STROKE OF GENIUS

New guidelines and statewide study spotlight local stroke response

ALSO:
Nasal Reconstruction
Lynch Syndrome
Graft vs. Host Disease

Phillip Scott, M.D., U-M emergency physician
On the cover: Phillip Scott, M.D., co-authored new national guidelines for treatment of stroke and directed a state-wide study evaluating the ability of community hospitals to administer tPA on time.

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**INSURANCE**

**Priority Health now accepted**

The University of Michigan Health System is now a participating provider with Priority Health, serving its HMO, PPO, POS and Medicare product lines. The contract, which went into effect March 1, adds more than 1,800 physicians and all U-M hospitals to the Priority Health provider network.

**ONLINE** For a full list of insurance plans accepted by UMHS, visit uofmhealth.org/insurance.

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**Teaching hospital**

The events listed below are just a sampling of upcoming CME opportunities available to clinicians practicing outside the UM Health System.

- Clinical Care Issues in the Care of Older Adults: Sept. 26 in Ann Arbor, Mich.
- 10th Annual IBD Update for the Practicing Physician: Nov. 2 in Plymouth, Mich.
- Practical Solutions to Common GI Problems: Nov. 16 in Plymouth, Mich.

**REGISTER** For a complete listing of CME opportunities or to register, visit ocpd.med.umich.edu/cme/course-calendar or call 734-232-3468.

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**TRANSPLANT**

**BEST CHRISTMAS GIFT EVER**

One organ donor saves lives of 999th and 1,000th pediatric transplant recipients

On Christmas Day 2012, early-morning phone calls delivered the best gift ever for two Michigan families. The calls from the University of Michigan Transplant Center notified two 15-year-old boys that organs had been donated to save their lives.

Within 24 hours, the boys became the 999th and 1,000th pediatric transplant patients at Mott. The recipients were Scott Simon, a freshman at Fowler High School, and Jacob Brancheau, a tenth-grader at Monroe High School.

For U-M, the boys represent a significant milestone. No other Michigan hospital has done as many pediatric transplants.

"Reaching 1,000 pediatric transplants is a point of pride. This story illustrates the amazing impact of organ donation. Two young men received the greatest Christmas gift ever: a second chance at life," says John Magee, M.D., transplant surgeon and director of the pediatric abdominal transplant program, who led the teams that performed both operations.

**ONLINE** Get transplant consult request guidelines and read more about the pediatric transplant program at Colleagues in Care Online at med.umich.edu/cic.
Expanding hope

An option for patients with severe aortic stenosis

Earlier this year, U-M expanded its use and testing of transcatheter aortic valve replacement (TAVR) procedures with the launch of the Medtronic CoreValve SURTAVI clinical trial, which includes patients with symptomatic severe aortic stenosis who are at moderate risk for aortic valve surgery.

The emergence of TAVR procedures in the U.S. is providing new hope for patients at high risk for surgery or who are not surgical candidates, half of whom could die within two years without treatment. The procedures allow access to the diseased aortic valve using a catheter, usually inserted through an artery in the leg, rather than through open heart surgery. The new valve is placed in the beating heart over the existing valve. Patients are home from the hospital in three to five days.

The SURTAVI trial is the latest TAVR trial to be taken on by the cardiac surgeons and interventional cardiologists at the newly renamed University of Michigan Samuel and Jean Frankel Cardiovascular Center. The U-M TAVR team is also participating in the Medtronic CoreValve TAVR trial for patients at high risk or who are ineligible for surgery, and is using the Edwards SAPIEN transcatheter heart valve, which is FDA-approved for use in high-risk or non-surgical patients.

The U-M TAVR program is led by Stanley J. Chetcuti, M.D., Eric J. Topol Collegiate Professor of Cardiovascular Medicine, Internal Medicine; P. Michael Grossman, M.D., professor of Cardiovascular Medicine, Internal Medicine; G. Michael Deeb, M.D., Herbert Sloan Collegiate Professor of Cardiac Surgery; and Himanshu J. Patel, M.D., associate professor of Cardiac Surgery.

The U-M Frankel Cardiovascular Center performs more than 600 surgical aortic valve procedures a year; more than any other Michigan hospital. And for TAVR, our team has the highest volume of implants in the state and is also among the top in the country in terms of volume.

M-LINE Call M-LINE at 800-962-3555 to find out if your patient may be eligible for a TAVR procedure.

ONLINE Learn more about the three TAVR options available at U-M and get consult request guidelines at Colleagues in Care Online at med.umich.edu/cic.

The SURTAVI clinical trial is testing the use of the Medtronic CoreValve on aortic stenosis patients at moderate risk for surgery.

CHOOSING WISELY

U-M cardiologist helps craft national vascular campaign

Recognizing that patients sometimes ask for tests and treatments that are not necessarily in their best interest, and that physicians often struggle with decisions about prescribing tests and procedures as a way of covering all possible bases, leading medical specialty societies have written lists of tests and procedures to question. These lists, under the umbrella of the Choosing Wisely campaign, are meant to spark conversations between patients and doctors about what care is really necessary.

U-M cardiologist and president-elect of the Society for Vascular Medicine James Froehlich, M.D., helped craft the list of five things to question about vascular medicine.

At the top of the list: avoiding preoperative stress testing for patients undergoing low-risk surgery and skipping clotting disorder lab tests for patients who suffer a first episode of deep vein thrombosis (DVT) when there’s already a clear cause.

“Lab tests to look for a clotting disorder will not alter treatment of a venous blood clot, even if an abnormality is found,” says Froehlich. “DVT is a common disorder, and recent discoveries of clotting abnormalities have led to increased testing without proven benefit.”

ONLINE See the complete vascular Choosing Wisely list at Colleagues in Care Online at med.umich.edu/cic.
THE KINDEST CUT

Minimally invasive surgery is the first choice at Mott

Minimally invasive surgery (MIS) is increasingly becoming the norm for children of all ages at C.S. Mott Children’s Hospital. It is now used on even the smallest patients, including premature infants and in utero. It is also becoming routine for complex procedures that previously required open surgeries.

Advancing technology that continues to shrink the size of MIS equipment is one reason for this change. But the key to offering this level of specialized expertise nearly across the board at UM is the commitment to the MIS approach among all the physicians.

“All the surgeons in our group have extensive experience in MIS, and are very comfortable with advanced laparoscopy,” says Marcus Jarboe, M.D., pediatric surgeon at Mott. “This creates an environment where we constantly challenge ourselves to find creative approaches to difficult cases.”

One way to achieve these goals is to leverage different disciplines where possible. For example, Jarboe is fellowship-trained as both a pediatric surgeon and an interventional radiologist. “When we are trying to solve a difficult problem, it’s very helpful to have a thorough understanding of all the different techniques available,” he explains. “Everyone brings his or her own expertise to the table, which helps us devise unique solutions.”

Another critical element for successful MIS is anesthesia. “Without the right anesthesiologists, using MIS on sick infants and children is not possible,” Jarboe emphasizes. “We have excellent anesthesiologists who are committed to making these MIS procedures possible, even on very tiny infants and patients with complications, such as heart defects.”

Another example of leading-edge surgery at Mott is fetoscopic surgery, which has expanded the possibilities for in utero treatments. The small tools and minimally invasive approaches are well suited to treat fetal disorders such as twin-twin transfusion syndrome.

In addition to physical benefits of MIS, such as less pain and faster recovery, there are also emotional benefits for children later in life. “A 2-centimeter incision in an infant can turn into a sunken 8-inch scar by the time the teenage years roll around. So, we plan for tiny incisions that make for tiny scars,” says Jarboe. “It’s not a vanity issue with the kids; it’s a confidence issue. So, it’s rewarding to be able to offer surgical solutions that have so many advantages.”

ONLINE Visit mottchildren.org/minimallyinvasivesurgery to learn more about the pediatric MIS capabilities at Mott. You can watch a surgical video, read a case study and get a list of MIS procedures performed at Mott.

Breathe Easy

Undiagnosed obstructive sleep apnea can be a major risk factor for airway collapse and related respiratory complications after surgery and procedures requiring sedation, according to U-M sleep neurologists and anesthesiologists.

Physicians should consider a patient’s apnea risk when referring them for elective surgery or even procedures such as colonoscopy. A simple questionnaire, known as STOP BANG, can help assess risk and determine whether patients should have a more formal obstructive sleep apnea evaluation before surgery.

UM screens elective surgery patients for obstructive sleep apnea. Patients who snore, are sleepy, have hypertension or have a large neck circumference may be at increased risk. Patients found to have a high risk of apnea are referred to U-M’s Sleep Disorders Center for further assessment and treatment, including fitting with CPAP (continuous positive airway pressure) equipment for use before, during and after surgery.

Patients who use CPAP at home should be encouraged to bring the equipment with them to the hospital or procedure unit, because anesthesia can compromise breathing.

Patients with apnea require special monitoring during operations and sedated procedures, and during the post-anesthesia period. UM sleep neurologist Shelley Hershner, M.D., notes that undiagnosed patients’ risk continues after discharge, especially if opioid analgesics have been prescribed for post-procedure pain.

ONLINE The STOP BANG questionnaire is available at stopbang.com. Get the Ambulatory Surgery Obstructive Sleep Apnea (OSA) Toolkit from the Institute for Quality Improvement and learn more about U-M’s Sleep Disorder Center at Care Online at med.umich.edu/cic.
If a community hospital partners with a primary or comprehensive stroke center, early treatment decisions can be made.

Phillip Scott, M.D.

When a patient begins experiencing symptoms of stroke, the nearest major stroke center could be miles away, and the patient may not recognize or act on the symptoms right away. That combination of delay and distance can keep patients from receiving optimal care, including timely tPA treatment for ischemic stroke.

But a new national guideline for emergency stroke care, and results from a statewide study of stroke treatment in 24 Michigan community hospitals, point to new possibilities that could benefit patients nationwide.

U-M emergency physician Phillip Scott, M.D., who co-authored the guidelines and directed the statewide study, says physicians of all specialties should be aware of the new recommendations and findings.

“Educating our patients about their personal risk for stroke, and about the need for rapid action if they experience stroke-like symptoms, could affect their long-term outcomes,” he says.
For patients taking aspirin or clopidogrel on a preventive basis, and their physicians, a new U-M-led study may ease concern about their eligibility for tPA treatment in the event of a stroke.

After adjusting for patient characteristics, researchers found no significant difference in the rate of symptomatic or asymptomatic brain hemorrhage on CT or MRI among such patients who received tPA for ischemic stroke.

The findings are based on data from 830 patients who received tPA in the INSTINCT study (see main story) or another four-hospital study, just under half of whom were using aspirin or clopidogrel before their strokes. U-M emergency physician William Meurer, M.D., M.S., and colleagues published the results in *Academic Emergency Medicine*.

The study did not include any patients taking more potent blood thinners, such as warfarin, heparin, dabigatran or rivaroxaban. The authors caution that the potential use of tPA in patients taking these drugs needs much more study.

“In light of the long-term benefit that patients receive from antiplatelet therapy, the small increase in risk of intracranial hemorrhage after tPA treatment should not be a game-changer for emergency physicians,” says Meurer. “This study from a broad range of hospitals provides solid evidence based on real-world use of tPA that physicians should not alter their decision-making based on aspirin or clopidogrel use when treating stroke patients with tPA.”

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**NEW NATIONAL GUIDELINES**

The new American Stroke Association guidelines, published in *Stroke*, extend the time window for tPA treatment to 4.5 hours, from the previous 3 hours. This longer period means that more patients may be eligible for tPA, which has been shown to improve long-term motor and cognition effects from stroke.

But the guidelines also put new pressure on hospitals to reduce the “door to needle” time for stroke patients to 60 minutes — including triage, brain imaging and preparation for tPA administration.

If a hospital isn’t equipped to provide tPA treatment, ischemic stroke patients should be rapidly transferred to the closest available certified primary stroke center or comprehensive stroke center, which might involve air medical transport, the guidelines say.
6 hours
The potential window for intra-arterial fibrinolysis in certain patients who aren’t candidates for intravenous tPA, but only at an experienced stroke center with interventional care, such as U-M Telemedicine and simple telephone support can provide real-time access to expertise. Phillip Scott, M.D.

“However, for patients brought to hospitals that don’t offer specialized stroke expertise, telemedicine and simple telephone support can provide real-time access to expertise,” says Scott. “If such a hospital partners with a primary or comprehensive stroke center, early treatment decisions can be made.”

MICHIGAN-WIDE STUDY
The role of community hospitals and physicians is made clear by recently published results from the study that Scott directed, called INSTINCT. It evaluated the ability of 24 community hospitals to deliver tPA, with training and 24/7 support available from U-M. The study was funded by the National Institute of Neurological Diseases and Stroke.

By the end of the study, the community hospitals that had the U-M experts as the “sixth man” on their teams did better at delivering tPA to eligible patients, without increased risk of hemorrhage, than those that didn’t. The findings of the randomized controlled trial were published in Lancet-Neurology.

Data from 22 of the hospitals show that tPA use more than doubled in the 11 hospitals randomized to receive assistance, versus a smaller increase in the other 11. Some hospitals even surpassed national targets for tPA use that large stroke centers don’t always reach — a true game-changing performance.

Across the U.S., less than 5 percent of stroke patients receive tPA — when more than 11 percent could — largely because of the time factor.

The INSTINCT results demonstrate that tPA can be used safely in the community hospital setting, and that more work needs to be done to expand public access to the only treatment approved by the FDA to reverse the effects of stroke.

As for other ischemic stroke treatments, such as stent retrievers used to remove large clots, the new guidelines call for further studies to determine if they improve patient outcomes before being seen as substitutes for intravenous tPA during the time window when tPA can be given.

ONLINE Get linked to more information about the new national guidelines and the statewide INSTINCT study at Colleagues in Care Online at med.umich.edu/cic.

M-LINE Refer patients to U-M’s Comprehensive Stroke Program by calling M-LINE at 800-962-3555.
The cosmetic results of the new single procedure are almost as good as with the double procedure.

New nasal reconstruction technique skips second procedure

The basal cell carcinoma growing on Carolyn Bohlmann’s nose was not aggressive, but it was deep and located right on her nostril. The tricky part was not the MOHS surgery to remove it, but reconstructing her nostril to good results, both cosmetically and functionally.

Bohlmann opted for a new reconstruction technique her surgeon, Jeffrey Moyer, M.D., was offering at the University of Michigan Comprehensive Cancer Center. Moyer removed cartilage from behind Bohlmann’s ear, and skin from her shoulder, and shaped it to create a new nostril.

“It healed up nicely. You can see a bit of a wrinkle, sort of a raised wrinkle. No one notices it unless I say something about having a surgery,” says Bohlmann, 69. Ten days after having the procedure done, she was back to work.

A ONE-TWO PUNCH

“The nose is a fairly complicated area to reconstruct,” says Moyer, an associate professor of otolaryngology at the U-M Medical School.

The most common method for nasal alar reconstruction uses ear cartilage to reshape the nostril and forehead or cheek skin to create a skin flap that provides a blood supply. The flap stays in place for about three weeks, after which patients come back to have it removed. Typical results look good, and the nostril functions correctly.

A SINGLE SURGERY

But what about patients who can’t — or don’t want to — endure two procedures? Moyer and his team started with one key question: Do we really need that blood supply from the skin flap?

The new procedure skips the skin flap — and the need for a second procedure — but still appears to allow for the cartilage to take hold and keep its place without the nostril either collapsing or pulling up. On a one-to-five scale, with one meaning excellent, the average cosmetic result was judged a 2.3.

“This could save both patients and surgeons a lot of effort and time. The last thing people want to do is return to the OR,” Moyer says. “It allows us to spare people multiple surgeries or a scar that dominates the cheek.”

Moyer says that the cheek flap technique has a somewhat better cosmetic result than his new procedure. But since many skin cancer patients are older, their co-morbidities may make that second procedure inadvisable.

“The incremental benefit with a cheek flap is not worth it for some patients. The ability to do something less but still get the same quality of results is important,” he says.

ONLINE Get linked to the study in JAMA Facial Plastic Surgery at Colleagues in Care Online at med.umich.edu/cic.

M-LINE Refer patients to U-M plastic surgeons by calling M-LINE at 800-962-3555.
WEIGHING THE RISKS

Prostate cancer risk rises in men with Lynch syndrome

Men with the inherited genetic condition Lynch syndrome face a higher lifetime risk of developing prostate cancer and appear to develop the disease at an earlier age, according to a new study led by researchers at the University of Michigan Comprehensive Cancer Center.

Lynch syndrome is linked to a higher risk of several types of cancer. People with Lynch syndrome have up to an 80 percent lifetime risk of colorectal cancer and are also more likely to develop endometrial, gastric, ovarian, urinary tract, pancreatic or brain tumors. Overall, about 1 in 440 people are carriers for the genetic mutation, making it one of the most common inherited cancer conditions.

THE IMPLICATIONS

The findings in prostate cancer have implications for screening younger men who may be at higher risk of the disease. Recent guidelines from the U.S. Preventive Services Task Force recommend against screening with PSA in men younger than 75 who do not have any symptoms.

“For men with an inherited risk factor for prostate cancer, they should still be thinking about prostate cancer screening. Our study is valuable for patients and physicians when weighing the risks and benefits of screening. We suggest men with Lynch syndrome might benefit from regular prostate cancer screening beginning at age 40,” says lead study author Victoria M. Raymond, a certified genetic counselor with the University of Michigan’s Cancer Genetics Clinic.

THE STUDY

The researchers looked at 198 families who have a strong family history of cancer and were enrolled in registries at the University of Michigan Comprehensive Cancer Center or at Dana Farber Cancer Institute. These family registries included 4,127 men who were included in this analysis.

Among men with a mutation linked to Lynch syndrome, the researchers estimated their lifetime risk of prostate cancer to be 30 percent, compared to SEER data that puts lifetime risk among the general population at 18 percent. Men aged 20–59 who carried this mutation also faced a higher risk of prostate cancer than the general public, with a hazard ratio of 2.5.

Earlier studies have suggested that Lynch syndrome might play a role in inherited prostate cancer, but studies to date have been controversial.

“It’s been tricky to figure out if prostate cancer is really associated with Lynch syndrome. It’s a very common cancer,” says Raymond. “When you see it occurring in families, it’s difficult to figure out if that’s because it’s associated with Lynch syndrome or just because it’s really common.”

The current study uses a more rigorous statistical analysis and pulls from a larger number of people. This same method has previously linked Lynch syndrome to endometrial cancer and pancreatic cancer.

Results of the study appeared in the Journal of Clinical Oncology.
Andrew Harris, M.D., is fighting graft vs. host disease at C.S. Mott Children’s Hospital for the second time. The first time, he was a teenage patient who received a bone marrow transplant from his sister. Today he is a pediatric oncologist.

Andrew Harris was a physically fit, 19-year-old college student and captain of his semi-professional soccer team. So he was surprised when he found himself having to stop to catch his breath with just a little exertion.

With his shocking diagnosis — acute myeloid leukemia — he began what has become a lifetime battle against the disease. The Ohio native checked into C.S. Mott Children’s Hospital at the University of Michigan, where his treatment began. After chemotherapy treatments did not work, Harris learned he needed a bone marrow transplant. His sister donated the bone marrow, but Harris soon had to tackle another roadblock: graft vs. host disease, in which the transplanted immune cells attacked his body’s cells.

“But all through it, I thought, if I survive this, I want to come back and do something with my life to make this better,” says Harris.

**HARRIS JOINS THE TEAM**

He was true to his word. Harris got his M.D. and now works on the pediatric cancer team at the same hospital where he was treated, with the same doctors who gave him his bone marrow transplant in 1998.

He’s studying the disease he beat: graft vs. host disease, a leading cause of death for kids who have had bone marrow transplants. In summer 2012, the Hyundai Hope on Wheels program provided Harris with a $250,000 grant to study graft vs. host disease in children who have had bone marrow transplants.

A lifetime battle against graft vs. host disease
“We want to see if we can stop this disease in its tracks,” says Harris, who today is father to three children and remains an avid soccer player. “Without this grant, this study would not happen. It is the first national study looking at whether we can predict which kids are likely to get graft vs. host disease.”

**A COMPLICATION TOO COMMON**

Graft vs. host disease often develops in bone marrow transplant patients, and it is deadly.

About half of the people who get bone marrow transplants get graft vs. host disease, and about 30-to-40 percent of them don’t respond well to therapy. Unfortunately, some of those patients die. Those who get immunosuppression drug therapy can face side effects from other life-threatening diseases.

At U-M, Harris and his research partners have collected a biorepository of more than 2,000 blood samples with matched clinical data. By studying the blood biomarkers, they have developed a promising working model for predicting which children are most likely to develop graft vs. host disease. Harris hopes to move this effort to a clinical trial soon, possibly with a pre-emptive trial at U-M.

**A MATHEMATICAL MODEL**

Harris is also working toward a universal mathematical model that can work at other centers. He hopes to collect samples from around the world, and is working on that effort through the Children’s Oncology Group, the world’s largest organization devoted exclusively to childhood and adolescent cancer research. He is also working on establishing a new international consortium dedicated to GVHD research. Just recently, researchers from Thailand visited C.S. Mott Children’s Hospital to learn about how to get involved with the research.

Harris and his research partners have developed a promising working model for predicting which children are most likely to develop graft vs. host disease. Harris hopes to move this effort to a clinical trial soon, possibly with a pre-emptive trial at U-M.

**RESEARCH** Find out about childhood cancer, leukemia and lymphoma and bone marrow transplant studies that could benefit your patients at Colleagues in Care Online at med.umich.edu/cic.

**M-LINE** Refer your patients to pediatric oncologists at Mott or for adult cancer care at the U-M Comprehensive Cancer Center by calling M-LINE at 800-962-3555.

**Andrew Harris, M.D., couldn’t back down from this challenge.**

One of his young patients, Kyle Peterson, was a champion for children’s cancer research as the Michigan Bay of the Year for the Leukemia and Lymphoma Society. Kyle took this role seriously, and asked Dr. Harris to launch his own fundraising campaign, nominating the doctor as Man of the Year for the LLS.

“I wouldn’t be alive without leukemia research, so it is fitting that I work to help raise funds for this incredibly important research,” says Harris, who cared for Kyle as he fought leukemia. Kyle completed therapy more than three years ago and is living a life full of sports, school and friends.

“As a leukemia and bone marrow transplant survivor, and as a children’s cancer doctor and research scientist, I know that researchers can’t do this alone,” Harris says. “We need support for these efforts, if we are going to be able to develop the next generation of cures for blood cancer.”

The contest ended in June, but Harris says he’s not focused on winning the Man of the Year title. He knows the need is constant for funding and just hopes to help contribute to those efforts — and show his patients he cares. More information is available at www.lls.org.

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