About 2.5 million Americans live with atrial fibrillation. It is a leading cause of hospital admission due to arrhythmia, and a leading cause of stroke. The Cardiac Electrophysiology Service at the University of Michigan Health System focuses on the diagnosis and treatment of abnormal heart rhythms. Patients come to the facility from all over the world.

With the opening of the U-M's Cardiovascular Center in 2007, the Electrophysiology Service more than doubled its capacity. “We were able to reduce our waiting period from 4-6 months to several weeks – a very positive impact,” says Hakan Oral, M.D., associate professor of internal medicine at Michigan, and director of the Service. The CVC’s patient coordination centers have streamlined everything from scheduling to post-procedure care. “Patients can reach us 24/7,” he says.

For cardiologists in communities all over Michigan and in surrounding states, the team at U-M can be regarded as an excellent EP resource – one with a full array of services, state-of-the-art technology and staff that are happy to help or offer an opinion, often at a moment’s notice.

The goal of the group is clear: to work in alliance with referring physicians – PCPs and cardiologists alike – to provide subspecialty advice and care for their patients – and then for the referring physicians to manage their patients in the long term, in their own communities.

A major research and clinical focus of the U-M electrophysiology group is atrial fibrillation. Says Oral, “This is a very complex arrhythmia and its mechanisms are multifactorial. Drug treatment of atrial fibrillation has not been very effective. Drugs do not appear to have high efficacy in maintaining normal rhythm. There may also be patient concerns that negatively impact compliance.”

This has led to the development of non-pharmacological treatment studies of atrial fibrillation. Today, the U-M Electrophysiology Service is a pioneer in the use of catheter ablation in the treatment of atrial fibrillation. More than 2,500 ablation procedures have been performed to treat atrial fibrillation at U-M in the last several years. “Today, we can successfully treat the vast majority of patients with atrial fibrillation,” says Oral. “This is very good news.”

David Pinsky, M.D., the J. Griswold Ruth, M.D., and Margery Hopkins Ruth Professor of Internal Medicine, and scientific director of the Cardiovascular Center at U-M, adds “Not only are we developing the techniques to manage and treat arrhythmias, but also techniques to make these procedures safer.”

Last winter, a team of 25 basic scientists was recruited to Michigan from the SUNY Upstate Medical University in Syracuse, N.Y. There's no disputing it was a coup for U-M, and for medical science. The team's research focus dovetails with that of the CVC's clinical arrhythmia group, exploring why people get arrhythmia, how these arrhythmias propagate, how they initiate, and also how best to image or map them so they can be ablated effectively and efficiently.

Clinical trials are another option for the patients of referring physicians. (Learn more about these trials at www.engage.org.)

continued on back page
Blayney elected ASCO president for 2009-2010 term

Douglas W. Blayney, MD, medical director of the University of Michigan Comprehensive Cancer Center, was elected president of the American Society of Clinical Oncology for a one-year term beginning in June 2009. He will take office as president-elect during ASCO’s 44th Annual Meeting in Chicago this June.

ASCO is the world’s leading professional organization representing physicians who care for people with cancer. With more than 25,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals.

Blayney, an internationally recognized expert in oncology quality, currently serves as professor of internal medicine at the University of Michigan Medical School. He is an active clinician in the Adult Hematology and Breast Care Clinics.

“I am honored to have been elected to serve as ASCO president, following in the very large footsteps of those who have served before me,” Blayney said. “ASCO is an exceptional organization and I look forward to working alongside my esteemed colleagues on the board of directors to continue improving the care and treatment of those living with cancer.”

Since joining ASCO in 1983, Blayney has demonstrated a comprehensive record of service to the society. He has served on the ASCO Board of Directors and The ASCO Cancer Foundation Board of Directors. Blayney has also been a member of two ASCO journals, and currently serves as editor in chief of the Journal of Oncology Practice.

In addition to his work with ASCO, Blayney is an active member of the American Society of Hematology and the Southwest Oncology Group. He currently serves on the Board of Directors of the National Comprehensive Cancer Network.

Motor neuron disease is a rare, devastating illness in which nerve cells that carry brain signals to muscles gradually deteriorate. One form of it, Lou Gehrig’s disease or ALS (amyotrophic lateral sclerosis), is familiar to the public in the lives of scientists Stephen Hawking and Morrie Schwartz, about whom Mitch Albom’s “Tuesdays with Morrie” was written.

For most MND patients, the cause is unknown. Figuring out why these people develop the disease, which causes muscles to weaken, atrophy and cease to function, is an important step in developing therapies to treat or prevent motor neuron disease.

Now a team of University of Michigan scientists has gotten a step closer:

They have discovered mutations in one key gene (neuropathy target esterase, or NTE) that cause a previously unknown type of inherited motor neuron disease.

The discovery paves the way for better diagnosis and research on treatments.

Most intriguing, the scientists found the mutations caused changes in a protein already known to be involved when people develop neurologic disorders as a result of exposure to toxic organophosphates – chemicals commonly used in solvents and insecticides and also as “nerve gas” agents. This discovery points to a new lead in the search to understand MND.

“We speculate there may be gene-environment interactions that cause some forms of motor neuron disease,” says John K. Fink, M.D., professor of neurology at the U-M Medical School and senior author of the new study, which appears in the March issue of the American Journal of Human Genetics. He also is a researcher at the VA Ann Arbor Healthcare System.

“Our findings support the possibility that toxic organophosphates contribute to motor neuron disease in genetically vulnerable people,” says Fink. He believes the results suggest that altered activity of the gene found in patients in the study may also contribute to other motor neuron disorders, possibly including ALS.

Motor neuron disease affects five in every 100,000 people.

The findings are an exciting first step in uncovering a possible link between the environment and motor neuron disease, says Shirley Rainier, a research assistant professor at the U-M Department of Neurology and the first author of the study. “Why does one person in a family get it, and another doesn’t?”

Piecing together a puzzle

In the 1930s, an estimated 50,000 people in the United States became lame or otherwise neurologically affected by neurotoxic organophosphates when they drank a contaminated batch of “ginger jake,” an alcohol-containing potion that was legal during Prohibition.

Ginger jake suppliers substituted a lubricating oil for the oil usually used, castor bean oil, when castor bean prices were high. People in the United States became lame or otherwise neurologically affected by neurotoxic organophosphates when they drank a contaminated batch of “ginger jake,” an alcohol-containing potion that was legal during Prohibition.

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More recently, there have been incidents in Fiji, India and Africa when accidental consumption of oils containing neurotoxic organophosphates (instead of cooking oil) caused death or nerve damage for tens of thousands of people. Although scientists don’t yet know the exact manner in which toxic organophosphate exposure leads to progressive and permanent nerve damage, they have learned that this process involves disturbance of an enzyme, NTE, contained within nerves.

Fink examined members of two families who had progressive weakness and spasticity (tightness) in their legs, as well as muscle atrophy in their hands, shins and feet. James Albers, M.D., Ph.D., a U-M professor of neurology and an expert in neuromuscular disorders, studied nerve and motor function. Rainier performed genetic studies and determined that the gene for the condition was on a region of chromosome 19.

Mark Leppert, Ph.D., co-chair of human genetics at the University of Utah, and his team performed genetic analysis that confirmed this location and excluded other areas in the genome. Among the many genes in this region of chromosome 19, one gene stood out as particularly likely: the gene that encodes for NTE. Because of its known role in organophosphate-induced neurological disease, the NTE gene was considered an important candidate gene and was studied immediately.

Analysis showed that the affected people in each family had NTE gene mutations. These mutations altered a critical part of the NTE protein called the esterase domain. Fink has named the inherited condition “NTE motor neuron disease.”

It begins in childhood and progresses slowly, with symptoms of weakness and spasticity in the legs and muscle atrophy in the hands and lower legs.

Next, Fink and his team want to learn if mutations in the NTE gene happen in other types of motor neuron disease such as ALS, and if the mutations make a person more vulnerable to neurological damage from organophosphate exposure. Fink’s lab is currently using fruit flies as a model to study the NTE mutations, with the goal of finding treatments for people with motor neuron disease.

Other authors include Melanie Bui, Erin Mark, Donald Thomas, Debra Tokarz, Lei Ming, Colin Delaney, and James W. Albers, M.D., Ph.D., of the U-M Department of Neurology; Rudy J. Richardson, D.Sc., associate professor of neurology at U-M Medical School and Dow Professor of Toxicology in Environmental Health Sciences at the U-M School of Public Health; and Nori Matsunami, Jeff Stevens, Hilary Coon and Mark Leppert, Ph.D. of the University of Utah.

A patent application for the use of the NTE gene and protein sequence for diagnosis and treatment is pending. The University of Michigan, through its Office of Technology Transfer, is actively seeking a licensing partner to help bring the technology to market.


**FIND MORE ON THE WEB**

www.med.umich.edu/neurology/

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**KEY POINTS**

- University of Michigan scientists have discovered mutations in one gene, neuropathy target esterase or NTE, that cause a previously unknown type of inherited motor neuron disease. This information advances understanding of the causes of motor neuron disease and improves prospects for better diagnosis and treatments.

- People with this form of inherited motor neuron disease have abnormalities in the same protein (NTE) that is involved in nerve injury caused by exposure to harmful amounts of organophosphates. The results raise the possibility that healthy people may have gene variants that make them vulnerable to nerve damage if exposed to these chemicals, which include insecticides. Organophosphate exposure has been raised as a possible cause of the increased incidence of ALS among Gulf War veterans.

- The study results also suggest that alterations in the same NTE gene may contribute to other motor neuron disorders, including ALS.
EXPLORING THE BODY’S “DARK CONTINENT”: NEW TECHNOLOGY AT U-M TREATS GI DISORDERS WITHOUT SURGERY

U-M now using double balloon endoscopy system to diagnose and treat small intestine disorders

“Using a scope instead of a scalpel to examine, as well as treat problems in the small intestine, will greatly improve the quality of life for patients and significantly reduce the number of invasive surgical procedures needed to treat small bowel disorders,” she notes.

Before technology like the double balloon endoscopy was available, the small intestine was an uncharted and often unseen territory within the body. Once referred to as the body’s “Dark Continent,” physicians previously were unable to access the small intestine without surgery – even colonoscopy and traditional endoscopy procedures were unable to provide a clear view of the small intestine.

Fisher’s non-invasive exploration of the small intestine began in 2001 when UMHS began using capsule endoscopy – a wireless, pill-size camera capable of producing 60,000 digital images of the digestive tract when swallowed by a patient. From the teeth to the colon, the tiny capsule can record its entire journey through the digestive tract – 25 feet in all – while closely examining the 15 to 18 feet of the small bowel.

Since the program began, more than 1,000 patients have used capsule endoscopy at UMHS.

“The capsule endoscopy system was revolutionary in the diagnosis of small bowel disorders,” says Fisher, director of U-M’s Capsule Endoscopy Program. “It’s allowed us to finally gain a clear view of polyps and other disorders in the small intestine such as bleeding..."
or Crohn’s disease. The challenge, however, was that we could see the problems, but couldn’t easily intervene to provide treatment. Surgery was the only option.”

Now, with the use of double balloon endoscopy, Fisher has the ability to diagnose gastrointestinal disorders in the small intestine, as well as cauterize lesions and perform biopsies of inflammatory lesions like Crohn’s ulcers, or potentially-cancerous tumors. It currently is the only technology available that allows for therapeutic intervention of the small intestine, says Fisher.

The double balloon endoscopy system features two balloons, attached to the end of a scope similar to a colonoscope used for colonoscopies, and the other attached to an overtube, which slides over the endoscope. Once inflated, the balloons hold onto the sides of the bowel and “shorten” the small bowel by pleating it over the endoscope. This allows the scope to advance through the bowel and permits full visualization and therapeutic intervention in the small intestine.

The procedure, typically done in a few hours under conscious sedation, can be performed on adults of any age. Most often, the scope is inserted through the mouth, although Fisher says the system is designed to be passed through the colon, too. Before undergoing a double balloon endoscopy, patients most often will need to have a colonoscopy and upper endoscopy, followed by a capsule endoscopy.

To speak to Dr. Fisher about this new technology, call M-LINE at 1-800-962-3555.

FOR MORE INFORMATION
about the double balloon endoscopy system, visit www.fujinonendoscopy.com

KEY POINTS
• Double balloon endoscopy is a great advancement for patients. Instead of invasive surgeries, Dr. Fisher can search hard to reach places in the small intestine using a scope, and perform interventions concurrently.
• The University of Michigan Health System is at the forefront of making these searches of the small intestine as minimally invasive for the patient as possible. In 2001, gastroenterologists began using capsule endoscopy and have seen approximately 1,000 patients.
• The double balloon procedure allows U-M gastroenterologists to not just see, but treat and intervene on the spot when lesions, tumors or ulcers are found.
BLADDER AND PELVIC FLOOR DYSFUNCTION

Treating urinary problems with sacral nerve stimulation

Proper urinary function, fecal elimination, genital response and the workings of the reproductive organs are made possible by the delicate choreography of muscles and organs in the pelvic area. The sacral nerves help to maintain healthy bladder and pelvic floor activity by sending directions to the brain via electrical impulses. When surgery, infections, genetic issues or childbirth upset the sacral nerves, they can begin to send distorted messages to the brain, resulting in bladder and pelvic floor dysfunction. Typical symptoms include urinary frequency, loss of urinary control or pelvic pain.

Bladder and pelvic floor dysfunction is often treated successfully with medication or behavioral modification. However, for millions of patients in the United States, these treatments are ineffective and quality of life is significantly diminished. In these cases, sacral nerve stimulation should be considered.

It works through an implanted device that transmits gentle but continuous stimulation over the sacral nerve. Nerve-to-brain communications are thus normalized and the symptoms of bladder and pelvic floor dysfunction are improved or even completely eliminated.

Other ailments that may be positively impacted by sacral nerve stimulation include irritable bowel syndrome, interstitial cystitis and urinary retention.

Safe, Effective, Life-Changing

This FDA-approved treatment is safe and effective and has been widely used since 1997. At the University of Michigan Department of Urology, over 30 of these procedures have been performed since the procedure was introduced in October 2007, with a success rate of 80 percent.

“Most patient’s resume prior activities within two weeks with a significant reduction in their urinary symptoms and improved quality of life,” according to Humphrey O. Atiemo, M.D.
Sacral nerve stimulation is a minimally invasive, two-stage process and can be performed in an outpatient setting with local anesthetic and sedation. A one-day recovery period after each stage is typical.

Stage 1 — Test Stimulator

Because sacral nerve stimulation is not effective for all individuals, a temporary stimulator is used to test the patient’s response over a two-week period. Two small incisions are made over the sacrum and in the upper buttock. A tiny electrode is inserted through the first incision and is implanted near the sacral nerve. The electrode is connected to a thin lead extending from the second incision. This lead is connected to a temporary pager-size stimulator worn on the waistband. The patient controls the intensity of the stimulation via a power dial on the stimulation unit.

With the test stimulator, pre- and post-test voiding diaries can be compared as a way to determine the level of improvement that may be expected. If the patient’s symptoms improve by 5 percent or more, the implantation of a permanent stimulator is recommended. If the test does not yield satisfactory results, the electrode and lead are removed and the incisions are closed. At this point, we work with you and the patient to explore other therapies.

Stage 2 — Permanent Stimulator

Assuming a successful test and the patient’s willingness to proceed, the temporary lead is removed. Using the same incision, a permanent stimulator about the size of a silver dollar is placed under the fat layer in the upper buttock. Because the unit cannot be seen and is not obvious to the touch, the patient can resume all normal activities. A remote device is used to make program modifications to the stimulator as needed.

If, for any reason, the patient chooses to discontinue the therapy, sacral nerve stimulation is completely reversible.

FOR MORE INFORMATION
To learn more about Sacral Nerve Stimulation or to refer a patient to the U-M Urology Department, please call M-LINE at 1-800-962-3555.

Most patients resume prior activities within two weeks with a significant reduction in their urinary symptoms and improved quality of life.
Electrical cardioversion, implantation of pacemakers and automatic defibrillators, AV node ablation, catheter ablation, open-heart surgery… Michigan’s Electrophysiology Service offers the latest, safest and best treatments for all types of heart arrhythmias. Most patients stay for just one night before returning home to their own PCPs and cardiologists.

Pinsky’s message to referring physicians: “We will make it easy, we will help your patients, and we will return them to you for further care.”

At the 2008 conference of the Heart Rhythm Society – to be held May 14-17 at the Moscone Center in San Francisco – the University of Michigan Health System will be well represented. Here are just a few of the U-M physicians who will be presenting at the conference this year:

**Thursday, May 15**, Hakan Oral, M.D., will chair a session titled “Atrial Flutter and Tachycardias Following AF Ablation.” Later that day, Frank M. Bogun, M.D., will present “Radiofrequency Ablation of Frequent, Idiopathic Premature Ventricular Complexes: Comparison with a Control Group Without Intervention.”

**Friday, May 16**, Jerome Kalifa, M.D., of the U-M’s Center for Arrhythmias Research, will present “Endoscopic Fluorescence Mapping of the Left Atrium: A Novel Experimental Approach for High Resolution Endocardial Mapping in the Intact Heart.”

**For more information** about the conference [www.hrsonline.org/](http://www.hrsonline.org/) sessions/HR2008