Beaumont Hospitals, Royal Oak, Troy and Grosse Pointe. He was Director of Continuous Professional Development for the University of Michigan Medical School and held faculty appointments at the University of Michigan/St. Joseph Mercy Hospital and the Wayne State University-Detroit Medical Center/Sinai-Grace Hospital. He also served as an attending physician in emergency medicine at Henry Ford Hospital. Dr. Kowalenko is an active researcher of workplace violence, quality measures and board certification. *Progressnotes* chatted with Dr. Kowalenko in May 2019.

What first attracted you to MUSC?

Part of what drew me to MUSC was the fact that the Department of Emergency Medicine is new, which gives me the opportunity to help grow and shape it. I was also attracted to the philosophy of the institution of expanding their footprint throughout the state, and I saw a real opportunity for the department to follow suit.

I was president of a 1,000-physician medical group for a couple of years, and MUSC also offered me the position of associate chief of the ACT [acute, critical and trauma] ICCE. That is intriguing because beyond emergency medicine, I can envision the whole system and where we fit within it.

Additionally, I recently became a CMS Quality Payment Program clinical champion. CMS picks 10 to 12 clinicians every two years to serve as consultants regarding quality payment programs, and I'm in the second

PHOTO: SON NGUYEN

cohort. I felt like MUSC would be a very good place to help share that experience.

What is your vision for the Department of Emergency Medicine?

My vision is for us to become a premier department that provides outstanding patient care. I am a very patient-centric individual because of two experiences that changed my outlook. One was trying to navigate through the complex health system when my dad was diagnosed with a brain tumor and died within nine months. The other was my son suffering a traumatic head injury. Being on the other side of the bed changed my view of medicine.

I'll be working with the chairs to help our patients navigate the system. When patients come into our emergency department, they think they're already in the hospital. But if you asked anybody who works in the hospital, they would say that they were in the emergency department, not the hospital. I think that we need to start seeing it more from the patient's perspective.

At Beaumont, mine was the first department to start a patient family advisory council (PFAC). We started meeting every month and would talk to families about issues surrounding the department. When we were designing the new department, they suggested ideas regarding aesthetics, comfort and convenience, like having phone chargers in every room. Little things like that helped us gain a patient's perspective, and I intend to do the same here.

I work very hard to build relationships so that we can work together to do what's best for our patients, and I view success based on my faculty's accomplishments. I'm a proponent of faculty development and mentorship. I'd like to expand our education and research portfolios and give as many opportunities as possible for faculty to have a regional and

national presence in clinical research and education.

Additionally, security and workplace violence have been my areas of interest and research for the last decade. I am on the workplace violence committee at MUSC, and I'm hoping to help make our workplace as safe as possible.

What drew you to your research focus of security and workplace violence?

I was president of the Michigan College of Emergency Physicians when we received a letter from a member who had been stalked by the mother of a patient. He was curious as to what we could do about it and if others were having this experience. We realized that we didn't have much information, so we designed a survey of Michigan physicians and published our results about their experiences. Some years later, I was introduced to Donna Gates, Ph.D., who was also doing work on violence. She was the principal investigator and I was the coinvestigator on a grant that looked at workplace violence, and we wrote several papers on it. I've continued working on this ever since.

What are the greatest strengths of the department as it enters its third year?

I think the greatest strengths are the people. I am incredibly impressed with the faculty, residents, fellows, nurses, technicians, clerks and all the people that work there. They are incredibly dedicated and hardworking. There are a lot of challenges to our environment, and the fact that they have stayed strong and worked through these challenges demonstrates their commitment to this department.

What are the challenges and your initial priorities?

I think the biggest issues we currently have are related to MUSC's growth. I am working

with my own faculty and other department leaders so we can continue to support patient throughput. We continually look at space to best support quality patient care, our staff and operational efficiencies.

I also want to align department goals with those of the institution and to be cognizant of faculty wellness. Burnout is prevalent among all specialties, but emergency medicine has consistently been in the top three for several years. Hopefully, improved wellness will translate into better patient satisfaction and more compassionate care.

Breaking down silos is critical to the success of any medical organization. It's important for us to engage our patients and our staff to make this a premier destination for emergency care. We will work on innovative approaches to improve the patient experience and throughput to ensure we are a resource to not just Charleston, but the entire state. As a tertiary or quaternary care center, we care for the most complex patients. We hope to work with all of the MUSC and non-MUSC facilities to provide the best possible care to all of our patients.

What would you like *Progressnotes* readers to know about you?

I'm honest, hardworking, dedicated, a team player, very patient-centric, and I believe strongly in building relationships. As a son of immigrants, English was not my first language. I was the first in my immediate family to attend college. I've worked in and around Detroit and Ann Arbor as well as in Africa, where I helped start the first emergency medicine residency in sub-Saharan Africa. I love my family and the outdoors. I hope to help the citizens of South Carolina and promote the success of MUSC.



Collaborative Spirit Lures Brain Researcher to MUSC

BY LESLIE CANTU

Hesheng Liu, Ph.D., jokes that he relocated to MUSC from Harvard University because he's originally from the South – South China, that is.

The fact is, when Liu first came to MUSC to give a talk, he had no idea he would end up moving to Charleston as the SmartState Endowed Chair in Imaging Science in the Brain Imaging SmartState Center or become the associate director for the MUSC Center

for Biomedical Imaging. But as he talked to people like **Kathleen Brady, M.D., Ph.D.**, vice president for research; **Peter Kalivas, Ph.D.**, chair of the Department of Neuroscience; and **Thomas Uhde, M.D.**, chair of the Department of Psychiatry and Behavioral Sciences, he realized that his work studying brain function through “resting-state” functional MRIs could have a ripple effect in multiple disciplines.

“I have a feeling that here it's a very collaborative environment. That's probably the most attractive thing,” said Liu, who earned his doctorate at Tsinghua University in Beijing and retains an associate professorship at Harvard.

And MUSC's researchers are delighted to have him here.

“He's an international expert on resting-state MRI measurements,” Kalivas said. “He's

developed methods for evaluating the data from resting-state MRI that are absolutely cutting edge.”

Brady said Liu’s technical expertise will bring MUSC’s imaging research portfolio “to the next level.”

“For a campus our size, we have a large number of people who are doing work in this neuroimaging area, and they’re doing it across disorders – everything from ADHD and Alzheimer’s to addictions – so I think he really saw the potential for collaboration here as very rich,” she said.

“The beauty of this technology is now we are not looking at the 1% signal. We are looking at the 99%. So it’s very robust.” —Hesheng Liu, Ph.D.

Liu’s work looks to create “fingerprints” of individuals’ brains by mapping out their functional architecture. Although researchers have long known the general areas of the brain responsible for language, motor skills and executive functioning, the specifics have been harder to capture. Functional MRIs, or fMRIs, provide a “window” into the brain to see which part is at work, but they have yet to prove their value to an individual patient facing a disease or diagnosis.

“After 27 years of development, it’s still limited to the research community. In the hospital, doctors cannot prescribe a functional MRI scan,” Liu said.

Doctors can get a regular MRI scan of a patient to check for anatomical changes, but they can’t get an fMRI scan to check for changes in the brain’s signals. That’s because the fMRI measures a signal increase that’s pretty tiny – maybe 1% – compared

to the nonstop, apparently random, activity happening in the brain. Because the signal is so weak, researchers can’t look at an individual’s fMRI but instead have to look for an average across thousands of fMRIs to come to any conclusion about the purpose of any particular brain signal.

Pushing fMRI toward clinical applications, Liu’s group uses resting-state fMRIs. The resting-state fMRI captures the nonstop activity in the brain, which Liu said may be the brain constantly checking its infrastructure by sending out test signals.

Instead of requiring a subject in a scanner to do a particular task – tapping a finger, solving a problem, moving her tongue – the resting-state fMRI simply requires the subject to lie there.

“The beauty of this technology is now we are not looking at the 1% signal. We are looking at the 99%. So it’s very robust,” he said.

His team has been working to develop the computational algorithms to understand what’s embedded in those spontaneous brain signals and then create a map of the brain.

An individualized map of a specific patient’s brain network could greatly improve brain surgery, and Liu believes this application could be ready for clinical use in a year or two.

Right now, he said, patients with epilepsy or brain tumors sometimes go through an awake surgery, a demanding task for both patient and surgeon. To ensure the surgeon

doesn’t damage functions like language, memory or movement, the patient is awake during the critical portion of the surgery and asked to perform specific tasks to demonstrate that those functional brain networks remain intact. Liu has been running trials with hospitals in China to compare their results from awake surgery with what his calculations would recommend, and he has found his calculations to be spot on.

“We’re going to see that we can get it really, really precise,” he said. “I believe our technology is almost ready, so we can prescribe an fMRI for that.”

Longer term, Liu thinks this technology has applications for checking on brain recovery after stroke, psychiatric care and maybe even one day for general health and wellness. He can envision a time when middle-aged people will go to their doctors for a checkup and not only get their cholesterol levels, blood pressure and weight checked, but also whether their brains are signaling at an appropriate rate or slowing down more quickly than expected.

Liu is also excited about the possibilities of collaborating with MUSC researchers working on drug addiction and brain stimulation. Furthermore, brain mapping with fMRI could also help in developing treatments for psychiatric disorders by classifying patients according to which networks are dysfunctional.

“The bottom line is, Dr. Liu is hoping to get fMRI-based biomarkers of neuropsychiatric disorders and then maybe, once that’s established, use those biomarkers to help refine therapy,” Kalivas said.



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