THE SKY’S THE LIMIT

New helicopters mark next era for U-M’s Survival Flight

ALSO:
Breast Cancer Stem Cells
Minimally Invasive Valve Replacement
Hepatitis C Treatment
Esophageal Cancer Surgery
**DEMENTIA**

**CONNECTIONS FOR MEMORY LOSS**

New phone line recommends resources to patients

It can be hard for patients with diagnoses that affect memory to get accurate information about their conditions and find resources to help them cope. That’s why the U-M Health System has established a new phone line that connects patients and their families, friends and physicians to memory loss and dementia services.

“We need to do a better job of helping our patients and families find their way,” says Henry Paulson, M.D., Ph.D., director of the Michigan Alzheimer’s Disease Center and professor of neurology at the U-M Medical School. “We don’t want patients, their families and friends to spend a lot of time on routes that don’t lead to answers. The new call center is a great start to solving that problem.”

The U-M Memory Connection is a one-stop resource to learn about and connect to U-M memory loss and dementia services in an easy, non-stressful way. Calls are answered by experts in conditions such as mild cognitive impairment, Alzheimer’s disease, Lewy Body disease, frontotemporal dementia and vascular dementia. They offer advice and information about multiple clinics and departments at U-M, including the Cognitive Disorders Clinic, Geriatric Psychiatry, Neuropsychology, Pharmacology and the Turner Geriatric Clinic.

**CALL**

The U-M Memory Connection line, at 734-936-8803, is answered Monday–Friday, 8:30 a.m.–4 p.m., with the goal of providing service within the next business day or sooner.

On the cover: Survival Flight will soon be retiring its fleet of Bell 430 helicopters and flying in new state-of-the-art American Eurocopter 155s, expanding range and improving safety, speed and patient care.

**A molecular model of amyloid protein fibrils, which are found in the brains of sufferers of Alzheimer’s disease.**

**Alzheimer’s clinical trials**

At the University of Michigan, our clinician-scientists are constantly striving to better understand memory loss, dementia and Alzheimer’s disease through cutting-edge research.

Currently, participants are needed for multiple studies. One study, led by Nancy Barbas, M.D., is focused on whether the drug bapineuzumab is safe and effective in treating Alzheimer’s disease. Another research project, led by Judith Heidebrink, M.D., is examining the usefulness of brain imaging and other biological tests in detecting Alzheimer’s disease and its progression.

For more information about these and other studies or to sign up for research alerts, go to [www.umclinicalstudies.org](http://www.umclinicalstudies.org) and type in Alzheimer’s as the search keyword.
Paul Lee Named New Chair of Ophthalmology

Paul P. Lee, M.D., J.D., a glaucoma specialist, has been appointed chair of Ophthalmology and Visual Sciences at the U-M Medical School and director of the W.K. Kellogg Eye Center, leading a faculty of 85 eye care providers and vision scientists. Dr. Lee holds the F. Bruce Fralick Professorship and maintains a referral practice for complex glaucoma patients.

Most recently, Lee served as vice chairman of Ophthalmology at Duke University and as the James Pitzer Gills III, M.D., and Joy Gills Professor of Ophthalmology. Previously, he was a consultant at RAND and an associate professor at the University of Southern California School of Medicine.

A graduate of the U-M Medical School, Lee completed his ophthalmology residency at the Wilmer Eye Institute of The Johns Hopkins Hospital and his glaucoma fellowship at the Massachusetts Eye and Ear Infirmary.

He has published over 200 papers and serves on the board of directors of the American Board of Ophthalmology, among other organizations.

M-LINE For more information or to refer a patient to Lee or another ophthalmologist at the W.K. Kellogg Eye Center, call M-LINE at 800-962-3555 or visit kellogg.umich.edu

Edward Bove Chairs New Department of Cardiac Surgery

Pediatric cardiac surgeon Edward Bove, M.D., has been appointed chair of the U-M Medical School’s new department of Cardiac Surgery.

During his 26-year career at U-M, Bove and the pediatric surgical team at the University of Michigan Congenital Heart Center have revolutionized surgical approaches to congenital heart defects.

“Dr. Bove has received national and international prominence for his contributions to cardiac surgery,” says James O. Woolliscroft, M.D., dean of the U-M Medical School and Lyle C. Roll Professor of Medicine. “His skill has changed the lives of thousands of families, and his ability to teach and mentor has developed a new generation of bright, proficient cardiac surgeons who are also leaders in the field.”

His patients are primarily children born with serious heart malformations such as hypoplastic left heart syndrome, but increasingly Bove cares for adults who survived their childhood heart defects and require monitoring as adults.

Cardiac surgery at U-M continues to develop new approaches for the treatment of a large spectrum of cardiac diseases, from congenital abnormalities to problems of the elderly. Today, U-M performs more than 2,000 heart operations a year.

M-LINE To refer a patient to Bove or another cardiac surgeon, call M-LINE at 800-962-3555.
THE SKY’S THE LIMIT

New helicopters mark next era for U-M’s Survival Flight

A Survival Flight team: (back row) flight nurses Lori Jacobs, Ben Tung, John Bollen and pilot Tony Eupizi; (front row) flight nurse Joe Mollinger and pilot Paul Shaka.
Three maize and blue Bell 430 helicopters darting across Michigan’s skies have been the icons of the U-M Health System’s Survival Flight program for more than a dozen years.

In their collective service, more than 10,000 critically ill and injured patients and donated organs destined for new hosts have passed through their cabin doors, each a unique story of pain and hope.

Now, the arrival of three new American Eurocopter 155 helicopters later this year marks the beginning of a new era for the 29-year-old Survival Flight program, which was the first medical flight service in Michigan.

They are the first EC155s to be put into emergency medical service in the United States.

ADVANCED FEATURES FOR INCREASED CAPABILITIES

The new helicopters, equipped with advanced avionics and safety features, have nearly 50 percent more cabin space for nurses and patients and all-glass cockpits. A 500-mile range allows them to fly as far as Syracuse, N.Y., or Louisville, Ky., without refueling, while a much shorter warm-up time shaves critical minutes from flights, as does a faster cruising speed.

In the past, picking up a patient in the Upper Peninsula was usually done with Survival Flight’s Citation Encore fixed-wing plane, which requires additional time because patients must be transported to and from an airport by ground.

Robert Doyen’s left arm tells a story. It’s a story of pain, progress and gratitude. From the top of his left shoulder to the middle of his bicep, Doyen proudly displays a tattoo depicting a Survival Flight Bell 430 helicopter and the words “Thank you all.”

“Survival Flight is a big part of why I’m still here today,” he says. “When I was in the hospital, I couldn’t believe how much everyone cared about my recovery.”

One Saturday last June, Doyen went to the local emergency room in Bay City, Mich., because the shoulder pain he had been experiencing for weeks got worse. He underwent an MRI, and when coming out from the machine, his arms erupted in pain. “They felt like they were on fire,” he recalls.

That’s the last thing he remembers until he woke up in the intensive care unit at U-M’s University Hospital two days later. In between, Doyen had been flown to U-M. His C5 and C6 vertebrae had collapsed, pinching his spinal cord and forcing him to undergo a cervical fusion surgery. He woke up Monday unable to walk. After six weeks of rehabilitation, he left the hospital under his own power.

Although his recovery isn’t over, Doyen says his tattoo is a daily reminder of his appreciation for U-M.

Gratitude that’s more than skin deep

Robert Doyen’s tattoo is a tribute to the care he received from Survival Flight and U-M’s University Hospital.
But the greater range of the EC155s allows them to pick up patients as far away as Marquette without having to refuel, and bring them directly to University Hospital or the helipad atop the new C.S. Mott Children’s Hospital and Von Voigtlander Women’s Hospital, which opened in 2011.

“We’re excited about the helicopters’ increased capabilities, but it’s also important to remember that the heart of Survival Flight will remain the same, and by that I mean our dedicated team of highly-skilled flight nurses, pilots, mechanics and communications specialists,” says Mark Lowell, M.D., Survival Flight’s medical director.

SPECIALIZED CARE IN THE SKY

“Survival Flight is about more than just getting a really sick patient from point A to point B,” he adds. “What matters is the highly specialized care our patients receive before, during and after transport.”

During each flight, the helicopter is staffed by two flight nurses who are also licensed as paramedics. The program is the only one in the state to require this high standard of dual certification. The 21 nurses of Survival Flight are cross-trained to treat everyone from newborns to geriatric patients.

“Our specialized capabilities are integrated into a robust Emergency Medicine program and directed by emergency physicians,” Lowell says. “We deliver pediatric and adult patients right to state-of-the-art Level 1 trauma centers.”

Chief flight nurse Donna Robinson says the new helicopters will make a big difference.

“The additional space and seating arrangement in the new helicopters is going to make it easier for flight nurses to stabilize patients,” she says. “And their increased speed is going to help us reduce the time it takes to get a patient to the treatment they need.”

What Sets Survival Flight Apart?

- Survival Flight staff provide specialized care in areas such as:
  - patients with cardiac assist devices
  - neonatal care
  - pediatric cardiology
  - advanced ventilation support (including nitric oxide therapy)
- Flight nurses are dual-certified as paramedics
- Nurses undergo quarterly surgical skills training
- Medical staff are UMHS employees and dedicated to the program full-time
- Additional specialists are available to assist with complex transports 24/7
- Staff maintains direct physician to physician contact

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**ONLINE** Learn more about the Survival Flight program on Colleagues in Care Online at med.umich.edu/cic
Perilous Approach

Anti-angiogenic drugs promote growth of breast cancer stem cells

Cancer treatments designed to block the growth of blood vessels were found to increase the number of cancer stem cells in breast tumors in mice, suggesting a possible explanation for why these drugs don’t lead to longer survival, according to a study by researchers at the U-M Comprehensive Cancer Center.

While anti-angiogenic drugs do shrink tumors and slow the time until the cancer progresses, the effect does not last, and the cancer eventually regrows and spreads.

“This study provides an explanation for the clinical trial results demonstrating that in women with breast cancer, anti-angiogenic agents such as Avastin delay the time to tumor recurrence but do not affect patient survival,” says study author Max S. Wicha, M.D., director of the U-M Comprehensive Cancer Center.

The researchers treated mice with breast cancer using the anti-angiogenesis drugs Avastin (bevacizumab) and Sutent (sunitinib). The researchers found that tumors treated with these drugs developed more cancer stem cells, which fuel a cancer’s growth and spread and are often resistant to standard treatment.

The researchers found the increase in cancer stem cells was due to hypoxia. They were also able to determine the specific pathways involved in hypoxia that activate the cancer stem cells.

The U.S. Food and Drug Administration recently revoked approval of Avastin for treating breast cancer. The reversal was in response to clinical trials showing that the drug’s benefit was short-lived, with breast cancer patients quickly relapsing and the cancer becoming more invasive and metastatic.

The current study, published in the Proceedings of the National Academy of Sciences, suggests the possibility of combining anti-angiogenesis drugs with a cancer stem cell inhibitor to enhance the benefit of this treatment. The researchers are testing this approach in mice, and preliminary data looks promising.

**ARTICLE** Get a link to the full text of the Proceedings of the National Academy of Sciences journal article or find out about current breast cancer and cancer stem cell clinical studies that may benefit your patients on Colleagues in Care Online at med.umich.edu/cic

Max S. Wicha, M.D., is director of the U-M Comprehensive Cancer Center.

Breast cancer stem cells in a region of hypoxia in a mouse treated with the anti-angiogenic drug sunitinib (Sutent).

About cancer stem cell research

Cancer stem cells are adult stem cells found in malignant tumors. They are believed to represent 1 percent to 3 percent of all the cells within a tumor but are the only cells capable of regenerating new cancer cells. U-M researchers believe current cancer treatments often become ineffective because they do not kill the cancer stem cells. The key to future treatments is to develop drugs that target and kill these cells.

Stem cells have now been identified in most cancer types. U-M researchers were the first to identify cancer stem cells in breast, pancreatic, head and neck and ovarian cancers and are currently working in virtually every cancer type. Clinical trials targeting cancer stem cells are ongoing in several cancer types, including breast cancer, pancreatic cancer and leukemia.
Minimally invasive aortic valve replacement a new option for previously inoperable patients

Each year, about 100,000 American adults are diagnosed with aortic stenosis, but one-third of patients, because of age or frail health, are considered too high-risk for traditional valve replacement surgery. Without a valve replacement, half of patients with severe aortic stenosis will not survive more than an average of two years after symptoms begin.

“Patients who do not receive an aortic valve replacement have few effective, long-term treatment options to prevent or delay their disease progression,” says cardiac surgeon G. Michael Deeb, M.D., director of U-M’s multidisciplinary Aortic Clinic and the Herbert Sloan Collegiate Professor of Surgery at the U-M Medical School.

TWO OPTIONS

The U-M Cardiovascular Center is among a select group of U.S. hospitals performing transcatheter aortic valve replacement, or TAVR, to replace a patient’s diseased aortic valve without heart bypass or open heart surgery. It is also referred to as TAVI, or transcatheter aortic valve implantation.

U-M surgeons and interventional cardiologists now offer comprehensive options to treat aortic stenosis, including the new FDA-approved Edwards SAPIEN Heart Valve and — through a clinical trial — Medtronic’s CoreValve prosthesis. The procedures allow access to the aortic valve percutaneously, usually through a femoral artery, rather than through open surgery.

“This gives physicians the tools to take care of patients who we were not able to take care of before,” says interventional cardiologist Stanley Chetcuti, M.D., director of the Cardiac Catheterization Lab at the U-M Cardiovascular Center.
Back in the swim

Michael Baker, 53, has a new view of what summers in Michigan can be like. Fishing and boating near South Haven will be a stark contrast to what life had been like living with severe aortic stenosis.

Because of the limited blood flow from his aorta, he would get out of breath tying his shoes, and he struggled to make his bed. But the former factory worker was among the one-third of aortic stenosis patients who cannot tolerate open-heart surgery to replace the aortic valve, and two balloon valvuloplasties produced limited results.

A team at the U-M Cardiovascular Center implanted Baker with the new FDA-approved Edwards SAPIEN heart valve, a transcatheter aortic valve replacement option.

“I can already get around better,” says Baker, whose Edwards device was implanted on January 6. He was discharged in four days. He said he misses waterskiing and would love to be behind a speedboat again, “but I think I’ll start with swimming first.”

RESEARCH CONTINUES
The Edwards valve is the only TAVR therapy approved for use in the United States, but some aortic stenosis patients at U-M are also being enrolled in the Medtronic CoreValve U.S. Pivotal trial.

“Studies such as the PARTNER trial with the Edwards valve have substantiated the benefit of TAVR to extend lives,” says U-M cardiac surgeon Himanshu Patel, M.D., associate professor of surgery.

Research published in 2010 in the New England Journal of Medicine showed that the Edwards SAPIEN valve had a significantly lower mortality rate than standard medical therapy. Seven out of every 10 inoperable patients were alive one year after the procedure, compared with five out of every 10 patients who did not receive a new valve. Patients treated with the Edwards SAPIEN valve also had improved heart function and improved quality of life at one year, as compared with the control group.

QUALITY OF LIFE IS KEY
The goal of aortic valve replacement for these high-risk patients is not only to improve their survival but also to enhance their lives.

“For most of these patients, their quality of life is quite impaired because of severe aortic valve disease. They physically cannot do the things that they want to do,” says interventional cardiologist Paul Michael Grossman, M.D., associate professor of Internal Medicine at U-M and director of the Cardiac Catheterization Laboratory at the VA Ann Arbor Healthcare System.

“We’re very hopeful that this technology will offer them the opportunity to get back some of the quality of life that they probably have lost in the last several years,” he says. “In addition to that, certainly the success will be measured in our ability to collaborate and to learn as surgeons and interventional cardiologists work together.”

The U-M aortic program, part of the nationally ranked heart and heart surgery programs at the U-M Cardiovascular Center, performs more than 500 surgical valve procedures a year — more than any other Michigan hospital.

This gives physicians the tools to take care of patients who we were not able to take care of before.

Stanley Chetcuti, M.D.
A new combination of investigational drugs successfully suppressed hepatitis C genotype 1 infection in a high percentage of patients who had not responded to previous treatment, according to research led by a U-M hepatologist.

The work of Anna S. Lok, M.D., was published in January in the New England Journal of Medicine. The study focused on hepatitis C genotype 1, which is predominant in the United States and is the most difficult to treat.

In this pilot study, patients with hepatitis C genotype 1 infection who had not responded to previous treatment with PEG-interferon alfa and ribavirin were given a combination of two investigational direct-acting antiviral agents (daclatasvir and asunaprevir) alone, or were given these two antiviral agents along with PEG-interferon alfa-2a and ribavirin.

All the patients saw their hepatitis C viral load drop rapidly, says Lok, professor of Internal Medicine in the Division of Gastroenterology at the U-M Medical School and lead author of the study.

All 10 patients given the four-drug treatment — two direct-acting antiviral agents (daclatasvir and asunaprevir) that block the NS3 and NS5A regions of the hepatitis C virus, plus PEG-interferon alfa and ribavirin — had sustained virologic response with undetectable virus at the end of treatment and at 12 weeks after stopping treatment. Four of the 11 patients given only the two direct-acting antiviral agents also achieved sustained virologic response.

“The two recently approved hepatitis C drugs — telaprevir or boceprevir — combined with PEG-interferon alfa and ribavirin, have limited success in patients who have not responded to previous treatment with PEG-interferon alfa and ribavirin. There is a necessity for new combination regimens that can increase response rates in that population,” says Lok, who also is director of Clinical Hepatology at U-M.

“The high rate of sustained virologic response in patients who received the four-drug regimen is very exciting. Although only four of 11 patients given the two direct-acting antiviral agents only achieved sustained virologic response, this is the first study to show that sustained virologic response can be achieved without the use of interferon or ribavirin. These data are very encouraging because PEG-interferon alfa and ribavirin are associated with many side effects and many patients with hepatitis C choose not to receive treatment for fear that they cannot tolerate those drugs.”

The study was funded by Bristol-Myers Squibb.

“Overall, these results suggest that further research into combinations of direct-acting antiviral agents, with or without PEG-interferon and ribavirin, should be encouraged,” Lok says.
Physicians are seeing more patients like Jack Selby, a 68-year-old retiree living in Lansing who had suffered from heartburn all of his life. Selby thought over-the-counter antacids had solved his problem, but they were only masking Barrett’s esophagus, which frequently leads to adenocarcinoma, a form of esophageal cancer.

The incidence of esophageal adenocarcinoma has increased by 350 percent over the last decade, making it the most rapidly increasing malignancy among white males.

“In patients who have ongoing gastro-esophageal reflux, the backwash of acid from the stomach into the esophagus for years and years can expose the lining of the esophagus to this bombardment of acid,” says Mark Orringer, M.D., professor of Surgery in the Section of Thoracic Surgery at the U-M Medical School. “The esophagus was never meant to hold up to acid, and this can have significant implications.”

Selby required an esophagectomy for Barrett’s mucosa and early stage esophageal cancer.

He was treated at U-M by a team led by Orringer. U-M is considered a national leader in performing a type of esophagectomy — transhiatal esophagectomy, or THE — which is less invasive than conventional esophagectomy requiring a thoracotomy.

U-M has performed more than 3,000 of these procedures. Compared with data compiled in the Society of Thoracic Surgeons National Database, U-M has a substantially better 30-day patient survival rate with fewer complications and a shorter length of hospital stay.

“Many years ago, the esophagectomy operation, the traditional operation done through the chest, carried upward of a 20 percent mortality rate,” says Orringer. “With the advent and the refinement of the transhiatal esophagectomy, the death rate from the procedure is around 1 percent at U-M.”

Transhiatal esophagectomy was developed and refined at U-M and involves removing the diseased esophagus and rebuilding it. The procedure is performed through an incision in the neck and the abdomen and eliminates the need to open the chest.

“I had a transhiatal esophagectomy done about 15 months ago and I’m doing great now,” says Selby, who weighed 260 before the esophagectomy. “I’ve lost about 70 pounds, have lots of energy and I feel very good.”

Complications within 30 days after operation

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<thead>
<tr>
<th>Complication</th>
<th>UM</th>
<th>STS Average</th>
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<tr>
<td>Death</td>
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<tr>
<td>Blood transfusion</td>
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<td>10%</td>
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<tr>
<td>Mechanical ventilator</td>
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<tr>
<td>Pneumonia</td>
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<td>Poor lung function</td>
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Complication rates are much lower at U-M than the Society of Thoracic Surgeons’ average.

Mark B. Orringer, M.D., is head of the Section of Thoracic Surgery.
With M-LINE, you can reach more than 3,000 doctors and 26 departments, 24 hours a day. Each service representative has the knowledge and expertise to guide you where you need to go and to what you need to know.

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