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Fall 2009

EMORY | health

PATIENT CARE, RESEARCH, AND EDUCATION FROM
THE **WOODRUFF HEALTH SCIENCES CENTER**

FINDING NORMAL

Emory's new hope for restoring brains after injury 2

Emory Health

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FROM THE EXECUTIVE VP

Out of the silos

The debate on health care has caught the attention of policy groups, insurers, and patients alike. As lawmakers grapple with the best approaches to transform our current system, academic health centers like the Woodruff Health Sciences Center at Emory already have been busy exploring and testing models and initiatives to overhaul health care.

As we refocus health care from the treatment of diseases to the treatment of individuals, and the management of health through prevention and wellness, one truth continues to emerge in successful models of health care delivery: interactive teams that span disciplines, specialties, and professions are vital to the process. When we break out of clinical specialty and academic silos, we discover a wide range of perspectives that can serve complementary and synergistic roles in providing the highest performance—in not only delivering health care but also educating students and conducting research.

Take, for example, Emory's approach in discovering progesterone for treating traumatic brain injury (TBI). This first new potential treatment in 30 years results from years of work by one persistent researcher, Don Stein, and a team of basic scientists, emergency medicine doctors, statisticians, neurosurgeons, trauma surgeons, and other colleagues at Emory. The team approach to validate what may be the first-ever effective treatment for TBI is now spreading across the United States to 17 trauma centers that are participating in a clinical trial led by Emory and funded by the NIH.

In the Emory ALS Center, the multidisciplinary team approach extends from the clinic to the research lab. Patients with amyotrophic lateral sclerosis attend a clinic where the physicians, nurses, social workers, respiratory therapists, nutritionists, and others all come to them. The center's team focuses on increasing independence and quality of life for those with ALS. The team puts the patient at the center of the experience, as the most effective way to manage a person's health. And behind the scenes, Emory researchers—including neurologists, geneticists, and biochemists—are looking for the breakthrough to cure this devastating disease.

Throughout this issue, you'll read over and over again of successful examples of health care that are working because of multidisciplinary and interdisciplinary approaches—from developing a treatment for TBI to improving the quality of life for people with ALS, from finding the earliest indicators of Parkinson's disease to Emory's comprehensive approach to heart failure and cancer. These stories confirm that academic health centers like the WHSC, with their broad range of services and disciplines, are the natural leaders in transforming health and healing—by working together.

Fred Sanfilippo, MD, PhD

Please share your feedback at evphafeedback@emory.edu.

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PATIENT CARE, RESEARCH, AND EDUCATION FROM THE **WOODRUFF HEALTH SCIENCES CENTER**

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ALS is like a lit candle: it melts your nerves and leaves your body a pile of wax.
–Tuesdays with Morrie, by Mitch Albom

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What do you think? ***Emory Health*** welcomes your comments—pro or con—about topics and issues covered in this magazine. Please send comments, letters to the editor, address changes, and other correspondence to ***Emory Health***, 1440 Clifton Road, 150M, Atlanta, GA 30322; email rhonda.mullen@emory.edu; or call 404-727-8166.

HIDDEN *in plain sight*

Progesterone offers the hope of being the first new treatment for traumatic brain injury in 30 years and the first-ever safe and effective treatment. **It was there, under our noses, the whole time.**

By Sylvia Wrobel • Phottography by Jack Kearse

The progesterone story began as a scientific puzzle, obstinately pursued by a stubborn Emory neuroscientist.

What caused some female rats to survive brain injuries virtually unscathed while males with similar injuries died or had severe problems finding their way around once familiar mazes?

Many colleagues thought Don Stein was too obsessed with a potentially career-killing research dead-end. Two Emory doctors—Art Kellermann, then head of emergency medicine, and David Wright, an ER clinician and researcher—looked at Stein's findings in rats and thought that maybe, just maybe, the scientist was on to something that could change the too often dismal outcomes of the traumatic brain injury (TBI) patients they saw in the emergency department. Other Emory doctors and researchers stepped up to help them find out, in a clinical trial funded by the NIH, conducted from 2001 to 2005 at Grady Memorial Hospital, where TBI patients arrive with heartbreaking regularity.

This winter, based on the promising results of that study, a second NIH clinical trial of the progesterone treatment developed at Emory will begin at 17 trauma centers across the United States, including at Grady. Headed by Wright, the study will enroll 1,140 TBI patients. If progesterone works as well as it did in the smaller trial, clinicians will have the first new treatment in 30 years, and the first-ever safe and effective treatment, for TBI. Progesterone could transform the way doctors treat head injury, not only in emergency rooms but also at the site of car wrecks or bombings and explosions in Iraq and Afghanistan, where TBI has become the signature wound.

The final answer could take five years, but hope of an effective treatment for TBI no longer sounds so crazy. Ask the NIH. Or, just ask **Marc Baskett** (left) and his parents.

The journey of progesterone as a treatment for traumatic brain injury began in Don Stein's lab decades ago. Turns out, he was onto something.

Coming to say goodbye

Three weeks before high school graduation, everything went dark for Baskett. He was riding in the car with his girlfriend near his hometown of Commerce, Ga. She had taken her eye off the road for an instant, then looked up to see a truck filling the windshield, crushing the passenger side of the car so completely that emergency rescuers at first thought Baskett had been thrown from the vehicle. Unconscious, unresponsive, he was airlifted to Grady, the region's only level-1 trauma center, some 70 miles away.

There, a shifting phalanx of doctors began to treat the 19-year-old's multiple injuries: damaged organs, cuts (650 stitches in his right arm alone), a metal rod through his knee into his shattered right femur, another rod to hold together his crushed ankle. But no effective treatment existed for his most devastating injury, that to his brain. Unable to open his eyes or respond to painful stimuli, Baskett scored 4 on the 15-point Glasgow Modified Coma Scale. He had almost no brain activity.

"Jeff and I believed we had come to Grady to say goodbye to our boy," says his mother, Johanna Baskett. "And not just us." It seemed as if half of the small town of Commerce had closed up shop and followed the popular young athlete to Grady. When a young woman asked to talk to the family about a study Emory was conducting, a dozen of Baskett's coaches and teachers joined them.

The study coordinator explained that the researchers did not know if progesterone could do for humans what it had done in lab rats. In fact, ProTECT (progesterone for traumatic brain injury–experimental clinical treatment) was a pilot study designed primarily to evaluate whether progesterone could be safely and reliably administered intravenously. The 100 participating patients all would receive state-of-the-art care; 80 would be randomly chosen to also receive progesterone. The cluster of family and friends agreed that the Basketts should sign. They had nothing to lose.

EMORY UNIVERSITY PHOTO

Emergency medicine physician David Wright is leading the national research trial tor progesterone, which patients will receive within four hours of traumatic brain injury.

Within minutes, a vial was added to the drip of medicines already flowing through Baskett's veins. Because the study was double-blinded, neither his family nor the researchers knew whether the numbered vial contained progesterone or saline, a standard research method to make sure researchers do not unconsciously score patients in the experimental group as doing better. As the researchers would find out when the data were analyzed, Baskett was one of the lucky ones.

For three days, a steady infusion of natural, sterilized, human-grade progesterone bathed Baskett's brain cells. Some cells had been killed outright by the impact and by the swelling that began even while paramedics rushed him to Grady. These cells would not revive (but other cells would take over some of their tasks). The progesterone treatment was intended to intervene in the post-injury destruction of injured cells or in further damaging healthy cells.

On impact, Baskett's brain had slammed back and forth inside the inflexible skull. Injured nerve cells began releasing free radicals, toxic by-products that punched holes in the walls of nearby still-functioning cells. Other brain cells called glia worked to mop up dead or dying cells, only to collapse and die themselves, releasing yet more toxins. Hemorrhages of tiny vessels freed blood cells into the brain, and immune cells struggled to repel these unfamiliar invaders, causing inflammation and then more swelling.

According to Stein's animal studies, progesterone should slow these processes down. And something appeared to be working for Baskett. After 2-1/2 weeks, he emerged from his coma, confused by the tubes, the blur of unfamiliar and familiar faces, but speaking, trying to smile. He had missed his high school graduation; his teachers brought his diploma to him. After three weeks, he was transferred to Children's Healthcare of Atlanta for rehabilitation.

Given the usual outcomes, he could expect to be in the hospital for at least a year. But Baskett's case was proving to be anything but usual. He left the hospital four weeks later, returning only to participate in a rehab program with a dozen others who had suffered car crashes, falls, a horseback riding accident.

"I didn't feel like I was going through what they were," says Baskett, "and I promised myself then I would do whatever I could to make sure other head injury patients had access to the drug that I knew I must have been given."

A persistent pursuit

Don Stein sometimes jokes that his becoming a scientist seemed unlikely. "If you grow up in an apartment complex in the Bronx," he once told a reporter, "the last thing your parents want you to do is to work with rats."

As a graduate student in the 1960s, Stein learned just how much those rats can contribute to science. His job was to surgically injure the brains of anesthetized rats to see how the brain damage would affect their behavior. At the time, this approach was the basic tool critical to understanding the functioning of the nervous system in health and disease. What fascinated him, however, was why about a third of the female rats recovered, while others with the same injury remained seriously impaired.

His professors, like all neuroscience leaders at the time, thought the findings were merely natural variation in brain injury outcome

"I promised myself then I would do whatever I could to make sure other head injury patients had access to the drug that I knew I must have been given."

because it was then taught that in the damaged brain, there was no possibility of repair or functional recovery. Stay focused, they urged. You have a PhD to complete, a career to build.

Thus began a kind of double life for Stein that would continue for more than two decades. He spent his days doing the more traditional "real work"—at the University of Oregon and MIT, where he completed doctoral and postdoctoral studies, at Clark University in Massachusetts, where he ran the brain research lab, and at Rutgers, where he was dean of the graduate school and associate provost for research. He spent his free time trying to solve the mystery of those injured but still normally functioning female rats.

When Emory brought him on board in 1995, it was not so much for his progesterone research but rather his administrative talents. Here too, for five years, he spent his days as dean of the graduate school and vice provost and his evenings in a research lab in a double-wide trailer previously discarded by the Veteran's Administration, not uncommon during Emory's then-building boom. With typical Stein humor, he purchased a stash of plastic flamingos from a nearby hardware store. The grounds crew would yank them up whenever they could, only to find a new pair gleaming in the morning sun. Stein finally decided he had been outsmarted when the crew replaced the lawn with a rock garden of artfully placed boulders.

When it came to his work with rats, however, he did not quit.

Since the females typically did better, Stein thought that the difference had to be hormonal. That helped explain anecdotal or single-case clinical reports that women were more likely than men to recover from similar brain injuries. Estrogen was the obvious candidate, but he observed no correlation between estrogen levels and recovery. He turned to progesterone.

"Progesterone was hidden in plain sight as a neuroprotective agent," says Stein. A naturally occurring hormone produced in the brains of both sexes, progesterone's protective properties become most obvious during pregnancy when levels shoot up dramatically and stay elevated until the baby is born. Stein and others began to recognize that many processes involved in fetal development are similar to those that take place during tissue repair after injury. Perhaps, Stein theorized, the higher levels of progesterone in females at the time of their injury accounted for their better outcomes. And since



"The drug and all the people who believed in it gave us back our son, with his mind, personality, and sense of humor intact."

progesterone levels fluctuate sharply during rats' estrus and women's menstrual cycles, perhaps the outcome depended on where females were in their cycle when injured.

By tricking the female rats' bodies into thinking they were pregnant (a little like birth control pills do), Stein was able to produce high levels of progesterone in the animals. It soon became evident that female rats injured when their progesterone levels were high did much better after injury than either males or females with lower progesterone levels. The first thing he and his students noticed was that the high-progesterone females had virtually no brain swelling compared with those in other phases of their estrus cycles. He was on the right track. But would it work for males? And if so, why?

In the years since Stein's graduate school days, science had advanced considerably. Brain swelling was recognized as a major cause of cell death after TBI. Many treatments, then and now, focused on preventing swelling to preserve still healthy brain tissue. In 1991, Stein and his laboratory put progesterone to the test. In earlier work, he had manipulated naturally occurring progesterone. Now he gave progesterone by injection to both male and female rats within 24 hours after identical brain injuries. The progesterone-treated male and female animals showed no signs of brain swelling.

Research elsewhere also had found that injured brain cells release free radicals and neurotoxins and that the immune response to injury causes inflammation. Stein showed that, in rats, progesterone also intervenes at these points.

Heroic attempt or pig-headed waste?

Although the scientific and medical world did not exactly beat a path to Stein's trailer door, first the CDC and then the NIH began to support his work. A few researchers in other labs repeated his findings, validating his results. But what really turned the corner, says Stein, was when he met Art Kellermann, a passionate advocate for public health who introduced him to David Wright. For Stein, the maverick scientist, and Wright, the former flight physician and rock band drummer, it was the beginning of "a beautiful friendship."

Wright wanted to believe that Stein had found something that would help brain-injured patients, but he also was a scientist. He had been part of the team that discovered the protein involved in Marfan's syndrome (a disorder many believe afflicted Lincoln). With appointments in emergency medicine, injury control, biological and biomedical sciences, and biomedical engineering at Emory, he had strong and cautious research instincts. He carefully repeated some of Stein's rat studies and got the same promising results.

After that, Wright too became convinced that progesterone held serious promise as a potential treatment for TBI. He and Stein worked with a statistician at Emory's Rollins School of Public Health and with clinicians from neurosurgery, trauma surgery, and other Emory departments to design a clinical study to see if progesterone would work on injured humans without causing serious side effects. Progesterone had a long track record of safety for treatment of other diseases, but not at levels the researchers believed would be most effective for treatment of TBI in humans. In 2001, the first of 100 patients enrolled in a three-year pilot study funded by NIH and headed by Kellermann and Wright. All had suffered TBI within 11 hours before arriving at Grady, and all had an initial Glasgow Coma Scale score ranging between 4 (severe TBI like that of Baskett) and 12 (moderate TBI).

At the end of the study, Wright and others on the team went to Washington, D.C., to find out the results from NIH analysts, the only people aside from the team statistician who knew which patients had received progesterone, which placebo. The researchers' nervousness was palpable. Were they closer to treatment?

Back in Atlanta, Stein was driving when his cell phone rang. When Kellermann told him to pull over before he heard the results, Stein's blood ran cold. What worked in rats did not always work in humans. Would progesterone end up in the graveyard of failed neuroprotective drugs? Had his research career been a heroic attempt or a pig-headed waste of time?

Not only had progesterone caused no side effects, but fewer than half the patients receiving progesterone (13%) had died compared with those on placebo (30%). Furthermore, functional outcomes and the level of disability were significantly improved among progesterone patients with moderate brain injury.

Soon after, a similar study in China also found progesterone to be completely safe and patients receiving it to have superior outcomes at three and six months after the injury.

And in September 2007, a front-page article in the *Wall Street Journal* reported on Stein's quest to heal brain injury.

Although not every progesterone patient in the Emory/Grady trial did as well as Baskett, there were a number of other marked successes, including a prominent businessperson who prefers that people don't know about the injury and a young man who continues to pursue a successful, prominent athletic career.

Saving time and brain cells

Results in hand, Wright, Stein, and the team began planning a larger clinical trial to more completely test progesterone's clinical effectiveness. The process involved six Emory departments and three schools (Emory's schools of medicine and public health and Morehouse School of Medicine). Wright then reached out to potential partner institutions in a plan the size and scope of a small military campaign. Last fall, the NIH awarded the proposal more than $27 million in funding—news that again made the pages of the *Wall Street Journal*.

During the next four years, 1,140 TBI patients will be enrolled across 17 different institutions, each at a level 1 trauma center. Participating institutions will work under shared protocols and operating and quality control standards developed at Emory. The progesterone, a natural substance, will be purchased from a pharmaceutical company and prepared, tested for quality control, and packaged in Emory laboratories, then distributed to all participating centers.

As in the earlier study, patients must be 18 or older, with blunt head trauma (no penetrating injuries). In the new study, however, patients will begin treatment within four hours of injury. Given the safety results of the first study, the FDA will allow the use of exception from informed consent—a special research allowance for cases where time to treatment is critical to the conduct of the research. Patients will be monitored daily for safety and clinical management. At six months, memory, cognition, and behavior will be measured, with outcomes stratified by severity of injury.

The safety of progesterone makes for numerous possibilities, say the researchers. Stroke, for example. Stein's recent animal studies suggest that progesterone is highly effective in reducing the size of blood clots and, unlike tPA, has no risk of causing bleeding in the brain. Wright and Michael Frankel, director of Emory's Stroke Center, are readying for a stroke trial.

Children with TBI were excluded from the first progesterone studies because researchers were uncertain how the hormone would affect development. Clinicians in the Emory-Children's Center, Emory Center for Injury Control, and Children's Healthcare of Atlanta have brought their expertise to studies now being designed.

Stein, Wright, and the other researchers also would like to explore getting progesterone to patients faster to save more brain cells. They are working with Emory chemists to create a stable, heat-resistant progesterone product. If an injection device loaded with progesterone became part of emergency response med-pacs at home and in the military, a person with a possible head injury could receive an injection of progesterone at the scene of the injury.

The progesterone story—the science, teamwork, perseverance, and ability to think outside the box—shows what can happen when science is at its best.

The Basketts take a more direct view. "This drug and all the people who believed in it gave us back our son, with his mind, personality, and sense of humor intact."

WEB CONNECTION *To see Marc Baskett on video, visit* **whsc.emory.edu/protect.cfm.** *To hear a podcast with Don Stein, visit* **whsc.emory.edu/soundscience/2009/stein.html.**

Smelling **Trouble**

By Quinn Eastman • Illustrations by Carol Dean Hatcher

The earliest harbingers of Parkinson's disease may be those ***we cannot see.***

Doctors first told John McCune that he had lost his sense of smell because of sinus blockages, but surgery to allow his sinuses to drain failed to help. He next tried large doses of zinc, but with no apparent benefit. Then several years passed before any visible sign of trouble arrived.

"Both my wife and my daughter noticed that my left arm didn't move while I was walking, and I had started to shuffle a bit," McCune says.

He was diagnosed with Parkinson's disease in 2006, more than a decade after first noticing that his sense of smell was weakening.

Today neurologists are recognizing that the loss of the sense of smell is one of a group of "non-motor" symptoms associated with Parkinson's disease. They include sleep disturbances, constipation, blood pressure changes, depression, and as the disease becomes more advanced, hallucinations and confusion.

These symptoms are like proverbial canaries in a coal mine, warning of danger years before classic signs of the disease such as tremors and stiffness.

Several Emory researchers are investigating these non-motor features of Parkinson's, ranging from degeneration of the nerves that regulate the digestive system to subtle changes in memory and decision-making. They are working both in Emory's clinics and with animal models developed to simulate the non-motor symptoms seen in humans.

"The field is moving in this direction because doctors realize that we have to address the effects of the disease in a more systemic way," says Emory neurologist James Greene, who is comparing digestive problems in animal models of Parkinson's. "Non-motor symptoms significantly affect patients' quality of life."

In addition, non-motor symptoms demonstrate that Parkinson's can cause damage to more than one part of the brain and more than one variety of brain cell. They provide clues to how the disease develops and how it might be delayed or prevented.

Getting to this point

The recent emphasis on non-motor symptoms reflects the history of treatment for Parkinson's, says Emory neurologist Mahlon DeLong, who has spent decades researching the disease and developing better treatments for patients.

"We've known about non-motor symptoms for a while," he says. "But they've remained in the background because of the considerable progress in treating motor symptoms."

In the 1960s, researchers discovered that the drug L-dopa had a dramatic effect on motor symptoms in people with Parkinson's. However, over time, L-dopa can lose its effectiveness.

Neurologists believe motor symptoms arise from loss of cells that make dopamine, especially in the part of the brain called the basal ganglia, which plays a critical role in regulating movement. Surgery with deep brain stimulation (DBS), which DeLong and others pioneered, targets specific areas of the basal ganglia in an effort to regulate them with electric current.

When Emory patient Bill Carroll couldn't smell the odor from an animal that died in his car, his family members became concerned. It was the first sign of Parkinson's disease.

Several medications available to treat the motor symptoms of Parkinson's have built on the success of L-dopa. However, these drugs have little effect on many non-motor symptoms, such as constipation and sleep disruption.

When Parkinson's affects the part of the brain that prevents people from acting out their dreams, for example, it leads to REM sleep behavior disorder, which in turn can lead to falls or other injuries. One Emory patient awoke in a closet after a nightmare.

Another patient, a retired bank executive, is unable to sleep at night and consequently nods off throughout the day. Not being able to get regular sleep "definitely makes the motor symptoms worse," he says.

Recent studies also indicate that the majority of hospitalizations for Parkinson's patients come from non-motor symptoms. "What drives Parkinson's patients into the hospital are things like hallucinations and confusion, or problems with balance, which can lead to severe injuries," DeLong says. "These can't be treated with L-dopa."

Although hallucinations can be addressed with antipsychotics, adding drug upon drug can create new problems, says DeLong.

Animal model for non-motor symptoms

By the time many patients consult a neurologist about classic Parkinson's symptoms, most of their dopamine-making cells already have been lost. DeLong says research must concentrate more on preventing or forestalling Parkinson's.

Prevention requires knowledge about the disease's causes and mechanisms, which are highly complex in Parkinson's, says Gary Miller, a neurotoxicologist at Emory's Rollins School of Public Health.

A small number of cases are clearly inherited, but most probably come from a mix of genetic variation, personal history, and exposure to environmental hazards such as pesticides. Miller, Greene, and other Emory colleagues are studying how pesticides injure certain brain cells.

Working with several Emory laboratories, Miller has developed a genetically engineered mouse that matches the pattern of non-motor symptoms seen in people with Parkinson's and thus could be a research tool in the search for medications to treat non-motor symptoms. "These mice are very useful for studying the major non-motor symptoms of Parkinson's because they have all of the symptoms together as a package," he says.

The mice are deficient in an enzyme that normally packages chemicals such as dopamine, norepinephrine, and serotonin into vesicles in order to deliver them to other cells. In the altered mice, the improperly stored neurotransmitters are thought to damage brain cells.

As part of a national clinical trials network, Emory is testing several proposed neuroprotectants that may have the ability to protect brain cells from Parkinson's damage. While some have failed to work, others seem to show early promise.

Before such a neuroprotectant could be used to help prevent or forestall Parkinson's, however, other questions need answering. How could people who could benefit from such a drug be identified?

Early warning sentinels

Emory is participating in a national study that aims to identify relatives of people with Parkinson's who are most at risk of developing the disease themselves. Known as PARS (Parkinson-associated risk study), it uses a mail-in scratch-and-sniff test as an initial screening device, followed by brain scans, if necessary.

With similar aims, clinicians have teamed up with neuroscientists Yoland Smith and Beth Buffalo at Yerkes National Primate Research Center at Emory. In parallel, they will use color- and shape-matching tasks to test people recently diagnosed with Parkinson's and monkeys treated with the neurotoxin MPTP (which simulates Parkinson's damage). The goal is to identify subtle changes in memory and attention that may help identify patients who can benefit from early treatment, Smith says.

Still, each patient's experience with Parkinson's and how it progresses is different. For every person who loses his or her sense of smell early on, another patient experiences classic tremors and stiffness first.

"Parkinson's is really a collection of several diseases," says Stewart Factor, director of Emory's Movement Disorders program at Wesley Woods Center. What they have in common, he says, is the pathology—the pattern of damage in the brain late in disease. But where that damage occurs first can vary, and many of the non-motor symptoms of Parkinson's can blend in with signs of "normal" aging.

Teasing out which symptoms came first—motor or non-motor—can be difficult. "Part of what we face is a recall bias or hindsight problem," Factor says. "A patient might tell me he's had recurring constipation for 10 years, but he wouldn't say anything to a neurologist about it until he starts having other symptoms."

For example, Emory patient Bill Carroll's fading sense of smell became most apparent when he couldn't detect a gas leak in his house or an animal that had died in his car, leaving family members puzzled and concerned. "I didn't realize it had to do with Parkinson's disease," he says. "I thought it was just part of me."

WEB CONNECTION *To make an appointment with a movement disorder specialist at Emory, call 404-778-7777, or visit* **emoryhealthcare.org/patient_info/healthconnection.html**. *For more information about Parkinson's disease, visit the American Parkinson Disease Association at* **apdaparkinson.org**. *For a video about the scratch-and-sniff test produced by one of Emory's collaborators in the PARS study, visit* **whsc.emory.edu/r_smell.htm.**

In memory

"What was most noticeable was that Worley lost his voice. He always had a strong voice."

That's Mary Louise Brown Jewell (above) talking about the Parkinson's disease that took her husband's voice, then his memory, then his life. Worley Brown, who was CEO of the Rock-Tenn Corporation, suffered from Lewy body dementia, a progressive form of Parkinson's that affects the ability to remember as well as to reason and carry out simple actions. It also causes hallucinations.

Jewell recently pledged $2 million to establish a chair in neurology at Emory to honor her late husband and a $500,000 gift to renovate a clinical research unit at Wesley Woods. Both contributions are lead gifts for an endowment to raise funds for Parkinson's and other movement disorders, and they are part of Campaign Emory's $1.6 billion fund-raising initiative.

"I want there to be a cure," says Jewell, "and through the research being performed at Emory, I believe that can be accomplished."

Every day, every way, Emory's clinicians and researchers are looking for a breakthrough to treat ALS.

on borrowed time

ALS is like a lit candle:
it melts your nerves and
leaves your body a pile of wax.
–*Tuesdays with Morrie*, by Mitch Albom

By Maria Lameiras • Photography by Jack Kearse

FIRST PERSON | **JUDY LOCHRIDGE**

Judy Lochridge was a nurse for 36 years when she started to tire on the job. Her hands were weak, and her shoulder hurt. She never expected ALS was the cause, but that was the diagnosis she got in the fall of 2007.

Since then, she has stopped work, but she and husband, Billy Lochridge, are trying to have a normal life. They've seen a daughter marry, attended their son's rock band opening at the Hard Rock Café, celebrated their 36th wedding anniversary, even traveled to Aruba. They know ALS is a terminal disease. "We have our crying times," they say. But having ALS, says Judy, has made her "look at the sunrise a little differently. All the special things that anyone does for me are a little more precious to me," she says.

See the photo essay and hear more patient stories at **whsc.emory.edu/r_als.htm**
For more information on the Emory ALS Center, visit **neurology.emory.edu/ALS**

FIRST PERSON | **JIMMY AND SONDRA EVERETT**

On a typical clinic day at Emory's ALS Center, director Jonathan Glass and his colleagues see a dozen or more patients with amyotrophic lateral sclerosis (ALS). This Friday is no exception. There are patients here dealing with all stages of the disease, some newly diagnosed, others confined to wheelchairs.

Newlyweds Jimmy and Sondra Everett are among the people in the center's lobby. They had planned to grow old together before ALS struck Jimmy, 55, a high school assistant principal, coach, and athlete from Tallahassee, Florida. "We've got to live with it," says Sondra. "We don't have a choice." Jimmy's words echoes those of his wife: "I have to accept it. It's a bad draw, but I just have to move on."

ALS is a bad draw. Commonly called Lou Gehrig's disease for the popular New York Yankees baseball player who died of it in 1941, ALS is a devastating disease that kills the motor neuron cells in the brain and spinal cord, causing the brain to lose ability to control muscles in the body. It inevitably leads to paralysis and problems with swallowing, eating, and breathing. The person's mental capacity remains intact, making the disease a cruel sentence for patients who are often otherwise healthy and active before being diagnosed.

"This disease is a horrific one," Glass says. "It hits people smack in the middle of their productive lives, and it affects not only the individual but the whole family."

For patients and their families, Emory's ALS Center provides multidisciplinary care, focusing on independence and quality of life. Together, Emory neurologists, nurses, a speech language pathologist, a social worker, dieticians, and occupational, physical, and respiratory therapists address all aspects and stages of ALS.

"We have created a patient-centered approach that has been successful for our patients," Glass says. "The family comes to us, and we bring the providers to them."

The axons of ALS

In addition to providing clinical services, Emory's ALS Center is searching for a research breakthrough to understand the disease. It partners with the Muscular Dystrophy Association of Georgia and the ALS Association of Georgia, bringing together clinicians and scientists familiar with a wide spectrum of human neurodegenerative diseases. It is one of five centers that participate in the national clinical research network to support ALS research.

"Instead of having silos of research in each area, we have them mixed together so we can learn from each other," Glass says. Believing that neurodegenerative diseases may all be related in some way, the Emory teams include specialists in Alzheimer's, Parkinson's, ALS, Huntington's, and other age-related neurodegenerative diseases.

In the ALS Center, research focuses on the basic mechanisms of motor neuron degeneration, genetics, and new experimental treatments. A main focus of Glass's laboratory is figuring out why ALS causes nerve fibers, called axons, to die.

"Axons connect the nervous system to the muscles and skin and give the body all of its interaction with the outside world," Glass says. "The ability to feel, move, do anything is controlled by the impulses that travel up and down the axons from the brain. The major feature of neurodegenerative diseases is that these wires die, disconnecting the brain center from the outside world."

FIRST PERSON | **NETTIE GREENE**

The thing that ALS patient Nettie Greene misses most is cooking. Known in her family for her home-baked pecan pies, coconut cakes, and banana pudding, now she has to rely on others to do her job in the kitchen. She feels a little guilty about that—"I should be the one in there, doing," she says—but ALS has made her too weak to stand for long.

More so than the disease itself is the dependency on others that is Nettie's biggest challenge, she says. The woman who used to work two jobs can no longer drive. She's recently transitioned from a walker to a wheelchair. She has trouble swallowing, which has caused her to lose weight.

Using cell cultures and animal models, Glass and his research team create models of the nervous system and ALS to identify factors that cause axon death. They then look at the pathways of cell death to find ways to prevent it from occurring.

With biochemists from Georgia Tech, Glass is working to develop new drugs to prevent axon cell death. The researchers are testing the potential of calpain inhibitors in mouse models to see if they can limit the toxic effects of the cancer drug Taxol (which causes axonal degeneration in humans and mice). Calpains are enzymes that are active in models of neurodegeneration, and Glass's research has shown that administration of a calpain inhibitor in mouse models seems to prevent axonal degeneration and preserve function.

Genetic links and breaks

Most current research focuses on familial ALS, even though only 10% to 15% of all ALS patients have the familial form. The rest have what is called sporadic ALS. Of all familial patients, about 20% have a mutation of SOD1, an enzyme present in all normal cells that detoxifies oxygen. The remaining 80% of familial ALS patients have a gene linked to ALS, but doctors and researchers do not know why the gene causes ALS.

"These indicators in familial ALS give us a place to start," says Glass. Since people with familial ALS are virtually indistinguishable from those with the sporadic form, what researchers learn about the genetic form will help them better understand sporadic ALS.

"Many believe that neurodegenerative diseases are all linked," says Glass. "The question is, how many ways are there to 'break' the nervous system? Probably, not many. Similar mechanisms have to cause it. If we can find out what causes axon degeneration in any situation, it could lead to prevention or treatments for the range of neurodegenerative diseases."

Glass also is working with Emory geneticists to find protein biomarkers that can predict the severity and progression of ALS, which impacts each patient with differing symptoms, severity, and rate of progression. Prognostic biomarkers could lead to a clinical trial to see how these protein biomarkers change in different patients.

At press time, Glass had just learned that the FDA has approved a phase I clinical trial to treat ALS with spinal cord stem cells. Emory is awaiting approval from its Human Investigations Committee to participate in this landmark trial.

A cure can't come too soon for the Everetts. As Jimmy puts it, "I hope Dr. Glass has a breakthrough soon."

FIRST PERSON | **SHIRLEY MORRELL**

Shirley Morrell's brothers travel from New Orleans to Eufaula, Alabama, to drive their baby sister and their mother to Shirley's visits at Emory's ALS Center in Atlanta. "We try to stick together," says her mother Geneva. Then she clarifies: "We don't try. We do it."

The family describes Shirley as a fighter, and the fighter in her is hanging in there in the face of ALS. She continues to work as a medical assistant in private practice, reminding herself to stretch and move to keep her limbs from stiffening. These days, she's doing more clerical work than standing on her feet. "I try to keep adapting," says Morrell. So does her family. It's hard, her brother Willie says, but "you try to adjust."

YOUTHFUL INSPIRATION

When people learn about Lou Gehrig's disease, when they meet someone who is struggling to keep a positive attitude in the face of death, they want to do something to help. Private support drives both research and patient care at Emory's ALS Center.

One of the center's patrons is Brian Duffy (above, left). Brian, 15, first learned about ALS while watching the Ironman triathlon in Kona, Hawaii, in 2005. That year, racer Jon Blais became the first person with ALS to complete the race. After watching televised coverage on Blais, Brian—a triathlete himself—told his parents, Karen and Mike, that he wanted to do something to help.

With their support, the teenager began a letter-writing campaign to family and friends in 2006, initially raising more than $2,200 for ALS research. His parents began running in triathlons to raise money for the cause, and his younger brother, Kevin, a golfer, began selling golf balls as a fund-raiser.

While at the ALS Association's Atlanta Walk, the Duffys met Glass, who took them on a tour of his lab and explained some of the research his team was working on. "After the tour," Karen Duffy says, "Brian turned to me and said, 'Mom, this is where we need to give our money.'"

At Brian Duffy's urging, the family held its first annual "Cure for ALS" 5K race in 2007. To date, they have raised more than $40,000 for ALS research and care at Emory.

Glass says donors like the Duffys provide a link to the community and let people know about the essential work being done at the center. "Brian's efforts are what really started his family's fund-raising efforts. He and his brother are amazing kids," Glass says.

Did you know?

America's best: In the most recent annual *U.S. News & World Report* guide to "America's Best Hospitals," Emory University Hospital has ranked among the nation's best hospitals in 11 specialties, including five top 20 rankings. Overall, Emory is one of only 170 hospitals, out of more than 5,400 medical centers in the country, to be named in the magazine's top 50 specialty rankings. It also is the only acute care hospital in Georgia cited in the list. It received a top national ranking in the following areas: ophthalmology, 9; psychiatry, 10; geriatrics, 13; heart and heart surgery, 13; neurology and neurosurgery, 14; ear, nose, and throat, 22; kidney disease, 25; diabetes/endocrinology, 31; gynecology, 44; urology, 44; and cancer, 46.

Challenging Crohn's: Emory and Children's Healthcare of Atlanta are teaming up to study the progression of Crohn's disease in children with a $5 million grant from the Crohn's & Colitis Foundation of America. The study will enroll 1,100 children who recently have been diagnosed with Crohn's, a chronic disorder that causes inflammation of the digestive or gastrointestinal tract and whose cause is unknown.

Healing tender tendons

During the 2008 Olympics in Beijing, Olympic champion Liu Xiang was forced to withdraw from competition in the 110-meter hurdles because of a tendon injury that failed to heal. Had he competed, he might have experienced a rupture with lifelong implications. Now athletes who endure chronic pain from tendon injuries may get relief.

Doctors at the Emory Sports Medicine Center have found that injecting platelets from a patient's own blood to rebuild a damaged tendon has proven successful in not only relieving pain but also jump-starting the healing process. The procedure is called platelet-rich plasma therapy.

Tendons are the rope-like structures that connect muscle to bone, enabling the bone to move. When a tendon is first injured, it can become inflamed, swollen, and painful. However most chronic tendon pain lacks significant inflammation as the tissue itself begins to break down, accounting for why traditional treatments like rest, ice, and anti-inflammatory medications often fail to provide long-lasting relief.

"Once a tissue like a tendon has been injured and athletes continue to overuse it, the healing process fails us, and we are left with an unhealthy tendon that will not heal on its own," says Emory orthopedist **Ken Mautner** (above).

"Some blame a lack of adequate blood supply to certain tendons. Some blame too much stress to the area. Whatever the reason, the tendon needs help to initiate the healing process. For years, the last resort for these problems was surgery to try to release or cut away the damaged tendon, procedures that met with mixed success. Platelet injections allow damaged tissue to regenerate and heal."

The procedure is performed in an exam room and takes less than an hour. The patient's blood is drawn and placed in a centrifuge for 15 minutes to separate out the platelets. The layer of platelet-rich plasma is then removed and injected into the diseased portion of the tendon with the guidance of an ultrasound machine.

Patients are put on a program of relative rest followed by physical therapy for the first six weeks. After six to 12 weeks, they are re-evaluated. Some patients with more difficult injuries may take more than one treatment to achieve successful outcomes. However, a majority of patients find that by three months they can return to most or all of the activities they were doing before the pain started—"sometimes activities they have been unable to do in years," says Mautner. —Kathi Baker

WEB CONNECTION *For more information, call 404-778-7777 or visit* **go.emory.edu/General/Sports_Medicine.html.**

The next breast thing

It's a call that any woman dreads. The results from her recent mammogram are back, and something has shown up that needs further investigation. The call-back produces anxiety and leads to another round of expensive screening tests.

Or for other women, particularly those with dense breast tissue, mammography may fail to detect a cancer altogether.

"With mammograms, it is sometimes hard to pick up breast cancer because we are putting a three-dimensional structure on a flat screen," says Emory radiologist Mary Newell. "We can miss cancers that are there or see things that aren't really there."

Enter a new technology—computed tomography (CT) scans of the breast. These new prototype CT scanners use cone-shaped X-ray beams combined with a digital flat panel detector to produce 3D images.

During the exam, a woman lies prone on a table, allowing the breast to hang through a hole rather than being squeezed between flat panels as in traditional mammography. Below the table, an x-ray source and detector rotate around the breast. The 10-second scan gathers digital information that produces hundreds of images.

Emory is one of only three sites in the United States testing the dedicated CT breast scanner manufactured by Koning Corporation. Emory radiologists Carl D'Orsi and Mary Newell are evaluating breast CT scans compared with diagnostic mammography as a tool for detecting cancer. In a second clinical trial, they are comparing breast CT scans (enhanced with contrast dye) with MRI to characterize newly diagnosed breast cancers. And in a third study, the researchers are looking at the effectiveness of breast CT scans in detecting how tumors are responding to chemotherapy treatments.

Newell believes the ability to tell whether a cancer is responding to a particular treatment is one of the most important potential applications for the new technology. "A doctor's hand exam is not as sensitive or specific as the dedicated CT scan may prove to be."

With the dedicated CT breast scanner, the researchers can reconstruct the breast from any angle, top down, and side-to-side. Computer post-processing allows them to focus in on calcifications, digitally remove the nipple or unnecessary background features, and manipulate the image in any way to sort out a real or false finding.

Dedicated breast CT may end up being used alone for routine screenings or in combination with other technologies for cancer diagnosis and treatment, says Newell. "The goal is to figure out the best way to see the breast in 3D. We think we're moving in the right direction."—Rhonda Mullen

WEB CONNECTION *For more information, call 1-888-WINSHIP or visit* **cancer.emory.edu.**

Stretching our spine services: Emory University Orthopaedics & Spine Hospital is now taking appointments for outpatient imaging services, including both CTs and MRIs, at its Tucker location. Patients also can walk in with no appointment for diagnostic x-rays at the hospital. Outpatient hours for the services are 8am–4pm, Monday through Friday. For more information, call 404-778-XRAY (9729). Emory orthopaedics also is expanding hours for musculoskeletal MRIs at its Executive Park location, the largest such outpatient facility in Atlanta. New Saturday hours are 7:30am–1pm. For an appointment, call 404-778-3350.

Emory's heart failure toolbox

Heart failure is a chronic, progressive disease that gobbles up a person's energy and breath, leaving them gasping, thirsty, and swollen with water retention. When a simple trip from bed to bathroom becomes a walk across a desert, their only hope may be a heart transplant.

"We have gotten better at keeping patients with heart failure alive longer," says **Javed Butler** (above), director of heart failure research at Emory Healthcare. "Mortality has consistently gone down, although prevalence is increasing. But in terms of quality of life, when a person spends years hardly able to walk across the room, that is not a successful outcome."

Indeed, heart failure now afflicts nearly 5.7 million adults in the United States. Incidence is steadily rising, with about 670,000 new cases reported every year.

But because heart failure is a syndrome that springs from a mishmash of different diseases, a treatment is not easy to come by. Simply keeping symptoms under control is the aim of most treatment plans. Prescription beta blockers keep blood pressure under control, a low-sodium diet prevents water retention and lung congestion, and exercise maintains the heart's strength.

However, to truly lessen the burden of heart disease, says Butler, prevention and early intervention are necessary. As deputy chief science adviser for the American Heart Association, Butler and others recently created a statistical model based on patient data to identify those at a high risk for heart failure. Butler hopes the risk tool will help pinpoint people at risk for heart failure despite its elusive causes.

He also has developed the infrastructure for a comprehensive study of patients with heart failure. A dozen researchers from across several disciplines already have begun collecting baseline data on patients at Emory hospitals and Grady Memorial Hospital.

Meanwhile the number of heart failure patients at Emory University Hospital (EUH) and EUH Midtown has ballooned so much that physicians have developed new ways to care for patients involving remote monitoring, says Andrew Smith, medical director of Heart Failure and Transplantation.

Remote monitoring saves patients time and gives doctors more information about the patient's condition. "About 85% of heart failure patients admitted to the hospital have salt and water retention," says Smith. "Remotely monitoring our patients' symptoms helps reduce hospitalizations."

A telemonitoring system sends the clinic a patient's weight via a cell phone every time the patient steps on a scale. Using an automated phone system, patients call a central number daily, enter their weight, and answer a list of "yes" or "no" questions. A nurse practitioner reviews the calls, and if she determines that weight gain is too rapid (more than 4 lbs. a day), she has the patient come in.

Surgically implanted pacemaker defibrillators help patients whose heart failure is complicated by heart arrhythmias. Sensor technology detects abnormal heartbeats, and the defibrillators pace or shock the heart back into rhythm.

One vendor even offers Bluetooth technology so that when patients step on a scale, the information goes to the defibrillator. At night, the information is logged into a central computer system, and the Emory heart failure team can track weight increases to spot a problem. Another remote device measures electrical signals across the lung, indicating fluid retention.

Smith is anticipating the completion of clinical trials now under way at EUH and EUH Midtown for several additional investigational devices.

Ultimately, the goal of Smith and Butler is to keep heart failure patients healthy. No one lives forever, says Butler. But keeping heart disease risk factors at bay can help people make the most of their later years.
—Valerie Gregg

WEB CONNECTION *To make an appointment, call 404-778-7777. To hear Javed Butler discuss heart failure treatments, visit* **whsc.emory.edu/soundscience/2009/butler.html.**

An alternative to craniotomy

ILLUSTRATION CAROL DEAN HATCHER

Brain surgery is a big deal, requiring a complex navigation of the organ that is the center of the nervous system. But Emory neurosurgeons have found a new approach to brain surgery that is less intimidating. They now are able to remove benign tumors from deep within the brain through openings in the skull no bigger than a pea.

The new endoscopic treatment is less risky, takes less time, and necessitates a shorter hospital stay than standard surgery. In Georgia, it is available only at Emory University Hospital Midtown.

The most common brain tumors removed by this method are colloid cysts, which can cause an increased buildup of cerebrospinal fluid (CSF) in the the brain. They account for approximately 1% of all intracranial tumors. Blockage of the normal flow of CSF can lead to increased intracranial pressure—resulting in headache, vertigo, memory impairment, limb weakness, and behavioral changes. The tumors can even cause sudden death.

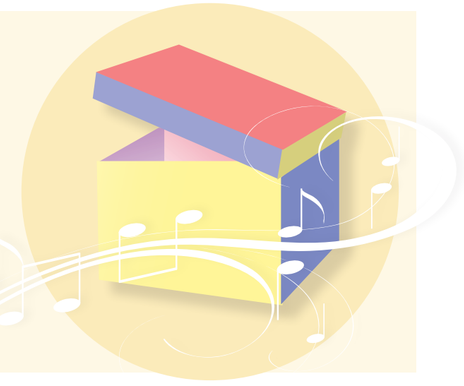
In most medical centers, surgeons perform a craniotomy to remove colloid cysts. The craniotomy involves a large incision and complete opening of the skull. By contrast, Emory neurosurgeon Costas Hadjipanayis removes these tumors through small incisions and openings in the skull through which he threads a 6-mm endoscope fitted with a fiberoptic camera. After identifying the location of the cyst using the endoscope, surgeons then pass 2-mm instruments through small openings to remove the tumor. They also are able to create new pathways to drain CSF so that no shunts for excess drainage are needed.

The endoscopic approach to brain surgery is one of many medical advances pioneered at Emory. Others featured on a new webpage (at emorythealthcare.org) include endoscopic heart surgery that allows surgeons to perform coronary artery bypass without opening the chest cavity and stopping the heart, a nutritional treatment for cancer that uses soy products to release cancer-fighting genes that have been silenced, and an alternative technique for hip replacement that minimizes removal of muscle from the bone and preserves hip stability.

WEB CONNECTION *To see videos of colloid cyst removal, visit* **emoryhealthcare.org/medicaladvances/index.html.**

Opening Pandora's Music Box

One of the hardest things about having an MRI is lying still for the 30 minutes or more that it takes to complete a scan. But recently Emory patient Ronnie Jowers found the experience a little easier by being able to listen to his favorite songs during his MRI. On Jowers' playlist? The Vogues, the Lettermen, Jim Croce, and the Mamas and the Papas. Emory's radiology department is offering the customized tunes on several MRI units through Pandora, an internet radio service that allows listeners to personalize their music. Now the only challenge is to keep patients from tapping their feet to the beat. To schedule an appointment, call 404-778-7777. For more information, visit radiology.emory.edu.



A faster response

Currently flu vaccines must be grown in chicken eggs, extracted, and then mass-produced. The process can take months when large supplies are demanded. However, at Emory, a team of scientists, led by microbiologist and immunologist Richard Compans, is working to rapidly speed up manufacturing of a flu vaccine.

How are they doing it? They are using virus-like particles (VLPs), empty shells that look like viruses but lack the ability to reproduce. VLPs are man-made decoys of natural viruses that prompt the immune system to fend off infection when exposed to the real thing.

While VLPs copy the structure of authentic viruses, they are not infectious, making them safer to produce than vaccines that use live, but weakened, organisms. When a person is exposed to the live virus, the immune system releases antibodies to protect against infection. That also happens with VLPs. They are recognized by the immune system as the "real" virus upon immunization, causing the body to produce antibodies, but not causing illness.

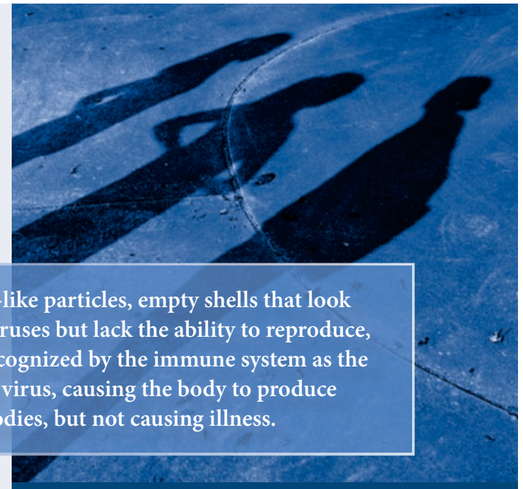
Emory began clinical trials of an H1N1 flu vaccine in August as one of eight NIH vaccine and treatment evaluation units. The trials tested both safety and efficacy and were critical in preparing for this fall's vaccination program.

In laboratory testing with mice, supported by the CDC and the Georgia Research Alliance, the Emory team has shown that a VLP vaccine could significantly cut the production time needed to manufacture the vaccine. Vaccines grown conventionally typically take up to six months to get to market. Not so with VLPs, says Emory microbiologist Sang-Moo Kang, who has been refining the VLP approach for eight years.

"After identifying the genes to constructing and making the VLPs, we can start to produce vaccines in four to six weeks," says Kang.

Another positive: The Emory researchers also found that immunity from the VLP vaccine in mice wore off more slowly than that induced by conventional flu vaccines in humans. "In a mouse, two years is the average lifespan," says Kang. "We have confirmed that the VLP immune system in mice can last 18 to 20 months. So this protective immunity is maintained throughout their lifetime." —Dana Goldman

WEB CONNECTION *For more info, visit* **emory.edu/flu** *and* **cdc.gov/h1n1flu/sick.htm.** *To hear James Steinberg, chief medical officer at Emory University Hospital Midtown discuss preparation for the upcoming flu season, visit* **whsc.emory.edu/soundscience.**



Virus-like particles, empty shells that look like viruses but lack the ability to reproduce, are recognized by the immune system as the "real" virus, causing the body to produce antibodies, but not causing illness.

The vaccine network

As part of a nationwide clinical trials network to develop vaccines, Emory participated in several clinical studies this summer and fall to gather data about this year's influenza vaccines. It was one of eight centers nationwide that tested two new vaccines for H1N1. The trials allowed the NIH to quickly evaluate the new vaccines to determine their safety and effectiveness.

Two clinical trials at Emory included healthy adults and seniors. In tandem, two pediatric clinical trials for the new vaccine unfolded at the Emory-Children's Center. "Children and young adults are considered among the most vulnerable populations for new and emerging strains of influenza, such as the current H1N1 pandemic," says Emory infectious diseases pediatrician Harry Keyserling, co-director of the Emory Vaccine and Treatment Evaluation Unit. "Vaccines are our most effective public health weapons against influenza." —Robin Tricoles

The flu patch

The small prick that comes with your flu vaccination might be getting a whole lot smaller.

Skin patches containing microneedles have proven as effective as traditional hypodermic needles in delivering vaccine and preventing influenza in mice. These patches are more convenient, less painful, and less costly than regular needles, and researchers from Emory and Georgia Tech believe they will increase vaccination coverage as a result. Their research is published in the April 2009 issue of the *Proceedings of the National Academy of Sciences* and the *Public Library of Science One* (March 10, 2009).

The way the patches work is straightforward: they contain tiny stainless steel microneedles that are covered with inactivated flu virus and pressed into the skin, where the vaccine dissolves after a few minutes.

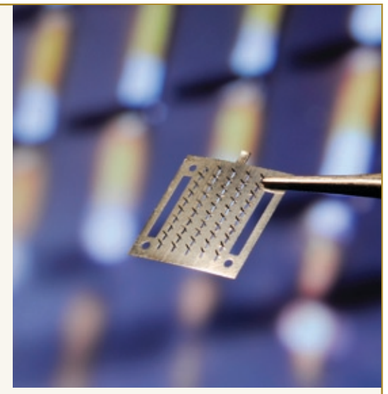
In their research on mice, the scientists immunized two groups of rodents, one with the microneedle patches and the other with hypodermic needles, and they exposed both groups to a high dose of influenza. All of the mice in the vaccinated groups survived, while those in a control group of unvaccinated mice did not.

In addition to the effectiveness of the flu patches, "vaccine delivery into the skin is desirable because of the skin's rich immune network," says Emory microbiologist Richard Compans.

Even though it stimulates the immune system and is effective in patients over 60, the technique of delivering flu vaccine directly to the skin has not been widely used. The reasons? It was inconvenient and required highly trained personnel to deliver the vaccine.

Delivery via microneedles changes that. Researchers say that the delivery system is so easy that patients themselves may be able to administer it. The small size of the microneedles also enables ease of transport and storage, making them ideal for use in developing countries. And finally, a format of one-use patches halts accidental re-use of hypodermic needles.

The study team has been working since the mid 1990s to develop a microneedle technology that delivers drugs and vaccine painlessly through the skin. Its next steps will involve additional testing in other animal models, such as guinea pigs and ferrets, before starting tests in humans. More studies are needed to determine the minimum vaccine dosage needed.



The work is complemented by a $32.8 million grant from the NIH to Emory and the University of Georgia to support a center on influenza pathogenesis and immunology research. The center focuses on improving the effectiveness of flu vaccine by studying how influenza interacts with its host and how flu viruses are transmitted. —Stone Irvin

When swine flu arrived in Georgia

Two hospitals. 41 days. 36 physicians, nurses, respiratory therapists, and physical therapy experts. One pandemic. One patient's life saved.

In April, as a new form of flu was emerging, Emory researchers were already at the forefront of studying the virus H1N1—tracking its spread across the globe, planning for its impact in the United States, and working to identify a vaccine.

But while Emory hospitals were prepared to treat patients impacted by the H1N1 virus, no one was expecting how sick the patient would be who arrived by helicopter in May. The 31-year-old mother of two young children was the first confirmed case of the H1N1 virus in Georgia. A resident of Kentucky, she already had spent more than 10 days in a hospital in Middle Georgia. She was suffering from respiratory failure with a dangerous blood clot in her lungs. Unable to breathe on her own, she needed the advanced care available only at a tertiary care center like Emory.

Atypical of other flu viruses, the one contracted by this woman was still present. "As a result, her lungs were stiffening – unable to expand and contract," says her Emory doctor, David Schulman.

Isolated in a special ICU room that is sealed from the rest of the hospital with a reverse filtered air flow, she was placed on a breathing machine called an oscillator. It takes literally hundreds of tiny breaths per minute into the stiffening lungs to deliver more oxygen into the patient's bloodstream.

"She was certainly one of the sickest early patients across the country," says Emory infectious disease specialist Bruce Ribner, who collaborated with several health agencies in studying the patient's case and outcome.

After two weeks, the patient improved enough to be taken off the ventilator and to transfer to Wesley Woods Hospital, an Emory facility noted for its expertise in the care of geriatric and chronic care patients. There, she relearned how to perform simple tasks (using a fork and spoon, typing on a laptop keyboard) that she had lost during a month in a coma.

Today, the patient is back home with her husband and children, and she still keeps in regular contact with many of her Emory nurses and doctors. —Lance Skelly

The rescue imperative: a conversation with Tim Buchman

Tim Buchman came to trauma surgery by the same route as many of his patients: injured. When a reckless driver plowed into his car, temporarily leaving him in a wheelchair, the trauma was "a personal epiphany" for the Johns Hopkins surgical resident. He discovered in himself what he calls "the rescue imperative."

Acting on that imperative, Buchman recently arrived at Emory as the founding director of the new Center for Critical Care—the first such center in the nation to focus exclusively on critical care. Emory's goal is to fundamentally change the critical care process to get better patient outcomes at lower costs. Emory is starting to do that by integrating all intensive care units (ICUs) throughout all its hospitals. While existing ICUs will remain geographically separate, the interdisciplinary teams who staff them will be linked under the new umbrella. That approach, says Buchman, will "standardize and harmonize clinical care, optimizing quality and making it easier for patients, families, and their personal physicians to understand and participate in the care process."

Tim Buchman wants to fundamentally change the critical care process to get better patient outcomes at lower costs in a brand new center at Emory.

As the newest interdisciplinary center at Emory's Woodruff Health Sciences Center, the Emory Center for Critical Care also will "fulfill the Emory mantra of discovered here, practiced here, taught here," says Buchman.

The new director has a unique set of education, training, and research skills that make him an ideal person to lead the effort. He holds PhD and MD degrees from the University of Chicago, and he is one of a select group of trauma surgeons in the country with research experience in molecular biology and genetics. His research passion is predictive biology, and he believes that with current knowledge and "data density," clinical science should soon be able to anticipate which patients will go into seizure or anaphylactic shock. Increasingly, he says, the clinician's job will be to see into the future of each patient and change that future for the better.

"We want to do for patient care what modern meteorology did for weather forecasting," he says. It combined unprecedented observational data with a better understanding of the laws of physics and began to allow people to make plans based on what was *going* to happen.

Buchman has not only the background but also the energy to carry out his charge. He lifts weights in Emory's Blomeyer gym at sunrise most mornings. In his office, he keeps open four computer displays to move easily among clinical care, predictive biology research, and mountains of administrative details. (Question: How many computers does he have at home? Answer: "You don't want to know.") He maintains an airline transport pilot's license, having learned to fly years before he learned to drive. His wife is Barbara Zehnbauer, an Emory adjunct faculty member who is branch chief of Laboratory Performance Evaluation and Genomics at the CDC.

Despite his high energy, Buchman appears serene, focusing his entire being on what is happening at the moment. When he sits down with a patient, family member, or colleague, he puts down the coffee cup that accompanies him everywhere and does not pick it up again until he is ready to go—an intentional gesture. His eyes do not wander. That person has his entire attention. Nothing is more important.

He knows doctors can be intimidating. He is not. He seldom wears a white coat. He often holds a patient's hand. He introduces himself as Tim. He shares puns, admittedly very bad ones. His mascot, given to him by a team member at his first job as director of the surgical ICU and trauma center at Hopkins, is a beanie baby beaver named, appropriately enough, Bucky. On clinical service in Emory's 5E surgical ICU, he begins rounds every morning at what is called Bucky's Corner, alongside critical care team members and young physicians in training.

"I'm the leader, not the owner; the coach, not the quarterback," Buchman says. "Critical care is best delivered by a team of geographically dedicated professionals, not just intensive care doctors but also nurses, respiratory therapists, pharmacists, nutritionists, and the list goes on. With the right people—our professional "family of choice"—exceptional care will yield great outcomes. That's our plan." —Sylvia Wrobel

For more information on the new center, call 404-712-2654.

a drive-by-tweet for health sciences

With new media on the Internet expanding in a flurry of tweets, pokes, podcasts, vlogs, and blogs, sometimes the advances are hard to keep up with. But despite the expanding new ways (not to mention words) available to distribute information online, Emory's health communicators have waded into the storm of vocabulary and new media with an array of Twitter accounts, Facebook pages, iTunes University features, YouTube videos, and health blogs.

"At the end of the day, it's about making our patients feel they are a part of the Emory community," says Jeffrey Molter, associate vice president for health sciences communications.

The cyber realm

Emory's Woodruff Health Sciences Center (WHSC) recently partnered with the *Atlanta Journal-Constitution* and CNN in the cyber realm. The Doctor Is In blog at ajc.com brings Emory's medical expertise to AJC readers, while CNNhealth.com features an interactive section where Emory neurosurgeon and CNN correspondent Sanjay Gupta leads a team of experts to answer health-related questions. Emory oncologist Otis Brawley and Emory psychiatrist Charles Raison have joined Gupta as two of the experts on the team. One of Gupta's recent posts, for example, shared his experience of contracting the H1N1 virus while on assignment in Afghanistan.

Visitors to iTunes University can now access a range of health information from Emory, including Sound Science, a podcast that highlights cutting-edge medical research. For those interested in a new and faster approach to fighting flu, a recent podcast with Emory Vaccine Center Director Rafi Ahmed is a must. (Hint: think monoclonal antibodies.) Now it's easy to work a favorite episode of Sound Science into the party mix, between T-Pain's Buy You a Drink and Rihanna's Umbrella, of course.

YouTube has created an avenue for the WHSC to carve out a space for news of medical advancements and research among the stream of pet videos, comedic short films, and goofy montages that have always found a home on the site. On Emory Health Source on the YouTube channel, viewers can watch videos about topics like El-E, a robot that assists people with motor impairments, or click through a range of other health-related features, like Emory's use of 3-D imagery to catch breast cancer early.

A glossary for the technically challenged

Blog (Contraction of weblog)—a website with regularly posted content, including commentary, events, graphics, or video

Blogosphere—collective term encompassing all blogs and their interconnections

Posting to the wall—when a Facebook user posts a public comment on another user's profile

Pokes—a feature without any specific purpose that allows users to virtually poke one another

Status—a short line of text that users post to their profiles to inform friends of current thoughts, locations, or actions

Podcast—an audio file made available on the Internet

Twitter—network of profiles that allows users to follow others and be followed

Tweet—a short status update of 140 characters or less

Live-tweet—posting tweets about a subject as it is happening

Tweet-dropping—eavesdropping on someone else's home page

Drive-by-tweet—a quick post in between tasks

Of twitters, pokes, and patients

Did you catch the analysis of health care reform by Emory's Kenneth Thorpe during the debate this summer? People who signed up for the health sciences' Twitter service did. Emory tweets about the latest in patient services and invites facebookers to write on its walls. Questions and comments range from the important (patients voicing questions about services) to the commonplace (the date of Emory's next Six Flags night).

Beyond Twitter and Facebook, the WHSC also has launched a health blog. Every story posted allows readers to share information across an array of websites to make the center's medical expertise available throughout the cyber world of social networking. A group of links (labeled "tag cloud") organize the site into an easily navigable nebula. There is even a Twitter-compatible sidebar that allows users to easily connect and share in a cacophony of tweets. The most recent news from Emory's various Twitter pages shows up at the top to entice online "birds" to follow up on the doctors instead of the other way around. —Stone Irvin

WEB CONNECTION *To explore Emory's cyber connections, visit:*

emoryhealthblog.com
blogs.ajc.com/better-health
itunes.emory.edu
twitter.com/emoryhealthsci
youtube.com/user/EmoryHealthSource
youtube.com/user/EmoryUniversity

Insulting injury: Emory joins CDC network

Consider these statistics: injuries are a leading cause of death for Americans of all ages, and millions experience an injury each year. More than 43,600 people die in traffic accidents. More than 37,000 people die of poisoning. And another almost 31,000 deaths are due to firearms. The number of emergency department visits for unintentional injuries is upwards of 27.7 million.

To address the challenges of preventing and treating injuries, the CDC sponsors a group of 11 Injury Control Research Centers throughout the United States. In July, Emory joined the network.

A $5 million five-year grant from CDC will allow the Emory Center for Injury Control to conduct research on a wide variety of injuries and their prevention and treatment. The center's activities will range from improved prevention and treatment of traumatic brain injuries to development of international public health surveillance systems and trauma registries. It also will undertake evaluation of programs to prevent child abuse and youth violence and to reduce motor vehicle injuries by addressing impaired driving and promoting use of protective helmets and safety belts.

Although the Emory Center is jointly located in the School of Medicine's emergency medicine department and the Rollins School of Public Health, the center's reach extends across campus and Atlanta. Partners in the effort include Grady Memorial Hospital, Georgia State, Morehouse School of Medicine, the Georgia Department of Human Resources, and local and state leadership.

The core and affiliate faculty, spanning several universities and areas of expertise, are widely recognized for work on a variety of topics, ranging from prevention of intimate partner violence and child abuse to promotion of sustainable pre-hospital trauma care systems worldwide.

"Connecting research to communities is a primary focus for CDC, and we are pleased the Center for Injury Control at Emory is now part of this critical research network," says Ileana Arias, director of CDC's Injury Center. "The work at Emory and in Atlanta will fill a critical gap and can help shape a better understanding of how to improve the lives of those affected so that they can live to their full potential."

WEB CONNECTION *For more information about research on injuries from the CDC, visit* **www.cdc.gov/injury.**

Making movies for monkeys

The plot: someone assembles a hat, adding stickers and other doodads, one at a time, and then dons the finished product. The audience: four rhesus monkeys at the Yerkes National Primate Research Center are quite intrigued, especially when a bit of the action changes. After viewing the movie only once or twice, the monkeys' eyes move to anticipate the next source of action, indicating that they remember the sequence in the movie, which was written, filmed, and produced by 10th-graders at the Gwinnett School of Mathematics, Science, and Technology who interned at Yerkes this summer. The production value: For Yerkes cognitive neuroscientist Elizabeth Buffalo, the ongoing eye movement studies suggest a possible way to diagnose mild cognitive impairment, a frequent precursor of Alzheimer's in humans. For the students, watching the rhesus monkeys respond to changes in their movies is proof positive that science can be fun, maybe even worth a lifelong career.

That means the eight-week Yerkes summer research and learning program was successful. Attracting students from all demographic groups to health-related sciences is both a national priority and the reason the NIH offered economic stimulus funds to selected NIH-designated primate research centers with experience in sharing the excitement of science with young students. Under a grant headed by Buffalo, the six students hired as interns spent two weeks learning the basic concepts of neuroscience. They then divided up to work under the tutelage of Yerkes neuroscientists studying topics such as cognition and memory, emotional processing, the role of the basal ganglia in Parkinson's, and how brain volume changes with age. Three high school teachers—including one from the Gwinnett school, where Yerkes director Stuart Zola serves on the board—also participated in the program, assisting in the labs and preparing lesson plans on what students learned to enrich the program at their own schools and those of other science educators in a state network. —Sylvia Wrobel

High school interns watch TV monitors (with Yerkes director Stuart Zola) to observe and record primates' reactions to the short movies they made during an educational summer program fueled by economic stimulus funds.

A Capitol rotation

While in medical school at Emory, Jackie Green (left) worked as a health policy intern at the Capitol, guided by Representative Sharon Cooper, who herself holds a masters in nursing.

Most fourth-year medical students expect their schedule to include rotations in a clinic, doctor's office, or hospital. But Jackie Green, a 2009 graduate of Emory School of Medicine, had something a little different in mind. She spent six weeks of her last semester of medical school at the Georgia State Capitol.

"Jackie was the first person with the insight to ask for a rotation at the Capitol," says Sharon Cooper, Georgia Representative of District 41, who supervised Green as a health policy intern in the Georgia House of Representatives. It was a first not just for Green but for the medical school as well.

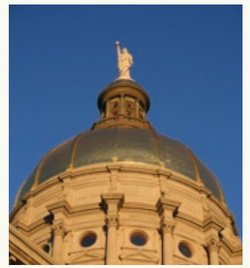
Cooper chairs the Georgia House Health and Human Services Committee, making her an ideal candidate to direct Green beneath Georgia's gold dome. A former college professor with a masters in nursing, Rep. Cooper wanted Green to get the most out of her time in the General Assembly. With Cooper's hands-on guidance, Green got a chance to work on several health policy bills and helped with the successful passage of the Medical Practice Act, which clarifies the roles and responsibilities of medical professionals.

While working with legislators on health policy was new to Green, working to influence policy was not. Previously she had served as an officer in HealthSTAT, a student-run, nonprofit group that influences health legislation. When HealthSTAT took an active role in an effort to keep Grady Hospital open, Green helped organize students for a campaign that drew attention to the hospital's plight. (See *Emory Health*, summer 2008.)

This passion for effecting positive change in health policy made Green's time spent with Rep. Cooper more than a learning experience. "It was great for me because I was invested in the policy decisions," says Green, who is now continuing her education as an internal medicine resident at Emory.

The precedent set by Green has paved the way for other Emory medical students to complete a health policy rotation with the legislature, underscored by a request from Cooper to work with additional Emory students.

> "It's the difference between watching a play and participating in the play as both a stage hand and member of the cast."
> —Arthur Kellermann



The new Emory health policy internship mirrors a long-standing program offered by the Robert Wood Johnson (RWJ) Foundation, which gives mid-career and senior health professionals an opportunity to work on health policy at a federal level. Arthur Kellermann, Emory's associate dean of health policy in the medical school, participated in the RWJ Health Policy Fellowship as a member of the U.S. House Committee on Oversight and Government Reform. He considers the knowledge gained from such programs to be crucial to medical professionals, giving a three-dimensional view of health policy.

"It's the difference between watching a play and participating in the play as both a stage hand and member of the cast," he says.

Although Georgia's Congressional delegation includes three congressmen with health care backgrounds (Representatives Tom Price and Phil Gingrey are both physicians, and Rep. John Linder is a dentist), most health care professionals shun or ignore health policy. Green's work with Rep. Cooper affirms what Kellermann describes as a duty for physician leaders to play a key role in shaping health policy for the benefit of patients, the state, and the nation. Now that Green has set the pace for future Emory medical students, there is hope that future generations of doctors in Georgia will be ready, able, and willing to do just that. —Stone Irvin

the nurse is in

An advanced nurse practitioner offers one solution for the health care crisis.

By Michelle Mott

There comes a time when we face a challenge that defines who we are— a time when meeting the demands of said challenge forces us to reexamine how we have been functioning. In health care, we are at one of those times now. Wherever we turn, the message is clear—improve quality, safety, and accessibility while making cost affordable.

Health care costs have risen to the forefront of national discussions as one of the economic factors contributing to the strain on American families, businesses, and health care providers. According to recent data from the Organization for Economic Cooperation and Development, health care costs comprise approximately 15% of the United States gross domestic product (GDP). By comparison, other major industrialized nations spend 8% to 10% of GDP on health care yet manage to make it available to a greater proportion of their citizens. Although the United States spends more on health care than other developed nations, we continually rank below peer countries when it comes to health care outcomes and patient satisfaction. Furthermore, we have a shortage of physicians, a rising number of people without insurance, and a financial crisis that may ultimately undermine efforts to address these issues.

As a nation, we are struggling to find answers. We need a solution whereby we have enough providers who can increase access to health services, provide quality care, and reduce costs. Enter the advanced practice nurse (APRN).

You may know the APRN as your nurse practitioner (NP), certified nurse midwife (CNM), certified registered nurse anesthetist (CRNA), or clinical nurse specialist (CNS). We may have worked with you or cared for you in the clinic, labor and delivery, the emergency department, or the inpatient setting.

All of these groups represent registered nurses who have masters or doctoral degrees, are nationally certified, and meet requirements for state licensure. NPs, CNMs, and CRNAs are licensed to assess, diagnose, treat, and prescribe medications for patients, and CNSs are the expert nurses in hospital units for evidence-based nursing care and interventions.

Regardless of the practice setting, our main goal is to address the patient's condition while integrating a holistic model of care. Spiritual and emotional well-being are important factors as we address a patient's concerns about disease or injury. We incorporate health promotion and health education for patients and their families in our care plan to empower them to make healthy lifestyle decisions.

In our practices, we work collaboratively with physician colleagues. The APRN-physician care model has been cited in economic, political, public health, medical, and nursing literature as a high-quality, cost-effective method to provide health care. APRNs often have lower administrative costs, and, through high-quality clinical skill and patient education, APRNs reduce costs to the health care system by assisting patients and families in making lifestyle changes that may ultimately reduce the need for costlier procedures and hospitalizations.

APRNs have a long history in the U.S. health care system, with nurse anesthetists and nurse midwives having practiced here since the early 20th century. The role of the CNS appeared as early as the late 1930s. The first NP practiced in 1965. All of these roles developed when our country needed providers with expertise to address issues ranging from improving safety and quality to increasing access to care for patients unable to afford or otherwise receive health care.

So, here we are, again, in one of those times. It is up to us as patients, providers, and administrators to funnel the frustration we feel over the state of the U.S. health care system to gain momentum. This momentum can help us reevaluate our mission, promote successful models, and create new methods of practice where others have stagnated or failed.

The APRN-physician practice model is one such model that has shown success. This dynamic approach is one of the more important ways to lower health care costs, improve quality, and foster more patient satisfaction. EH

*A certified family nurse practitioner, **Michelle Mott** is associate chief nursing officer at The Emory Clinic. An NIH-funded researcher, she holds faculty appointments at Emory in both nursing and public health. Previously, Mott coordinated the Nurse Practitioner in Emergency Medicine program at Emory University Hospital and Grady Hospital.*

Using the "r" word

Serious, and particularly honest, discussions about reforming the U.S. health care system (*Emory Health*, Summer 2009) represent a sociopolitical minefield. Health care needs are virtually infinite while resources for treatment are finite. Consequently, in the interest of equality and fairness, this must involve costs/benefits analysis in the allocation (rationing) of health care resources. With the sophistication and accuracy of available metrics, quite conceivably a monetary value can be placed on a human life. How many politicians or voters would support the use of such parameters to determine who receives medical treatment? Further, U.S. politicians at the highest levels of government have been admonished not to use the term "rationing" since this is considered a politically threatening word. But not using "rationing" is disingenuous, and no issue can be effectively resolved until all obvious facets of the issue are honestly considered. Given that political efforts to resolve a spectrum of critical issues facing the United States have produced only marginal results, any meaningful health care reform will (A) not likely occur or (B) consist of politically expedient measures that accomplish little beyond shoving the issue(s) down the road. A rather bleak—but honest—assessment.

Dale E. Hunt, Professor Emeritus
of Dentistry, Atlanta, GA

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Have a plan.

GROWING UP ON A FARM in Cuthbert, Georgia, Viola Castleberry learned simple but important lessons: be honest, work hard, and be responsible. And so she took responsibility for her younger brother, Bill, who has a learning disability.

Now he is 84 and living with Parkinson's disease, and she is taking responsibility for advancing a cure.

Castleberry's bequest to the Yerkes National Primate Research Center will support the nation's best scientists as they work to unravel the mysteries of neurodegenerative diseases such as Parkinson's and Alzheimer's.

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