Threats of pandemic flu, bioterrorism, natural catastrophes: how the university is preparing to cope
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**GETTING TO KNOW YOU**

Fred Sanfilippo, MD, PhD, arrived to lead the Woodruff Health Sciences Center on October 1, as Michael Johns, the center’s CEO from 1996 to 2007, transitioned to Emory University to serve as chancellor. This new leader (see opposite page) joined Emory from Ohio State, where he was senior VP and executive dean for health sciences, overseeing the OSU Medical Center with an annual budget of $1.6 billion and 2,500 faculty and 12,000 staff members. Well-known as a transplant immunologist and predictive health promoter, he also has served at Johns Hopkins and Duke.

**What do you think?** *Emory Health Sciences* welcomes your comments and responses to our inaugural issue. Please send your feedback, address changes, letters to the editor, and other correspondence to *Emory Health Sciences*, 1440 Clifton Road, Suite 318, Atlanta, GA 30322; send email to: rhonda.mullen@emory.edu; or call 404-727-8166.
The good side of change

Emory University and the Woodruff Health Sciences Center are places in constant flux. We are charting new waters in health care, redefining the way 21st-century medicine is delivered, and creating models for the health care of the future. Change also is afoot in our schools, as we open new buildings, develop new curricula, and send students around the world to learn to solve global health challenges. Change likewise is coming to our publications.

Many of our readers are familiar with our magazine Momentum. That publication, which was the brainchild of Michael Johns, my predecessor here at Emory and now chancellor of the university, captured more than 20 national and regional awards and was warmly received by its audience of faculty, staff, and friends of the health sciences. Now we want to share the big picture health care issues and challenges, the ground-breaking research, and the clinical care updates regularly covered in Momentum with an expanded audience—in our community and across the country.

We’re excited to continue to share our discoveries and vision of 21st-century health care with you in Emory Health Sciences, a retooled magazine focused on the Woodruff Health Sciences Center. In its pages, we highlight the remarkable work being done throughout our center in education, teaching, research, and patient care. We pledge to bring to you a quarterly publication packed with new cures for old ills, the latest health care policy analysis, cutting-edge breakthroughs in basic science that can be translated into patient care, and novel ideas on how to revitalize medicine to put the patient at the center of all we do.

In this issue, you’ll see that we’re doing just that. Our cover story takes you behind the scenes to see the steps the university is taking for emergency preparedness. Emory is a major resource for our region not only for excellent health care every day but also in the case of extraordinary or catastrophic events. We must be prepared for the worst, and we must all share and build the knowledge and experience to respond under the most challenging circumstances. Emory Health Sciences also allows readers to spend a night with the trauma team at Grady Hospital, the only level-1 trauma center in north Georgia. We’ve also included science features on a simple new test for colon cancer now in development and a common compound that may help boost the immune system to fight against flu.

In my first few months here, I can see that taking on difficult and important challenges is something that comes naturally in the health sciences at Emory, something reflected in these pages. I look forward to tackling change with you in the months and years ahead.

Fred Sanfilippo, MD, PhD
Executive Vice President for Health Affairs, Emory University
CEO, Woodruff Health Sciences Center
Chairman, Emory Healthcare
Walt Orenstein, director of vaccine policy and development for the Emory Vaccine Center and former director of CDC’s National Immunization Program, is helping Emory prepare for a pandemic of bird flu.

Threats of pandemic flu, bioterrorism, natural disasters: how the university is preparing to cope

By VALERIE GREGG • Illustrations by BRIAN HUBBLE
In September 1918, a doctor at an Army base near Boston sent a colleague his thoughts:

“These men start with what appears to be an attack of la grippe or influenza, and when brought to the hospital, they rapidly develop the most vicious type of pneumonia. Two hours after admission, they have the mahogany spots over the cheek bones, and a few hours later you can begin to see the cyanosis extending from their ears and spreading all over the face…. It is only a matter of a few hours then until death comes, and it is simply a struggle for air until they suffocate. It is horrible. One can stand it to see one, two, or 20 men die, but to see these poor devils dropping like flies sort of gets on your nerves. We have been averaging about 100 deaths per day…. My total time is taken up hunting rales—rales dry or moist, sibilant or crepitant or any other of the hundred things that one may find in the chest—they all mean but one thing here: Pneumonia. And that means in about all cases, death.”

By the next year, the Spanish Flu was everywhere—New York, Atlanta, San Francisco. In Philadelphia, 13,000 died in a matter of weeks. Gravediggers were in such short supply that family members paid funeral homes to dig their relatives’ graves themselves.

This particularly lethal and contagious strain of influenza infected people on every continent and eventually killed more Americans than World War I. More than 20 million people died worldwide.

While pandemics are rare, they can have devastating consequences. During the 20th century, influenza reached pandemic proportions three times. While pandemics in 1957 and 1968 fell short of the deadly strain of 1918, they still did their fair share of damage.

“Concerns about pandemic influenza have intensified recently because of an unprecedented sustained outbreak of a highly virulent new influenza virus called H5N1 among birds on three continents,” says Walter Orenstein, Emory infectious diseases expert. “The virus has led to more than 300 human cases and more than 190 deaths.” There is fear that this virus or a variant may adapt to humans and lead to widespread transmission from person to person, resulting in a pandemic.

Infectious disease experts agree that it’s not a matter of
if a deadly flu pandemic will occur, but when, according to Orenstein. Estimates from the U.S. Department of Health & Human Services predict that approximately 30% of the U.S. population (90 million) would become ill, with half of those seeking medical attention. Between 865,000 and 9.9 million would need hospitalization, and between 200,000 and 2 million would die.

**Disaster 911**

It can be as quiet as a virus taking hold in a person’s lungs or as loud as the Twin Towers crashing down in New York City.

Either way, catastrophe is nearly always unexpected. Whether caused by a terrorist, microbe, or cataclysmic force of nature—the punch in the most devastating disasters lies in their ability to catch victims unaware.

Controlling catastrophe, or at least taking out the sting, is the goal of a new Emory Office of Critical Event Preparedness and Response (CEPAR). Born of a task force charged with bolstering Emory’s capacity to respond to pandemic flu, CEPAR has a broad challenge. Its charge is to develop plans and responses for all hazards, from public health emergencies such as pandemic influenza to a plane crash that might bring large numbers of casualties to campus.

Fresh after an all-night shift in the Emory Hospital emergency department, CEPAR Executive Director Alexander Isakov offers perspective on the enormity of his mandate. “Emory has a wealth of expertise and resources,” he says. “CEPAR will help the university make the best, most efficient use of all these assets during times of great need, and it will facilitate greater collaboration with the broader community.”

Those resources at Emory include two disaster preparedness centers, located in the Rollins School of Public Health (RSPH). The Center for Public Health Preparedness and Research—funded by the O. Wayne Rollins Foundation on the heels of 9/11—studies a wide array of current and emerging public health crises and trains students, corporate employees, and public health officials to answer those threats both locally and internationally. The Academic Center for Public Health Practice, which works closely with the state of Georgia, is part of a CDC network to train front-line public health workers to respond to major public health events.

In times of crisis, CEPAR will coordinate the university’s response from an operations center at the former American Cancer Society building on Clifton Road. The university has devoted four full-time positions to the effort, including Isakov, who also directs Emory’s pre-hospital and disaster medicine section, and Robert Nadolski, former vice president for Grady’s emergency medical services and Level I trauma center, who is CEPAR’s senior administrator. They will continue their long-running emergency preparedness work with groups like the Atlanta Regional Commission and the Atlanta Metropolitan Area Council of Governments.
the Georgia Emergency Management Agency’s All Hazards Council, the Department of Homeland Security’s Atlanta Urban Area Security Initiative, and the state’s Regional Coordinating Hospital System.

“CEPAR will be a physical place, but it also will be one centralized source for understanding Emory’s activity relative to emergency preparedness. We’ll then see how all of our efforts might best be integrated,” says Isakov. “It’s a concept of operations, and it’s also a framework for development of protocols and thresholds for various types of responses.”

What if…?
On April 16, 2007, in Blacksburg, Virginia, a shooter blocked the doors to Burrus Hall. No police in. No students out. More time to kill. He went by the moniker Question Mark and had already killed two classmates in a Virginia Tech dorm earlier that morning. He took the stairs to the second floor and opened fire, Columbine-style, into classroom after classroom, killing 32 and wounding 25 before killing himself. The deadliest school shooting in history, this tragedy left students, staff, and faculty on campuses everywhere asking, “What if…?”

Emory had long considered emergency response strategies even prior to CEPAR’s creation, says Isakov. However, the events at Virginia Tech gave planners cause to reflect further on those strategies.

“The university already had invested in communications technologies designed to facilitate a more robust emergency notification process,” says Isakov. “Obviously, having a hospital emergency department on campus gives us an edge. We also have our own emergency medical first response unit manned by students 24/7, under supervision of the Emory Police Department. It’s a unique program, where students can take a course and become state certified as emergency medical technicians.”

The unit’s average response time is 3.5 minutes to answer calls for a territory including the Emory campus, CDC, Yerkes National Primate Research Center, and Wesley Woods Center. Two quick response vehicles and a reserve vehicle are always on call. The dispatcher handling a particular 911 call will send DeKalb County Fire and Rescue if further expertise or patient transport is needed.

Integrating “gems” like this program into emergency response plans is an important part of CEPAR’s role. Emory began an enterprise-wide risk management program more than a year ago, and CEPAR has an integral role in that process, says Isakov.

Ebola for chickens
In 1997, a three-year-old boy died of a strain of bird flu, bringing on the mass slaughter of domestic chickens and geese. Since then, the flu strain otherwise known as H5N1 has killed more than 60 people in Asia.

Scientists have closely followed H5N1, which has been responsible for the deaths of millions of birds on every continent except the Americas. So far, the virus has shown a 50% mortality rate among humans but is actually very difficult
Pandemic viruses can arise in two ways. A bird (avian) virus can mutate until it becomes adapted in humans (as happened with the 1918 strain). Alternatively, both an avian and human-adapted virus can infect a host, such as a pig, at the same time. The exchange of genes gives rise to new viruses, which are easily spread from human-to-human and to which virtually all humans are susceptible. This scenario, known as reassortment, led to the 1957 and 1968 pandemics. Future pandemics could arise from a combination of both mechanisms.

Some similarities between H5N1 and the deadly flu strain of 1918 raise concerns. Both are extremely virulent when they infect humans, and unlike annual seasonal outbreaks of flu that tend to more severely impact the elderly, these viruses cause severe disease in young, healthy adults. “What is worrisome about this H5 virus is that it is distributed widely in nature and has mutated and become more virulent over time in birds,” says Orenstein, director of vaccine policy and development for the Emory Vaccine Center and former director of CDC’s National Immunization Program. “If you’re a chicken, it’s a real disaster. It’s highly fatal and geographically widespread in Asia, Africa, and Europe. The fear is that bird-adapted virus would be carried by wild birds from Siberia to North America. Or it could arrive in North America in the wild bird trade and then come directly to the United States through migration.”

The virus has caused severe illness among people in 12 countries and killed people in 11 countries. The greatest number of cases has been reported from Indonesia and Vietnam, but human cases have occurred in places extending from Egypt and Nigeria. The numbers are small thus far because the virus does not reproduce well in the nose and throat. Instead the current H5N1 viruses must get all the way down into the lungs, leading to pneumonia and an ensuing immune “cytokine storm” that often kills victims through acute respiratory distress syndrome and shock.

The virus would have to undergo significant mutations to become more infectious among humans and create a pandemic, Orenstein says. However, because it is now so widespread in birds, those opportunities to mutate are present. “One problem with influenza viruses is that they are not faithful to each other,” he says. “They mutate easily.”

That’s why it’s so difficult for health officials to forecast even the next year’s form of annual flu, much less pandemic flu. “We can either do nothing and hope we’re lucky,” says Orenstein, “or we can prepare in ways that will help us anyway, such as establishing a vigorous annual vaccination program. Building vaccine production capacity and the infra-

Bruce Ribner supervises a special quarantine and treatment program that Emory runs for CDC employees who become sick with serious communicable diseases in the field.
structure to deliver vaccine would help tremendously should we need to vaccinate large numbers of people quickly in the event of a flu pandemic.

21 days
This past June, the first quarantine order in 40 years was issued for an Atlanta business traveler diagnosed with extensively drug-resistant tuberculosis (XDRTB). He was transported from Hartsfield International Airport in a special Grady Health System ambulance to a locked isolation unit that Grady operates for the Georgia Department of Corrections. “We have developed a special team to transport people with serious communicable disease in support of Emory, the CDC, and the airport. It’s a real community asset,” says Isakov, who directs the Biosafety Transport Unit.

Tuberculosis, even XDRTB, is one thing. Marburg hemorrhagic fever is quite another, says Bruce Ribner, hospital epidemiologist and director of a CDC special containment unit at Emory Hospital.

In 2005, a CDC doctor stopped in Johannesburg before flying home from a six-week assignment in Angola, where he had been working on an outbreak of Marburg, one of the deadliest, most contagious, and most feared diseases. When his plane refueled at Cape Verde in the middle of the Atlantic Ocean, the doctor called CDC to report symptoms he knew could land him in hospital isolation for 21 days: diarrhea, vomiting, fever, and chills. All precursors to Marburg.

CDC called Emory.
“CDC pays for us to be in a state of constant readiness in case one of their employees gets sick,” says Ribner. “Luckily, this young man turned out to have something like traveler’s diarrhea.”

CDC has renovated three patient rooms in Emory Hospital with state-of-the-art pathogen-containment capacity. Ribner supervises the operation, which includes a cadre of 21 nurses trained to work in this unit and 20 Grady EMS special operations paramedics trained to transport a sick person to this unit. The unit has served as a prototype for others across the country.

“CDC has about 350 research labs in the city of Atlanta and hundreds of epidemic intelligence officers investigating disease outbreaks with very serious communicable diseases,” says Ribner. “They needed an appropriate place for them to be treated and quarantined, if necessary. Before Emory, all they had was a two-bed unit in Fort Dietrich, Maryland. They obviously needed something local.”

While the Grady isolation unit locked the XDRTB patient
in, the Emory Special Isolation Unit aims to keep people out. Several layers of doors are alarmed from the outside in. Glass-covered lab facilities are built into the unit’s nursing station so patient specimens are impossible to mix with those of the general hospital population, and the air flows directly outside through sensitive HEPA filters.

“Anyone can do airborne isolation,” says Ribner. “We already have up to 30 airborne isolation units here for simple contagious diseases. But for extremely contagious, serious infections, we need this unit.”

**Fighting forgetfulness**
The field of disaster preparedness can be difficult because people tend to forget how bad things can get. “Planning fatigue,” Isakov, a former Navy doctor, calls it.

Just after 9/11, the skies were empty, commutes were short, and suburban streets were eerily quiet. A month later, weapons-grade anthrax mailed in letters killed three U.S. postal workers and contaminated Congressional offices. A common fear held Americans rapt.

Imagine the country’s fear in 1919, at war with the world for the first time and people dying of an influenza that left a blood-tinged foam about their mouths and nostrils. The public was amenable to measures that today might seem draconian. In San Francisco, it was illegal to leave the house without a gauze face mask, and people largely stayed home en masse when told to do so. The threat of death hung all around.

Such public obedience is not likely in this day and age. In fact, drive-thru flu booths are one of the more creative recommendations of Emory’s Pandemic Flu Task Force.

Remembering disasters past, taking inventory of what went wrong and what went right in the aftermath, is only the first step. Hospitals and universities can take the lessons learned and place them in context. They must ask the right questions and muster the right forces. Emory Healthcare and Emory University have a leg up, says Isakov.

“We should all recognize Emory’s substantial commitment to safety and emergency preparedness. As I like to say, ‘There’s no billing code for disaster preparedness.’ It’s not a revenue generator. It requires leadership with vision and acu-
The Friday Night Gun and Knife Club, the Monday morning rush hour wreck, the Tuesday afternoon construction site fall: Grady’s trauma team sees the most serious injuries in north Georgia.

In the Red Zone

It is late afternoon on a Friday in early fall when the paramedics wheel a young woman into the trauma room at Grady Memorial Hospital. Barely conscious, she has just survived a car crash, her vehicle rolling over before coming to a stop. The paramedics have called ahead, and the trauma team is ready. They don’t know much yet, but as the stretcher passes through the double doors, a scene unfolds. The paramedics call out vital signs, and a nurse simultaneously transcribes the information. The woman is rolled to Bay 2, and the trauma group springs into action—surgeons, emergency physicians, nurses,
x-ray technicians, and medical students moving together in a well-rehearsed dance. They assess the patient's level of consciousness, check her airways, look for bleeding. Someone takes x-rays while others pitch in to stabilize the patient. The images are processed, the blood work examined, the tests quickly completed, and a plan takes shape based on the woman’s condition.

Such a scene occurs daily inside Grady’s Red Zone. This is the threshold to the hospital’s trauma bay, where those with the most severe, life-threatening injuries find help. Grady is where patients want to be if they’ve been shot, stabbed, severely burned, or seriously injured in a car wreck. The Red Zone is where they have the best chance of staying alive.

**Beyond a place**

“Critical care is a concept, which takes hold the moment a patient arrives,” says Grace Rozycki, Emory’s chief of trauma/surgical critical care at Grady. “Critical care is not a place. It is not a unit. It is a concept, and that concept moves with the patient during the entire course of treatment, including rehabilitation.”

Most trauma patients are routed from the trauma area to the operating room or directly to intensive care. They eventually wind up in rehabilitation. Although there are various stops and stages of their care, the process is a continuum, says Jeffrey Salomone, the Emory cardiothoracic surgeon who is chief of general surgery at Grady. Both doctors and nurses keep a close eye on patients’ progress, sometimes following up even after patients have returned home.

Located in downtown Atlanta, Grady has the only level-1 trauma center between Macon and Chattanooga. A level-1 trauma center gives patients immediate access to critical care and vital resources, such as on-site surgeons, trauma and intensive care nurses, emergency physicians, pharmacists, the latest diagnostic equipment, and operating rooms. That translates into a better chance of survival for those with the most severe injuries. Without Grady, Atlanta would be the only top 10 metropolitan area in the United States without a level-1 trauma center.

**What's hurting you, sir?**

Later that Friday night, a middle-aged man is wheeled into the trauma room, Bay 3. Georgia clay splatters his face, arms, and clothes, the result of a motorcycle accident. The trauma team peppers him with questions: “What’s hurting you, sir? Does this hurt? Does that hurt? Are you allergic to anything, sir?”

The man’s clay-caked helmet and clothes lay in an orange heap on the floor alongside the gurney.

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“When the patient comes to us, he’s a blank sheet,” says Rozycki. “We don’t know what’s wrong. Many can’t tell us about their symptoms, and even if they can, there’s a certain level of mystery because these aren’t the best of circumstances.”

Point of fact, in Bay 2, doctors are trying to determine if the woman from the car accident has internal bleeding. Her x-rays reveal facial fractures, a broken pelvis and arm, and swelling to her face.
The sickest of the sick

Last year, Grady admitted 4,000 trauma patients. Of those, approximately 3,000 stayed more than 24 hours, according to Salomone. That includes 425 patients who were admitted to Grady’s burn unit, one of only two regional burn centers in Georgia. “It’s the most badly injured or the most ill who get admitted,” Salomone says. “We’re here to take care of the sickest of the sick.”

The patients who come to Grady for emergency treatment fall into three categories: those who meet trauma criteria and are sent to a trauma bay, those with unusual symptoms who are examined by both emergency and trauma physicians and then admitted to the hospital, and those with relatively minor symptoms such as broken bones and cuts who need emergency care but not that of the trauma team.

“Trauma medicine goes beyond emergency medicine because it involves a broad spectrum of disease,” says Rozycki.

While many people think of trauma doctors as handling gunshot and stab wounds, those make up only a small percentage of cases at Grady. “Car wrecks, motorcycle crashes, and falls make up at least 70% of trauma care seen in the hospital,” says David Feliciano, an Emory surgeon who is Grady’s chief surgeon.

What’s more, he adds, trauma is an injury that is a surgical disease. It can be blunt—as in car accidents—or it can be penetrating—gunshot wounds, stab wounds, and impalements.

Surge capacity

In July 1999, Grady’s trauma team got word of an office shooting in the Buckhead neighborhood of Atlanta. Of 21 people who had been wounded, nine were dead at the scene. Seven of the gunshot victims came to Grady, and six of those needed emergency surgery. Although the tragedy occurred during a shift change at the hospital, the nurses and anesthesiologist on call stayed so that all six patients were able to be taken to the operating room on arrival. “We were running the equivalent of six emergency ORs at 3:00 in the afternoon,” Salomone remembers. “There’s no other hospital in this town that can do that.”

While needing this capacity is not an everyday event, it does occur repeatedly. For example, in March 2007, a chartered bus carrying the Bluffton, Ohio, college baseball team to a tournament in Florida overturned on an exit ramp off I-75 and crashed to the interstate below. The accident claimed the lives of five students, the bus driver, and his wife. Dozens of other players needed immediate treatment. “The day of the Bluffton bus crash, the media kept asking, ‘How many people...
did you call in to help?’” Salomone says. “None. We took care of things with the people who work here. What we have is surge capacity—the ability to accommodate people who show up at your door all at once.”

That ability is enabled by trauma surgeons who staff the hospital 24/7, required for level 1 status and reinforced by Feliciano as chief surgeon. Salomone himself lives less than a mile from Grady, a factor that he considered when purchasing a place to live. That proximity also helps him in his volunteer duties to care for any police officer who becomes seriously injured on the job.

**Those of us who go into trauma medicine** like to take people who are critically ill and contribute each day to them getting better, going back to work, and returning to their lives. —Trauma surgeon Jeff Salomone

**Don’t move**

It’s after 10 pm, and the motor vehicle accidents keep rolling in. The latest casualty, a young man with his hair damp with blood from facial lacerations, is told to lie still in Bay 4. “Just answer yes or no,” they tell him. “Don’t move.” Then come the questions: “Any pain here? Any allergies? Any drug use? What about anything to drink?”

Now on pain medication, the motorcyclist in Bay 3 is asleep. Soon he will be admitted for observation and further care, but chances are he will not need surgery.

However, the woman in Bay 2 will. Her surgery will take place in one of Grady’s 16 ORs, 14 of which are usually in use during daytime hours. Available just outside the OR are 48 units of O negative blood, more than most hospitals keep in their blood banks. Two surgical nurses are on duty, awaiting a minute’s notice to ready the OR when a patient needs emergency surgery.

After surgery, trauma patients are transferred to a 20-bed surgical ICU, where the woman in Bay 2 is eventually bound. “This unit has nurses with the strongest intellect and capability in the city,” says Salomone. “They work 12-hour shifts with some very sick patients, and they are the primary reason many of these patients get better.”

**The job doesn’t stop here**

“Those of us who go into trauma medicine like to take people who are critically ill and contribute each day to them getting better, going back to work, and returning to their lives,” says Salomone.

The woman in Bay 2 did recover and return home to her everyday life. Likewise, all but five of the Bluffton kids returned to Ohio and the ballpark. Salomone and his colleagues even made a trip recently to see the team play. As they sat in the stands months after the bus crash, they felt the continuum of care had come full circle from the Red Zone to real life.

**WEB CONNECTION** Grady Hospital is experiencing a serious financial and governance crisis. For the latest update on the status of the hospital, see [www.emory.edu/grady/](http://www.emory.edu/grady/).
Robin Bostick wants to do for colon and rectal cancer what earlier scientists did for heart disease. He is working to develop a simple blood test to detect biomarkers of risk that can be treated before disease occurs. The epidemiologist already has identified biomarkers that predict colon cancer in apparently healthy people. And he has evidence that some of these can be modified in as little as six months with supplemental calcium.

But does altering the biomarkers of risk alter the risk itself? Bostick believes it does. He is studying more than 1,300 people to see if calcium and vitamin D will alter the biomarkers and prevent the recurrence of colon polyps, a precursor to colon cancer. His findings could change dramatically the screening for and prevention of colon and other cancers.

The parallel with heart disease
After decades of research, biologic measurements of risk for developing cardiovascular disease have become a standard part of medical exams. Cholesterol, blood pressure, blood sugar, and body size/shape are simple and relatively inexpensive to measure and monitor. Drug treatments and lifestyle changes such as diet, exercise, and stress reduction have immediate, quantifiable effects on biomarker “scores,” helping reinforce healthy behaviors. As a result, death rates from heart disease have been falling, sometimes dramatically, for close to three decades.

By contrast, the statistics for colon cancer are less encouraging. It is second only to lung cancer as the leading cause of cancer death in the United States for both men and women. Deaths from colon cancer have experienced only a modest decline, much of that due to earlier diagnosis and diligent removal of precancerous polyps. No clear biomarkers of risk for colon cancer have been found.

Not, that is, until Bostick discovered a panel of biologic changes and differences in the mucosal tissue of people who later developed colon cancer, which differed significantly from those who remained cancer-free.

A calcium escort
When Bostick became interested in the impact of calcium on disease, a link between calcium and colon cancer was still a far-flung concept. However, epidemiology studies tracking people who emigrated from countries with low colon cancer rates indicated high correlations with the disease and Western diet and lifestyle.

Bostick also noticed the complex molecular pathways from normal to cancerous cells contained multiple points where diet, calcium, and vitamin D can have an effect, both singly and in tandem with other interactions. For example, the body produces bile acids when it digests fat. While these acids can cause damage to the colon, dietary calcium can intervene and bind to the bile molecules, escorting them out of the system before they cause harm. Vitamin D not only enhances the absorption of calcium but also stimulates the production of
an enzyme that degrades bile acids. It also directly affects the cell cycle and immune system.

Bostick became so interested in this research that he made a life-changing decision to close his medical practice in Beaufort, South Carolina, and pursue a research career. That eventually led him to Emory, where he is a Georgia Cancer Coalition scholar and a professor in the Rollins School of Public Health.

He has continued to hone in on identification of new biomarkers for colon cancer. Among these discoveries are early alterations in the genes involved in the normal structure and function of the colon; subtle aberrations in the normal growth, repair, and death cycle of the cells themselves; the appearance of inflammation; and the rise of potent growth factors, hormones that stimulate proliferation and differentiation of cells.

Growing evidence

Bostick's hunch about the chemopreventive effects of calcium is no longer a far-fetched hypothesis. In an initial groundbreaking study of 200 participants, he analyzed mucosal tissue to demonstrate that cell proliferation is a powerful biomarker of risk for developing colon cancer. He recently completed a study of the effects of calcium and vitamin D, separately and combined, on a panel of biomarkers in 88 Emory Clinic patients with precancerous colon polyps. The biomarkers are of protein expression such as p21 (colon cancer differentiation, or maturation) and COX-2 (colon cell inflammation). Initial data analysis indicates that treating patients with both calcium and vitamin D has a synergistic effect on the biomarkers.

Although the approach works for biomarkers, will it work in clinical outcomes? Bostick and colleague Jack Mandel are trying to find out as principal investigators of the South Carolina and Georgia components of a multicenter study involving 2,457 people who have regular colonoscopies. Headed by Dartmouth’s John Baron, the study investigates whether adding vitamin D to calcium supplementation will reduce polyp recurrence.

Bostick also won additional funding from the National Cancer Institute to piggyback biomarker research with this study. The additional research will confirm whether treating biomarkers actually leads to decreased polyp occurrence in a large population. It also will examine questions such as if and how the biomarkers vary over time, whether they appear differently in different places in the colon, and if the biomarker response to treatment varies in people with different vitamin D receptors or in those taking nonsteroidal anti-inflammatory medications.

Just a little finger prick

Bostick is ready to take the next steps toward development of an effective biomarker screening test. That step involves a large prospective study of people who have never had a polyp, much less any sign of colon cancer, to determine if biomarkers can predict who will develop colon problems. As a part of this process, Bostick wants to develop a simple and easy test, such as identification of biomarkers in blood, urine, or mucosal tissue.

Nanotechnology may enable him to make such tests fast and cheap. Working with the quantum dot technology available at Emory and Georgia Tech, he is creating software that automatically scans slides to quickly and accurately quantify the presence and quantity of biomarkers in mucosal tissue. What used to take a researcher six hours can now be done by a machine in 15 minutes.

If Americans followed the American Cancer Society’s recommendations for regular colonoscopies, gastroenterologists would be unable to meet the demand. While the finger prick screening test that Bostick envisions would not do away with colonoscopies, a cheaper, easier biomarker test would more likely be accepted and used by more people. The biomarker screening will provide better information on who needs a colonoscopy when and how often, and will provide additional motivation for those who most need a colonoscopy to get one, says Bostick.

So get ready to hold out your finger.
It may not protect against a bad case of flu, but glutathione may just be the answer to fighting off a mild viral load of influenza. That’s what the manufacturers of Sucrets Defense are counting on, based on research by Emory biochemist Dean Jones. Glutathione is the active ingredient in the popular over-the-counter cold and flu remedy that promises to boost the immune system and fight off infection.

The first line of defense

By Rhonda Mullen • Illustration by Annie Lunsford

“You don’t see the science on the box because the FDA doesn’t want to overstate its promise,” says Jones. “But I think glutathione does work, and well beyond influenza, in enhancing our defense system.”

Glutathione is a central tissue antioxidant and the major chemical in the body to detoxify cells. It discourages cells from oxidative stress, a toxic accumulation of too much reactive oxygen in cells. Abundant circumstantial evidence indicates that oxidative reactions contribute to many consequences of aging and major disease processes, according to an article by Jones, published in the journal Antioxidants and Redox Signaling (2006). The far-reaching impact of these oxidative reactions extends to diabetes, cancer, and neurodegenerative, pulmonary, and cardiovascular diseases.

The usual primary source of glutathione is diet. In the mid-1980s, a graduate student in Jones’s lab discovered that the body could transport glutathione. That started Jones, who directs the Clinical Biomarkers Laboratory in Emory’s medical school, on a search to see if the body could use dietary glutathione in a protective way.

Early studies by Jones and Emory colleagues found that consuming dietary glutathione failed to significantly increase amounts of the compound in the bloodstream. However, the researchers did discover that even low levels of glutathione helped protect against oral and pharyngeal cancer. For Jones, that indicated the GI tract was protected even though the entire system failed to show increased protection. The association led the researchers to more studies to find out why
metabolism and absorption of glutathione are more important for the oral and GI tract than for the rest of the body.

**Bottom’s up: beer’s contribution to flu protection**

As Jones continued to explore the impact of dietary glutathione, he received a related proposal from an interesting source. A Japanese beer maker invited him to help find a use for yeast cakes, a by-product of the fermentation process. These nutrition cakes, which contain approximately 2% glutathione, promised a regular commercial supply for a product if an application could be identified.

Jones, who himself had eaten yeast cakes for their nutritional value as a high school wrestler, set about to find such an application. He wondered if the cakes could offer various viral protections and, if so, along which route. More specifically, if he added glutathione to a supplement, could it protect against flu?

Jones developed a study using human epithelial airway cell cultures and later a mouse model to see if the hypothesis held. He found that glutathione failed to protect against influenza with a high viral load. However, at lower levels of infection, the glutathione supplement did produce a noticeable protective effect.

“The glutathione allowed the epithelia to provide the first line of defense,” says Jones. “It changed the character of those cells, blocking activation of virus particles and stopping a conversion of the cells to an active form.”

Emory received a patent for the findings, then licensed use of that research to a commercial firm, which sublicensed it to produce and market related products. Sucrets Defense is the first product to bring the discovery to market.

**Fluctuating levels of protection**

Jones’s research on glutathione is hardly over. He is working on several projects with colleagues throughout the Woodruff Health Sciences Center to see how far glutathione’s protective effects extend. These investigations include the role of glutathione in an overactive immune system with immunologist Cornelia Weyand, glutathione’s role in gastrointestinal health with endocrinologist Tom Ziegler, its relationship to atrial fibrillation with cardiologist Sam Dudley, glutathione’s effects on fibrotic lung disease with pulmonologist Jesse Roman, and the role of glutathione on neurologic disease with neurologist Gary Miller.

In one recent study, Jones tracked oxidation levels, finding that they are higher in the morning, placing people in a vulnerable state in which their bodies are less able to guard against infection. However, as the day begins, as people rise and eat, their oxidation levels fall and they become more resistant to infection. At night, the levels rise again while people sleep.

Jones has an explanation for the changing levels. “We run out of food during the night,” he says. “Our defenses decline because there are only minimal reserves of dietary glutathione to carry on the fight.”

He believes that concept bolsters the argument that a glutathione supplement will work. “If you are able to pop something in your mouth at vulnerable times of oxidation, you may be able to use your first line of defense to fight off infection,” he says. “The supplement can mitigate the risk, which is manifest in times and places where infection occurs—when people are tired and stressed, when they are using public transportation, or even when they are sitting in the sun at a baseball game. This approach is very different from a vaccine, which offers long-term immunity. Yet it can still be effective.”
The fever was moving through villages in southeastern Congo at an alarming pace. More than 400 people were sick, their vital organs ravaged, blood seeping from their eyes and ears, and 187 would die by November 2007. Both the CDC and WHO sent emergency response teams to control this outbreak of Ebola hemorrhagic fever, a highly infectious disease for which there is no known treatment. Time was of the essence: the last major Ebola outbreak in Congo—some 12 years ago—killed 245 people. This latest outbreak raged for more than eight months.

By Kay Torrance  •  PHOTOGRAPHY by J.D. Scott and Jack Kearse
One of the first steps scientists took upon arrival was to obtain samples of the virus and send them to a laboratory especially outfitted to handle such a deadly pathogen. These biosafety level 4 (BSL4) labs, as they are known, require the most stringent construction and operating standards, such as independent, single-pass air-handling systems with a HEPA-filtered air supply and exhaust air as well as a liquid decontamination system for lab waste water. Scientists working in these labs handle the most life-threatening pathogens ever encountered, viruses such as Ebola, Lassa fever, or Marburg. Researchers in these labs must follow safety practices carefully to minimize the risk of infection.

The laboratories are vital for progress against infectious diseases, according to Ruth Berkelman, director of the Center for Public Health Preparedness and Research at Emory’s Rollins School of Public Health. Infectious diseases cause more than 15 million deaths worldwide each year and have risen to become the third leading cause of death in the United States. Bioterrorism also remains a threat. Although the labs are critical for learning how to prevent and control threats, the agents studied in the labs may pose a hazard to workers.

For example, during the SARS epidemic in 2003 and 2004, researchers in three separate laboratories became infected. The last incident occurred when a graduate student, working in China’s top SARS laboratory, came down with the respiratory disease. Unfortunately, she failed to be tested for SARS until three weeks later. In the interim, the incident led to seven other people being infected, including her mother, who died. More recently, a researcher at Texas A&M University came down with brucellosis in February 2006. It was later revealed that she lacked proper authorization and training to work with the pathogen. Such events are causing scientific institutions to put biosafety practices center-stage.

Laboratory exposures are usually the result of several controls failing, usually because of human error. That fact underscores why biosafety training is so important.

While the CDC requires training for those handling the most life-threatening pathogens in U.S. labs, training generally is left up to individual facilities. New researchers and lab staff often listen to lectures, watch videos, and train alongside co-workers to gain the necessary experience. But Emory has a new program that is changing the way training is done.

“We are trying to provide a safe environment where we assure that certain safe practices become ingrained,” says Berkelman.

Emory’s approach to training focuses on changing behavior. Since it opened the world’s first mock BSL 3/4 laboratory designed for simulation training, Emory has trained more than 300 people, some in the mock laboratory and some at their own institutions. People have come from as far away as Pakistan, India, Singapore, and the Philippines to participate in training in the mock lab.

Emory’s mock lab was the brainchild of David Stephens, vice president for research in the Woodruff Health Science Center. After the anthrax attacks in 2001, the NIH allocated additional support for biodefense research and construction of high security labs. Stephens helped Emory partner with
other Southeastern universities to form a Southeastern Center for Excellence in Biodefense and Emerging Infections. He saw a need to create better training opportunities for new BSL4 laboratories on the horizon and for workers in existing BSL4 laboratories, and Berkelman took the idea from there.

Currently there are only a handful of BSL4 labs in the world, but with the threat of emerging infectious diseases and the ease with which new pathogens travel, the need for more BSL3 and BSL4 labs is being recognized around the globe.

As those new labs come online, they’ll be able to draw on the new training model at Emory. “We have changed how training is done,” says Sean Kaufman, the public health educator who does the bulk of the training in Emory’s mock laboratory. “Previously, training was behavior-based with little or no simulation training. With hands-on training, we can move people from being novices, we can put them safely in settings of a laboratory emergency, and overall, we can begin to create experts.”

Kaufman and colleague Lee Alderman, a former biosafety officer at CDC for 30 years, have taken their program on the road, training at numerous institutions in the United States, from California to Texas to South Carolina. In addition, Berkelman and her team have received an award of $400,000 to take the training to five overseas institutions in Asia next year through a grant from the National Institute of Allergies and Infectious Disease and the NIH.

The CDC and Boston University also have caught on to Emory’s pioneering program and will soon start their own mock labs for training. “We are excited to see others emulate our program,” Berkelman says. “There is so much need out there, and we believe training with established competencies is the way to go.”

A dark room, an unconscious person, a life-threatening emergency

The 14 people in the Emory mock BSL4 lab have been in training for several days now. They’ve learned the layout of the lab and can find their way around the biosafety cabinets, test tubes, and needles. They’ve covered the finer points of “PPE,” or personal protection equipment. They’ve had the order on

“The students realize that they are thinking at the speed of light, but they’re moving at the speed of a turtle.”

—Sean Kaufman, biosafety lab trainer

how to don and doff the equipment drilled into them, and they’ve connected their supply hoses. They’ve even practiced going through the decontamination showers. Today is a test of the progress they’ve made.

Kaufman and Alderman huddle in a corner to go over the day’s game plan. Who is to be the decoy, the one who will drop to the floor, serving as the unconscious victim? They decide on Mark Sloan, a tall, 240-pound military scientist from Texas with a take-charge attitude that inspires his classmates to follow his lead. Without Sloan, the others will be forced to regroup.

All the students except Sloan are kept busy in a side room with animal cages, chasing a loose golf ball that represents
Walking in another’s shoes

Research scientists and biosafety officers have different, immediate, and sometimes conflicting goals. While both groups want to avoid accidents, scientists want to get their research completed as soon as possible while biosafety officers are charged with making sure that researchers follow all the safety rules, which, on occasion, can interrupt delicate work.

No one knows this better than Lee Alderman, who has worked on both sides in the laboratory, as a biosafety officer at CDC and as director of Emory’s Environmental Health and Safety Office. A good working relationship comes down to face-time, respectful interaction, and establishing a true relationship, he says. “I’ve known biosafety officers who sat behind their desk all day,” he says. “They weren’t effective or respected.”

In the mock training laboratory at Emory, both scientists and biosafety officers take classes alongside each other in the first place to bring both groups together to train in safe practices. They are part of an effort by the mock lab’s leaders to revolutionize interaction between the two professions.

Besides reducing the risk of lab accidents, Emory’s course seeks to foster the relationship between researchers and biosafety officers. “Good biosafety officers see themselves as consultants, helping scientists do their work safely, not simply as enforcers of rules,” says Alderman.

“It’s very important that ‘biosafety’ is seen as an integral part of the whole scientific research enterprise, the purpose of which is to improve human welfare,” says Ruth Berkelman, who directs the mock lab. “Everybody has the same mission—to advance science and protect workers at the same time. If biosafety is seen simply as rules to follow, it increases tension.” The assessment of risk also is best accomplished by scientists and biosafety professionals working together, she adds.

When biosafety officers train in the mock lab, they get to “walk in the shoes” of lab researchers. Or in this case they get to walk in the protective booties and space suits of another. The insight that results is worth perhaps as much as all the rules combined in arriving at true lab safety.

an infected mouse that has escaped. Kaufman and Alderman brief their accomplice. When the exercise commences, Kaufman throws the others for a loop. “Mark, go down,” he yells. The first person to reach Sloan is told to drop as well. Then the third.

“Why did you go over when two people are down?” Kaufman asks. “Something is wrong here. If you don’t call out, nobody is going to know you’re here. When you see someone who approaches the person also go down, get out and find help.”

On the other side of the room, meanwhile, Alderman is running a sharps accident. One student supposedly has cut a finger (complete with fake blood that stains the hand) and becomes woozy from the loss of blood. Two people help the victim to the sink to submerge the finger in disinfectant. Then they make their way as a group around a corner to get out of the lab, struggling to doff foot coverings once they arrive in the “clean zone.” Alderman gives the group a “good job,” but he has more advice. “Suppose you have a catastrophic event. Forget decontamination,” he says. “Just get out of Dodge. Your life is the most important.”

Back to the exercise with the unconscious person, Kaufman observes that the group is learning to think and calming its initial inclination to panic. When a victim collapses,
“Good biosafety officers see themselves as consultants, helping scientists do their work safely, not simply as enforcers of rules,”

—Lee Alderman, biosafety lab trainer

the students hesitate on taking the next step: Should they move the person or use the defibrillator?

“Wasting time, wasting time,” Kaufman shouts. “We have a defibrillator.” One of the students grabs it. “Put the defibrillator back,” he says. “You haven’t checked to see if the person is breathing.” He then shows the class how to use plastic trays to move an unconscious co-worker.

Next on the agenda, Kaufman has everyone gather on one side of the lab and put brown paper bags over their headgear. They will need to form a conga line to find their way out of the lab, essentially blindfolded. The exercise is meant to simulate a power outage or visual impairment when people must get out of the lab safely while they are unable to see. Although the students have the layout of the lab firmly imbedded in their minds, they know better than to think it will be an easy test to pass with Kaufman in charge. The instructor doesn’t disappoint, setting off ear-piercing alarms before shouting, “Go.” He pulls one person off the back of the line. Will the person’s co-workers notice? He also scuttles in front, moving equipment into the path. A large metal rack throws the line off, and the students walk directly into a cement wall. The lead person has to feel her way along a countertop.

“I bet three days ago you wouldn’t have thought you could do this in the dark,” says Alderman, who has watched the group snake itself around the corner to find the way out.

**Giving up control**

In fact on the first day of training, these same students averaged only 33% on a pre-course subject knowledge test. By the end of the one-week session of 12-hour days, they will have an average score in the 90%+ range. That increase is typical of other classes taking the intensive course, which mixes the hands-on lab experiences with classroom lectures.

What else have the students learned? That they “may not always be in control,” Kaufman says. Just squatting to pick up a dropped object is an exercise in strength and balance. Students are tethered to air hoses and are yanked back if they try to walk across the room. As simulated exercises progress, frustration mounts. “The students realize they are thinking at the speed of light, but they’re moving at the speed of a turtle,” he says.

A few students have found that the course steered them away from working in a lab. But for the majority, they’ve learned not only how to successfully navigate a biosafety lab but also how to deal with the unexpected. Most important, they’ve learned how to protect themselves and the community from life-threatening pathogens.

**WEB CONNECTION**  For an audio slideshow on the mock biosafety lab, visit [http://www.whsc.emory.edu/biosafetylab.htm](http://www.whsc.emory.edu/biosafetylab.htm)
Driving out HPV

Your teenaged daughter has begun to drive on her own. She’s completed driver’s education, passed her test, and signed a parent-teen contract to drive safely and carefully. You know she’s a reasonably careful driver. But she’s also human, and human beings make mistakes. Plus, she isn’t the only driver on the road. Now imagine that three souped-up soybeans could prevent her death in a head-on collision. Would it save her from all mistakes or protect her from every kind of accident? No, but it would eliminate one deadly possibility. Given that possibility, wouldn’t you want her to swallow those tiny pieces of protein?

This illustration, albeit far-fetched, has an actual, clinical equivalent. Now available to adolescent girls and young women is a vaccine, engineered around a surface protein that blocks the spread of the human papillomavirus [HPV] in females. In protecting against four strains of HPV, Gardasil, marketed by Merck, has proven highly effective in eliminating the primary cause of cervical cancer, historically one of the deadliest cancers in women. Advanced cervical cancer still has no cure, and 10 women die in the United States every day of this cancer, with rates twice that high in Fulton County, Georgia. However, with approximately 70 million girls and women now vaccinated, the vaccine has sustained an almost 100% rate of efficacy over its five years of availability, with no serious side effects.

“As a cancer vaccine goes, this is the best we have,” says Kevin Ault, associate professor of Gynecology and Obstetrics at Emory. “In four or five generations, we have gone from cervical cancer being the most common cause of cancer death in the United States for women to being a vaccine-preventable disease.”

Ault has worked on the disease for more than a decade, culminating in development of the vaccine and his contribution to landmark papers on HPV in the New England Journal of Medicine in May and Lancet in June. His interest began during his tenure at the University of Iowa, when he heard of a possible link between the HPV and precancerous Pap smears.

As a clinical trial investigator, Ault found testing of the vaccine to be challenging on several fronts. First, HPV does not grow easily in a lab. Then there were technical questions: how many injections would ensure the vaccine achieved its full effect, and how would investigators accommodate changing technology and guidelines for Pap smears? Beyond those difficulties were privacy issues of enrolling adolescents and college students in the study. To answer these challenges, the researchers tested and tracked a large experimental group, approximately 20,000 people.

The announcement of an effective HPV vaccine raised concerns in some circles that vaccinating girls amounted to handing them a license to have sex. Ault, the father of two daughters, responds to that concern with data from a study of teenagers who chose not to engage in sexual intercourse [Abma et al., 2004, Vital and Health Statistics, 23:24]. “You usually get the answers, as a parent, that you’d want to hear. It’s against their morals. They haven’t found the right person. They don’t want to get pregnant. Those are usually the Top 3, and sexually transmitted infections are somewhere lower on the list. Given that, it’s hard to believe they’d change their behavior if they’re not thinking about them anyway.”

According to the CDC, more than half of men and four-fifths of women will contract HPV during their lifetimes. Addressing the potentially devastating effects of the virus, the CDC recommends vaccination for females between the ages of 9 and 26. Although both men and women can, and do, become infected with the virus, more men than women seem to slough the virus without a problem. Those who come down with HPV may develop such serious symptoms as genital warts or precancerous lesions on the cervix, vulva, anus, or penis. Absence of active symptoms, however, does not necessarily indicate the absence of the virus. HPV can, often does, remain dormant for years before erupting into full-blown disease.

No current test will confirm the presence of the virus prior to the emergence of the disease's symptoms. Around the world each day, approximately 750 women die of cervical cancer. Through vaccination and continuing research on ways to prevent and treat HPV, the human papillomavirus could go the way of smallpox, eradicated globally.

Ault would celebrate HPVs disappearance. So would the daughters and sons of the women who live long enough to enjoy the ride. –Perky Daniel
Tea, turmeric, and Taxol for cancer prevention

Can green tea play a role in preventing head and neck cancer? How about curcumin, the principal ingredient in the Indian curry spice turmeric?

Emory's Winship Cancer Institute researchers are searching for the answers to these and other questions as they embark on four avenues of investigation in the prevention and treatment of head and neck cancers. The projects are part of a five-year, $12.1 million Specialized Program of Research Excellence (SPORE) grant in head and neck cancer from the National Cancer Institute (NCI).

SPORE grants are large, highly competitive, multidisciplinary grants that fund scientific research to bring new laboratory findings quickly to the clinic. The first SPORE grant ever received in Georgia, this is one of only five head and neck cancer SPORE grants in the United States.

With an expected 40,000 new cases and 11,500 deaths in 2007, squamous cell carcinoma of the head and neck accounts for 4% to 5% of all newly diagnosed cancers in the United States. More than two-thirds of head and neck cancer patients have locally advanced disease before they are diagnosed, and consequently they have a poor five-year survival rate after treatment with surgery, radiation, or chemotherapy. According to the NCI, the Southeastern states rank among the highest in the nation in head and neck cancer incidence.

The incidence of lung cancer and head and neck cancers will remain high for the next two to three decades, predicts hematologist/oncologist Dong Moon Shin, principal investigator of the grant. Although smoking has declined overall in the population, a large number of aging smokers and ex-smokers may still develop these diseases, says Shin.

Emory's SPORE program includes four translational research projects. The first uses a combination of polyphenon E (a chemical substance found in plants and extracted from green tea) and erlotinib (a growth factor inhibitor) to prevent advanced precancerous lesions of the head and neck. The second project is directed at developing therapies that block cellular pathways that allow cancer cells to metastasize and proliferate.

In the third project, Winship researchers have modified the chemical structure of curcumin to produce a more powerful analog than the original compound. Curcumin has shown anti-cancer activity in earlier studies, but its effects have been limited because it induces cell death not only in cancer cells but also in healthy cells.

In the final area, Winship and Georgia Tech investigators are working on development of a new class of biodegradable nanoparticles that will carry Taxol to targeted head and neck cancer cells, while avoiding unwanted side effects to normal cells.

Directions from Mars to Venus

Why and how do males and females solve spatial problems differently? That's what Rebecca Herman and Kim Wallen at the Yerkes National Primate Research Center wanted to know.

What they found is that the two sexes use different parts of the brain to navigate. For example, when finding a location, men generally use north and south coupled with distance estimates, suggests Herman, whereas women prefer physical cues such as street names, signs, and buildings.

In the April 2007 *Hormones and Behavior*, the researchers point to subtle hormonal changes that occur as the brain develops to explain these differences. They compared normal female and male rhesus macaques with those that differed in prenatal exposure to male hormones.

The researchers arranged boxes baited with food, varying the consistency of food locations (spatial information) and the presence of colored markers (landmarks). Males and females performed the same when both markers were present, but the females performed better than the males in locating the food when only the landmark information was present. The male monkeys whose testosterone exposure was blocked early in gestation were better at using the landmarks than the control males.

A better understanding of sex differences in cognitive performance may shed light on why men and women experience disorders such as Alzheimer's disease and autism differently.
Training the trainers

Forrest Pecha is no novice to international sports. As head athletic trainer for the U.S. men's alpine ski team, he watched the skiers take two silver medals in the 2002 winter Olympics. He has worked on rehabilitation and strength programs for Ruud van Nistelrooy from Real Madrid soccer team, and he served as an athletic trainer for the U.S. men's U-20 national soccer team in Panama in 2006. This July Pecha headed with the team to Canada to help keep the athletes healthy during the youth world cup tournament.

Since 2005, Emory Sports Medicine—where Pecha serves as program manager and director for athletic training services—has provided athletic training services to the U.S. Soccer Federation (USSF) through its certified athletic trainer (AT) program. Emory ATs have worked with both the U.S. men's and women's national teams as well as the federation's youth national and development programs. “It’s a way to give our ATs on-the-field experience at the highest levels and for U.S. soccer to get the highest level of care,” says Pecha. “It’s a good fit.”

Certified athletic trainers are mid-level care providers. If an athlete gets hurt on the field, the AT is the first person to assess the injury, determining if the athlete needs rehabilitation or further consultation with the team doctor. Outside of game time, ATs concentrate on treating injured athletes and on conditioning programs to prevent injuries.

At Emory, the sports medicine program is raising the bar for certified ATs, offering advanced education through a one-year fellowship for four fellows each year. The third class of fellows graduated in July.

“We’re preparing athletic trainers to support the orthopedic and sports medicine physician,” Pecha says. At a minimum, applicants already must hold masters’ degrees, be board certified as an AT, have state licensure, and have traditional athletic training experience. During the fellowship, the ATs are immersed in all aspects of a clinical orthopedic practice. They gain scrub privileges to assist physicians in the operating room, each assisting with approximately 250 surgeries per year. They learn to interpret radiographic findings, and they complete a research project, such as a recent fellow’s study on ACL injury prevention. They also travel with the national soccer teams, ski teams, or other high-level sports teams one month out of every four during the fellowship.

It’s hard to beat that experience, says Pecha. “Our program is a flagship. In fact, we’re working with the National Athletic Trainers Association to develop national accreditation standards for AT fellowship and residency programs.”

In addition to affiliations with the USSF, Emory’s ATs work with the Tour de Georgia cycling race, the U.S. Ski and Snowboard Association, the Southeast All Star Football Camp, collegiate athletics, and high school varsity and club sports teams.

“If you’re going into the field of athletic training, you have to have a passion for athletics,” Pecha says. “But more than that, you have to have a passion for making people healthy.” —Rhonda Mullen

WEB CONNECTION To hear Emory sports medicine physician John Xerogeanes talk about ACL injuries in female athletes, visit emoryhealthcare.org/mediapodcast/podcasts/New_Innovative_ACL_Treatment-_Part_1.html

Varsity high school players in Georgia benefit from the same athletic training services as the U.S. Soccer Federation. Both are supplied by Emory Sports Medicine through its certified athletic training program, which is helping develop national accreditation standards.
A genetic predictor of heart attack

Working with an international team, Emory researchers have found a common genetic variation is linked to a substantial increase in the risk of a heart attack. The variation is found on chromosome 9p21 and is the first common variant that’s linked to a substantial risk of heart attack in study groups of those of European descent. The findings were published last spring in the online and print editions of Science.

Researchers found that people with the variation have a 1.64-fold greater risk of suffering a heart attack and a 2.02-fold greater risk of suffering a heart attack early in life. Approximately 21% of people of European descent carry two copies of the genetic variation (one from each parent).

Heart attacks are the leading cause of death in industrialized countries. Nearly half of men and one-third of women who reach the age of 40 will suffer a heart attack in their lifetime. If the genetic variation was absent in the general population, there could be 21% fewer heart attacks, according to researchers.

The study was led by the Icelandic genomics company deCODE Genetics, with researchers from Emory, Duke, and the University of Pennsylvania.

“The gene variant we have linked to heart attack points us to a major biological mechanism that substantially increases the risk,” says Emory cardiologist Arshed Quyyumi, one of the study’s authors. “Discoveries like this one greatly heighten our understanding of the role genetics plays in heart disease.”
Rioting feet

Emory’s alliance with a company in the world’s hot spot for genetics research led to a breakthrough for restless legs syndrome (RLS) this summer.

Collaborating with deCODE Genetics in Iceland, Emory neurologist David Rye helped track down a gene variant responsible for at least 50% of all RLS cases. Study results were published in the July 19 online and August 16 print editions of the *New England Journal of Medicine*.

“We’ve got a slam-dunk,” answers Rye to those who have questioned whether RLS is a legitimate disorder. “But more work will be required to translate these findings into improved patient care.”

Those with severe RLS have trouble sitting still for any length of time. Plane rides, long meetings, and sleeping are often interrupted by an intense need to wiggle, kick, and jerk the feet.

Rye has worked with deCODE scientists on several sleep-related research projects for nearly a decade. For the RLS study, Rye added clinical details from Emory RLS patients to data from Icelandic patients. deCODE processed DNA from blood samples for their genetic fingerprints and crunched the numbers. To confirm diagnoses of all the RLS patients in the study, Rye validated a novel tool that incorporated accelerometers to measure the number of times a person’s legs twitch during the night.

After an RLS diagnosis was confirmed, nurses recruited and then interviewed extended family members about signs and symptoms of RLS. Patients were, in many cases, overjoyed that someone recognized their problem and offered treatment options. (Dopamine agonists, used to treat Parkinson's disease, often work well.)

“These people were in dreadful shape,” says Rye. “RLS is a real problem if you have it. To those who are unfamiliar with the disorder, it sounds trivial, even fanciful or ridiculous.”

Coming up with a term in Icelandic for RLS was a challenging first step. “We had to introduce a new word to Icelanders for newspaper ads to attract study participants. ‘Fótaóeirð’ literally translates as ‘a foot with no rest,’ which doesn’t resonate to someone without RLS. Icelanders unaffected by RLS might interpret this word as a ‘riot’ in one’s foot.”

A new method of analyzing large amounts of genetic information helped the researchers pinpoint the RLS gene variant. Referred to as genome-wide association, the technique allows scientists to probe for gene variants in more than 300,000 single nucleotides of the genome.

Iceland has more sheer capacity for genome processing than anywhere else in the world, and Emory scientists are collaborating with deCODE by providing clinical expertise and access to the diverse genetic profiles of Americans, says Rye. deCODE’s mission is to conduct population-wide genetic studies to uncover major genetic contributors to common diseases. Translating these discoveries in human genetics into new drugs and diagnostic tools is deCODE’s forte. The uniformity of the Icelandic population, totaling only about 300,000, helps researchers isolate and connect genes with clusters of disease.

In 2002, Emory and deCODE signed a formal “strategic alliance” and continue to collaborate on a variety of genetic studies, primarily in cardiovascular disease and the neurosciences. —Valerie Gregg

WEB CONNECTION To view a slide show about RLS, visit http://www.whsc.emory.edu/rls.htm
Public health places

In less than 12 years after the Rollins School of Public Health moved into its first home, the school has maxed out the room for growth in its current facility. With a tripling of the number of students, faculty, and research dollars, the school’s classrooms, offices, and laboratories now extend to five buildings scattered across the Emory campus. However, those satellite locations are about to be brought together in a newly planned building that will add more than 160,000 square feet of space to the school.

As with the first Grace Crum Rollins Public Health Building, this second building is made possible by a commitment from the O. Wayne Rollins family, for whom the school is named. Not only will the $50 million gift enable the school to double its physical size but also it will be instrumental in attracting the highest caliber of faculty and students.

Named for Claudia Nance Rollins, Wayne’s mother, the new building will be a multi-use facility, including more laboratory space, technologically sophisticated classrooms, conference spaces, and an auditorium. New conference capabilities will enhance specialized training, distance learning, and professional exchange programs that spread public health solutions around the world. The schematic design phase is nearing completion, with construction scheduled to begin next summer. When it opens in 2010, the new structure will link to the current building through a pedestrian bridge.

The Rollins family’s contributions to the school include major funding toward the Grace Crum Rollins Building, significant endowment and faculty recruitment gifts, and creation of the Center for Public Health Preparedness and Research. With the naming of the new building, five generations of the Rollins family are now recognized at the school.

Cutting ribbons and breaking ground

The Emory School of Medicine opened its new $58.3 million education building in August, empowering it to train the next generation of doctors to provide 21st-century patient-centered care. The state-of-the-art building enables implementation of a new curriculum that integrates basic and clinical sciences and allows students to acquire clinical experience through interaction with real and simulated patients.

The curriculum teaches the fundamentals of science within clinical settings and immerses students in clinical experiences from their first week on campus. With 160,000 square feet of space, including auditoriums, seminar rooms, and classrooms, the entirely wireless building has allowed a 15% increase in the size of the entering freshmen class to 133 students.

The 1915 Society is one of the groups supporting the new building with a brick engraving program. Named in honor of the year the medical school first moved to the Emory campus, the society offers membership to those who donate $1,915 to the medical school for scholarships. In turn, first-time members are eligible to name a paver around the foundation of the building.

So far, more than 150 people have become members of the 1915 society, and the first tier of 133 pavers was in place for reunion weekend and dedication of the building in August. The second tier of named bricks will be installed this winter.

To participate in the program, contact Heather Pharris, director of alumni relations and development for the Emory School of Medicine, at 404-727-5932, or hpharri@emory.edu.
Think pink

This year marked a milestone for cancer treatment in Georgia—the first ever statewide cancer clinical trial for breast cancer. Coordinated by the Georgia Center for Oncology Research and Education (Georgia CORE) and Emory’s Winship Cancer Institute, the study is the first of its kind in Georgia in which an investigator from an academic medical center will collaborate with community-based oncology practices and other academic centers to enroll patients in a statewide clinical trial for early-stage breast cancer patients.

Although the American Cancer Society (ACS) reports cancer death rates have dropped steadily since 1990 due in part to earlier detection and better treatments, breast cancer remains a serious health risk for women. In fact, the ACS estimates that 180,510 new cases of invasive breast cancer were diagnosed in 2007, and the chance that breast cancer will be responsible for a woman’s death is about 1 in 33.

Fortunately, cancer clinical trials are making progress against breast and other cancers by testing and finding effective new treatments. At Winship alone, more than 200 clinical trials are currently under way to find cures for brain, lung, gastrointestinal, and prostate cancers as well as other malignancies. Winship’s goal in pursuing these trials is to promote translational research—taking the latest discoveries and putting them to work as quickly as possible to treat people with cancer.

Building relationships with community doctors to help educate patients and their families about new cancer treatment options, including clinical trials, is key to this progress, according to Winship hematologist and oncologist Ruth O’Regan. “Our vision is that patients throughout the state have access to the most innovative treatment opportunities regardless of where they live,” says O’Regan, who is principal investigator of the study. “This is an important step forward toward that goal.”

Sponsored by Georgia CORE and supported by Sanofi-Aventis, the Phase II clinical trial is currently enrolling early-stage breast cancer patients. The randomized study’s goal is to compare two different methods for administering the anti-cancer drugs docetaxel (brand name Taxotere) and capecitabine (Xeloda) to see if the regimens produce the same or different outcomes. After the drug treatment cycles are completed, the patients have surgery.

“We are delighted to be able to work with the community oncologists on this exciting project. To date we have accrued almost 30 patients, half of which are African-Americans,” says O’Regan. —Sherry Baker

The statewide clinical trial will be available at the following sites:

- Winship Cancer Institute (Atlanta)
- Georgia Cancer Center for Excellence at Grady Health System (Atlanta)
- Emory Crawford Long Hospital (Atlanta)
- Augusta Oncology Associates (Augusta)
- Central Georgia Cancer Care (Macon, Warner Robbins)
- Charles B. Eberhart Cancer Center at DeKalb Medical Center (Decatur)
- John B. Amos Cancer Center (Columbus)
- South Atlanta Hematology Oncology (East Point, Riverdale, Stockbridge)
- Suburban Hematology Oncology (Duluth, Lawrenceville, Snellville)
- Wellstar Health System-Georgia Cancer Specialists (Marietta, Austell)
- Wellstar Health System-Northwest Georgia Oncology Centers (Austell, Carrollton, Marietta).

For more information, patients and referring physicians may contact Georgia CORE’s Research Director Diane Hicklin at dhicklin@georgia-core.org or 404-588-4082.
It's been a busy year so far in Emory’s Heart Failure and Transplantation Program. In the first eight months of 2007 alone, Emory surgeons transplanted more hearts than during any similar period of the previous 18 years. And clinicians are treating approximately 600 heart failure patients each month.

Why the increase? For one thing, heart failure remains the only major cardiovascular disease in the developed world that is increasing in incidence and prevalence. In this country, more than 550,000 patients are diagnosed annually, and 5 million currently live with the disease. The aging of the baby boomers is a contributing factor, with those over 65 at greater risk for developing heart failure.

Emory is responding to this public health challenge with new inroads in heart failure research and technology, along with a booming transplant service that performs between 68% and 75% of all heart transplants in Georgia. “The size and scope of our program is unmatched in the state,” says medical director Andrew Smith.

On the research front, cardiologist Javed Butler is studying how to better define whether patients will progress to heart failure based on results from physical exams, blood tests, echocardiograms, and genotyping. If patients already have a diagnosis of heart failure, Butler, director of heart failure research, is using this battery of information to accurately determine their prognoses. Another key research area involves monitoring disease progression and outcomes of heart failure patients after transplantation.

The heart failure program is using ventricular-assist devices (VADs) as destination, or lifelong, therapy for end-stage heart failure in patients who are not candidates for transplant. The VAD serves as a replacement for the heart, pumping a normal amount of blood to support circulation and allowing a patient to lead an active life. Smith predicts that VADs will be so advanced in a decade that the number of VAD implants will rival transplants performed.

In heart muscle regeneration, cardiologist Arshed Quyyumi and hematologist/oncologist Edmund Waller are conducting a clinical trial at Emory Crawford Long Hospital using stem cells of patients who have recently experienced an acute heart attack. Bone marrow is harvested from the patient’s hip, spun to sort out progenitor cells, and reinfused into the patient’s heart muscle through cardiac catheterization. The goal is for the stem cells to grow new blood vessels or repair damaged ones, improving blood flow and heart function.

In technology advances, Emory Hospital was the first in the state to use two types of VADs as permanent therapy for heart failure. Last year, the hospital also became the first in Georgia to offer a non-surgical device for patients who have experienced severe heart attacks or who need support to improve their health enough to be placed on the transplant waiting list. In this procedure, the VAD pump, which remains outside the body, is attached to two tiny cannulae that are threaded through the femoral artery and implanted in the heart to restore blood flow, giving it and other vital organs a chance to heal.

Emory also is pursuing telemedicine monitoring systems to help decrease hospital stays for heart failure patients. In the past, doctors had to monitor ventricular or pulmonary artery pressure in the ICU. The new technology includes a wireless pressure sensor implanted in patients, who then use an external monitor to transmit wireless, web-based data from their homes back to Emory. Program nurse managers monitor the data and alert any patients who need follow-up care. Another monitoring device will transport web-based data to Emory every time a patient steps on the scale to monitor weight gain from fluid retention. —Lee Jenkins

WEB CONNECTION To locate a heart failure expert or to refer a patient to the Emory heart failure program, see emoryhealthcare.org or call 404-778-7777 or 1-800-753-6679.
In everyday life, public health nurses seem almost invisible as they work in communities to promote health and prevent disease. But in times of emergency, these nurses assume leadership roles to create strategies and find resolutions to imminent challenges.

Trained as a disaster nurse, I volunteered at the Red Cross Center on Monroe Drive during Hurricane Katrina, helping process and get aid for victims of the storm. In all, approximately 120,000 people flooded Red Cross Centers in Atlanta, seeking aid. The first casualties arrived by plane from New Orleans hospitals, some with no diagnosis, no treatment plan, and no medicine. Some of the patients included unaccompanied children. We found beds in local hospitals for the sick and set up shelters for those who were mobile and homeless.

Normal Red Cross policies stop short of providing medical care. However, many of the people in the shelters had health problems that needed attention, so the Red Cross allowed us to bring in Emory physicians to treat hypertension, diabetes, and all manner of chronic problems. Emory nursing faculty and students also provided 24/7 support for the Salvation Army shelter on North Druid Hills Road and in Emory’s own hospitals.
to handle the influx of evacuees.

Responding to emergency situations such as Katrina has long fallen in the disaster nurse’s portfolio, but in recent years, with threats of bioterrorism, impending pandemic flu, and the recurrence of Category 5 hurricanes, the need for nurses trained in emergency response has escalated. Recognizing this need, the U.S. Department of Health and Human Services provided a grant to the Nell Hodgson Woodruff School of Nursing to design a program to train nurses to handle a wide scope of emergencies. The resulting master’s program in Public Health Nursing Leadership is the only one in Georgia and one of only a few in the country to offer a detailed focus on emergency preparedness.

The U.S. government has made preparation for terrorism a priority, yet until recently the health care sector was left out of these preparations. Input from health care professionals is critically important in developing plans for response to disasters and terrorism. Public health nurses in particular can contribute significantly to the design of disaster response. For example, if nurses had had proper training in disaster preparation before 9/11, they could have played a larger role in the emergency response to that national catastrophe, communicating with disaster management teams and helping with standard triage.

Leadership in tumultuous times requires creativity. And public health nurses call on creativity and training to provide care with limited resources in nontraditional settings to large numbers of patients under stress. Nurses trained in disaster preparation are essential in managing mass smallpox vaccination sites, administrating medicines from the Strategic National Stockpile, or assisting with health care in the aftermath of a community contamination by a toxic substance or infectious agent.

Biologic or chemical terrorist attacks require more sophisticated response than that provided by traditional health care delivery systems. Because release of a biologic agent may fail to be identified immediately, victims may be scattered far and wide before the first symptoms appear. Public health nurses are key players to assess patients during such a crisis. However, recognizing a chemical attack and working for and in the community under such circumstances would challenge the resources of most nurses.

The Public Health Nursing Leadership Program at Emory takes on this challenge by having students complete three semesters of courses in topics such as epidemiology, environmental health, health policy, terrorism and public health preparedness, disaster nursing, and public health nursing. Students spend one class suiting up in biohazard safety suits to see what it is like to deliver CPR or give a shot under such conditions. In addition to core master’s level work in the classroom, they complete 500 clinical hours in the community with agencies such as the American Red Cross, CARE, The Carter Center, and state and local health departments.

Graduates of the program receive an MSN in Public Health Nursing Leadership and may complete 32 additional hours in the Rollins School of Public Health leading to a dual MSN/MPH degree. They go on to work in the community, such as two recent graduates who were hired straight out of school to be assistant chief public health nursing officers for Georgia.

When Katrina struck in the fall of 2005, Emory was already training nurses with an emergency preparedness focus. One of the students, assigned to disaster health services at the Red Cross, walked headlong into the middle of Katrina’s chaos and finished his clinical hours with on-the-job training in one of the worst national disasters we’ve ever experienced. Since that time, the nursing school has trained 20 students, with eight more in the pipeline, a small but growing cadre of nursing professionals trained to mitigate disasters. These public health nursing leaders will be on the front lines when the next catastrophe strikes.

Disaster nurse Linda Spencer shares her expertise with students who are training to respond to health care needs during emergencies.
Mind-body connections: a 100-year project

Yin and yang is how Emory psychiatrist Charles Raison describes the Emory-Tibet Science Initiative (ETSI). “We’re learning from them, and they’re learning from us,” he says.

Just what Emory brings to this historic partnership is development and implementation of a comprehensive science education curriculum for Tibetan monastics. What the monks are sharing with the academicians grows out of a deep knowledge of the health benefits of meditation.

Led by Geshe Lhakdor, director of the Library of Tibetan Works and Archives, the initiative originates from the vision of His Holiness the Dalai Lama, the spiritual and temporal leader of the Tibetan people and a distinguished professor at Emory. The Dalai Lama has a passion for training monks in science, says Raison, who applauds “the boldness of a world religious leader to build bridges and a dialogue between science and religion. The involvement of the Dalai Lama takes this initiative to get science and spirituality in dialogue on a world scale.”

The first demonstration of the science curriculum, which is being developed by faculty in the sciences and humanities at Emory and other universities, will be rolled out before 2,500 Tibetan monks at the dedication of a monastery in January 2008. But it won’t stop there, with groups of monks being trained 50 at a time in scientific principles, approaches, and techniques. The Dalai Lama has described the initiative as a 100-year project.

A growing body of scientific research indicates that psychological stress affects the immune system, which in turn can trigger some of today’s most challenging illnesses, including cancer, heart disease, and diabetes. “If we can introduce behavioral strategies such as meditation to find new ways to lessen stress, then we’ll have healthier people,” says Raison. Already he is engaged in testing that theory. An ongoing research study is evaluating whether Tibetan meditation in a secular form can benefit Emory freshmen in coping with stress. Early results showed the students who practiced meditation experienced dramatically less measurable stress than those who did not.

In the long view, those involved with the Emory-Tibet Science Initiative believe it will create a better paradigm for optimal living. “In a sense, we are developing a shared language and creating a new kind of intellectual in deeply trained monastics who can interface with the latest scientific research and thought,” Raison says. “In turn, we can learn to better frame our science by study of meditation. The interaction between the academy and the monastic world will synergize both disciplines for the betterment of all.”