A fish out of water

page 16
Madara to head Medical Center
This past June, James Madara, MD, dean of the Biological Sciences Division and vice president for medical affairs (positions he has held since 2002), was appointed chief executive officer for the University of Chicago Medical Center.

Madara is “the right person to lead Chicago Medicine at this critical time,” said University of Chicago President Robert Zimmer. “He has demonstrated the ability to recruit exceptional faculty and study cautioned that rage could be a seriously underappreciated mental disorder—overshadowed by others, such as anxiety and depression, probably because society interprets anger as a behavior that should be controlled.

“Our new study suggests IED is really out there and that a lot of people have it,” Coccoo told the Chicago Tribune in June. “That’s the first step for the public to actually get treated for it, because if you don’t think it’s really a disorder, you’re never going to get treated for it.”

In this latest study, Coccaro and Ronald Kessler, a professor of health care policy at Harvard, found that as many as one in 20 Americans might have chemical imbalances in their brains that leave them susceptible to unjustified rage, often resulting violently in road rage, domestic violence and other extreme outbursts where rage takes over.

They conducted face-to-face interviews with more than 9,000 people aged 18 and older from 2001 to 2003 as part of a government-funded epidemiological mental health study. Between 4 percent and 7 percent of those involved had the disorder, which equates to about 16 million Americans. Lifetime attacks per person came to 43 on average and caused each person an average of $1,359 in property damage.

People who experience anger attacks multiple times yearly show an apparent shortage of the chemical serotonin, a deficiency also implicated in depression. In addition, they produce brain image scans with abnormal signaling in the amygdala—bunches of nuclei hidden in the temporal lobes that are responsible for

In Madara’s four years as dean, research funding from the National Institutes of Health has increased almost 75 percent.

Since 2002, clinical and research space have increased dramatically, capped by the recent opening of Comer Children’s Hospital and the Gordon Center for Integrative Science, the largest research building on campus, to be followed soon by the Comer Center for Specialty Care and the Knapp Center for Biomedical Discovery, opening in 2008. Fourteen new department chairmen have revitalized the academic mission and brought in dozens of stellar young scholars.

—Larry Arbeiter

Raging mad
People’s violent and repeated outbursts are the result of their own lack of self-control, right?
Maybe not, according to a recent study from researchers at the University of Chicago and Harvard University. The study, released in the June issue of Archives of General Psychiatry, shows that the reason for people’s rage lies more in what they scientifically can’t control—the chemical reactions underway in their brains.

It’s a psychological disorder that Chicago’s Chairman of Psychiatry Emil Coccoo, MD, calls intermittent explosive disorder, or IED. Coccoo’s preliminary

People who experience anger attacks multiple times yearly show an apparent shortage of the chemical serotonin, a deficiency also implicated in depression.
 Blocking signals may protect mice from MS

A new way to preserve the cells that surround and protect nerves could lead to new treatments for demyelinating diseases such as multiple sclerosis, a research team reports in the May 10, 2006, issue of the Journal of Neuroscience.

The approach grew out of a novel explanation, quickly gaining followers, for the mechanism of nerve damage caused by multiple sclerosis. Instead of concentrating on the alterations that result in autoimmune assaults on the nervous system, researchers led by Brian Popko, PhD, at the University of Chicago have focused on a set of factors that prevent recovery from the inflammatory attacks.

A series of papers from Popko’s lab has demonstrated that interferon-gamma—a chemical signal used to activate the immune system—plays a critical role in damaging the cells that produce myelin, the protective coating that lines healthy nerves. Interferon not only leaves these cells, called oligodendrocytes, incapable of repairing the damage, but also can kill them directly.

“Interferon-gamma is not normally found in the nervous system,” said Popko, the Jack Miller Professor of Neurological Diseases at the University of Chicago, “but it can gain entry after an inflammatory flare-up. We previously showed how it harmed oligodendrocytes. Here we confirm its direct harmful effects on those cells and demonstrate one way of protecting them.”

The researchers used a series of transgenic mice: In one set they introduced genes that produced interferon-gamma within the central nervous system; in another set they also introduced a gene (known as suppressor of cytokine signaling 1, or SOCS1) that blocked the response of myelin-producing cells to interferon-gamma.

Although transgenic mice with low levels of interferon-gamma showed no symptoms of nervous system damage, 18 out of 20 mice exposed to higher interferon levels developed difficulty walking, including mild to moderate tremors, within two weeks of birth. Only four out of 20 mice with both high interferon levels and the SOCS1 gene had symptoms.

Autopsy showed mice with high interferon levels in the nervous system had severe loss of oligodendrocytes, ranging from 20 to 40 percent. Those with the protective SOCS1 gene lost only 8 to 15 percent.

High interferon levels also were associated with loss of myelin sheaths around nerve connections and unprotected axons in the brain. Again, SOCS1 was able to reduce the damage.

“Together, these data demonstrate that oligodendroglial expression of SOCS1 protects mice from the clinical and morphological consequences of IFN-gamma expression in the central nervous system during development,” the authors wrote in the journal paper.

“We found this tremendously encouraging,” Popko said. “SOCS1 prevented or reduced the harmful effects of interferon-gamma on myelin-producing cells. This study solidifies our suspicions about

Photo by Dan Dow
interferon’s specific role in demyelinating disease and suggests ways to block it.”

Although there is currently no reliable way to deliver SOCS1 directly to the nerves of a patient with multiple sclerosis, this protective approach could be combined with stem-cell therapy to repair nerve damage. Several research groups already are studying the use of stem cells to repair damaged myelin sheaths, but in the long term, those stem cells would be vulnerable to ongoing immune-mediated damage.

But if stem cells could be engineered to resist harmful signals such as interferon-gamma, they might be protected from the “harsh environment” present in immune mediated demyelinated lesions, Popko said.

The National Institutes of Health and the Myelin Repair Foundation supported the research. Additional authors are Roumen Balabanov and Ji Yeon Lee of the University of Chicago, Krystal Strand of the University of North Carolina and April Kemper of Wake Forest University.
—John Easton

Approaches to patient spirituality vary
Although more than nine out of 10 doctors believe it is appropriate to discuss religious or spiritual issues when a patient brings them up and three out of four encourage patients’ religious beliefs and practices, only half inquire—even occasionally—about a patient’s faith, researchers from the University of Chicago report in the May issue of the journal Medical Care.

Only 10 percent of physicians routinely mention their religious beliefs and experiences to patients. Fewer than a third endorse praying with patients; 80 percent say they do so “rarely or never.”

But if half of physicians do not inquire about religious beliefs, the other half do. Ten percent of them do so “always.” And while 80 percent said they rarely or never pray with patients, the remainder do, “sometimes or often.”

“We found no consensus among physicians about what is customary or appropriate,” said study author Farr Curlin, MD, assistant professor of medicine at the University of Chicago. “Despite efforts to standardize many aspects of the doctor-patient relationship, patients are likely to encounter very different approaches.”

These differences in attitude and behavior closely reflect physicians’ personal religious and spiritual characteristics, the study found. “The close ties between belief and behavior,” Curlin said, “suggest that physicians are unlikely to reach agreement any time soon about what is suitable.”

The researchers surveyed 2,000 practicing U.S. physicians from all specialties about their own attitudes and how they affected the clinical encounter. They asked physicians about their religious traditions, the extent to which they try to live out the teachings of those traditions and about barriers that might hinder discussion of religious or spiritual topics with patients.

For patients, religion often comes to the fore during an illness. Some doctors have argued that physicians should honor those feelings as part of patient-centered care, maintaining that such discussions, and even prayer, can be attentive and comforting.

Of the 1,144 responding physicians, 18 percent described themselves as being neither religious nor spiritual, while 17 percent identified themselves as being both highly religious and highly spiritual. Thirty-nine percent of the physicians were Protestants, 22 percent Catholics, 16 percent Jewish, 13 percent other religion and 11 percent reported no religion.

Physicians who said they were highly religious and spiritual differed from less religious and spiritual doctors on every attitude and behavior. Seventy-six percent of the most religious doctors asked about their patients’ beliefs compared with 23 percent of minimally religious physicians. Seventy-six percent of highly religious doctors pray with patients compared with 30 percent of less religious physicians.

Although the level of religious commitment was more important than the particular religious tradition, Protestants were the most likely to inquire about patients’ beliefs and the most likely to pray with patients.

For patients, religion often comes to the fore during an illness. Some doctors have argued that physicians should honor those feelings as part of patient-centered care, maintaining that such discussions, and even prayer, can be attentive and comforting. Thirty-eight percent of those surveyed thought doctors spent too little time addressing spiritual needs.

Others see it as a violation of boundaries. Because religion, like politics, can be divisive, many insist that physicians should avoid such topics. Nevertheless, only 1 percent of doctors thought they spent too much time in such discussions.

A previous study by Curlin’s team found that physicians were more religious than expected. Seventy-six percent of doctors believe in God, 59 percent believe in some sort of afterlife, and 55 percent say their religious beliefs influence how they practice medicine. Most doctors, though, were hesitant to “apply their religious beliefs to other areas of life,” the researchers found.

Sixty-one percent said they “try to make sense of a difficult situation and ‘decide what to do without relying on God,’” compared with only 29 percent of the general population.

The Greenwall Foundation and the Robert Wood Johnson Clinical Scholars Program funded this study. Additional authors are Marshall Chin, Sarah Sellergren, Chad Roach and John Lantos of the University of Chicago.

—JE
Surgical robot makes prostate removal safe for obese men

The use of a robotic system could make surgery for prostate cancer an option for thousands of obese men who might otherwise be turned down, report researchers from the University of Chicago in the April 2006 issue of the journal *Urology*.

The prostate's protected location deep in the pelvis makes surgical treatment for obese prostate cancer patients challenging, even for experienced surgeons. Because profoundly overweight patients often have surgical complications, many physicians advise such patients to postpone the operation until they lose weight—which they seldom do—or to consider radiation therapy instead of surgery.

However, using the robotic surgical system to remove a cancerous prostate "enables us to work under the abdominal wall muscles and fat, avoiding many of the problems that make open prostate surgery so difficult in this group of patients," said Arieh Shalhav, MD, associate professor of surgery at the University of Chicago and director of the study.

The study looked at all 150 men who had a robotic laparoscopic radical prostatectomy by Shalhav and Gregory Zagaja, MD, at the University of Chicago Hospitals between February 2003 and November 2004.

Patients were divided into three groups according to weight. Group one consisted of 39 men with a normal body mass index (BMI) of 25 or less. Group 2 included 65 overweight men, with a BMI between 25.1 and 30. Group 3 contained 46 obese men with a BMI over 30, including three men over 40 and one over 50.

The only statistically significant differences noted among the groups were that the operation took, on average, 60 minutes longer and blood loss was 70cc (2.4 ounces) higher in the obese patients. Otherwise results were similar for all three groups in terms of complications, hospital stay, cancer control and resumption of urinary control and sexual activity.

"We found," the authors wrote, that this operation "can be completed safely in overweight and obese patients, with results similar to those in a cohort of normal-weight patients."

Overweight men were the quickest to regain urinary continence and sexual function. Six months after treatment, 80 percent of overweight men in this study had full urinary control, compared with about 75 percent of normal or obese men. And six months after surgery 75 percent had normal sexual function, compared with 50 percent of normal weight men and 70 percent of obese men. By 12 months, however, 80 percent of normal-weight men had regained their baseline sexual potency.

Longer treatment for toxoplasmosis

Treating acute congenital toxoplasmosis—a parasitic infection acquired through cat feces, raw meat or garden soil—throughout the first year of life improves long-term outcomes for children with the disease, according to the national Collaborative Chicago-Based Congenital Toxoplasmosis Study. Funded by the National Institutes of Health, the study followed 120 infants from the United States and Canada who were diagnosed with toxoplasmosis soon after birth. Eighty percent had clinical abnormalities at birth, some severe. Prior studies had shown that untreated children or children who received a short course (one month) of therapy performed poorly.

The longer-term treatment eliminated eye lesions, seizures, and cognitive and motor-function impairment, providing "compelling evidence" for prolonged treatment and for a more compre-hensive plan for neonatal screening for congenital toxoplasmosis, the authors wrote. About 85 percent of American women of childbearing age are at risk of acquiring the infection and transmitting it to their fetuses. Contributing authors include Douglas Mack and Shawn Withers of the University of Chicago.

Six for six

The lung transplant team recently recruited to the University of Chicago has completed its first six transplants in the new setting. All six patients are home and doing well. The first patient, Allen Leonard, 44, received two new lungs in a seven-hour operation. Leonard, a Chicago lakefront bicycle policeman, had suffered from scleroderma-associated pulmonary fibrosis. He was placed on a waiting list in March after his condition worsened, just a month after the team received approval for heart/lung transplants by the United Network for Organ Sharing. The 11-member team includes transplant physicians Sangeeta Bhorade, Edward Garrity and Wickii Vigneswaran, who said they were attracted to the university by its nationally recognized research and clinical programs in pulmonary biology and lung disease.

Obese prostate cancer patients may not be candidates for surgery because their weight puts them at too great a risk. However, a new robotic surgical system might change that.
This study shows that we can extend those advantages to men who were not previously considered good candidates for prostate surgery because of their weight," he said. "We now think robotic prostatectomy is the best surgical option for overweight and obese men, who have become the majority of our patients." Almost 75 percent of the men in the study were overweight or obese.

Other than skin cancer, prostate cancer is the most common type of cancer found in American men and the second leading cause, after lung cancer, of cancer death in men. The American Cancer Society estimates that there will be about 234,460 new cases of prostate cancer in the United States in 2006. Almost half of those men will choose surgical removal of the prostate.

At the University of Chicago Hospitals, Intuitive Surgical's da Vinci robotic system also is used for several other urologic applications, as well as by general surgery, cardiac, vascular and thoracic surgeons.

Additional authors of the paper include Albert Mikhail, Benjamin Stockton, Marcelo Orvieto, Gary Chien, Edward Gong, Kevin Zorn and Charles Brendler, all from the section of urology at the University of Chicago. The study was supported in part by an unrestricted independent medical grant from Pfizer Pharmaceuticals.

—JE

Prescription flip-side for medication withdrawal

Although thousands of scientific papers evaluate and compare new and established drugs each year, providing evidence to help doctors prescribe safe and effective doses, almost no studies focus on when or how to stop these medications, even late in life.

In the March 27, 2006, issue of the Archives of Internal Medicine, four University of Chicago physicians propose the first general framework for withholding or discontinuing medications, adding life expectancy, goals of care, treatment targets and time until benefit to the usual equation of drug pluses and minuses.

"Our framework was designed to help patients and physicians decide when to stop taking even safe and effective drugs in situations that are often radically different from those where the medications were started," said geriatrician Holly Holmes, MD, instructor of medicine at the University of Chicago and lead author of the study.

"We wanted to provide a road map that would steer people away from the prescribing cascade that is common for patients late in life and guide them past the barriers that prevent removal of treatments that may no longer be effective," Holmes said.

The impetus for the guidelines came from some misguided advice. The authors care for patients at a nursing home. The pharmacy that supplies the nursing home monitors physician-prescribing practices and offers suggestions. After one review, the pharmacy sent a fax pointing out that, according to accepted guidelines, two patients at the nursing home ought to be taking a statin—a cholesterol-lowering drug that can, over time, reduce the risk of heart attack.

“One of those patients was more than 100 years old, quite frail, with advanced cancer and multiple other medical problems,” Holmes said. “The other one was dead. It made us wonder whether something wasn’t missing from those guidelines.”

Well-tested algorithms exist for prescribing drugs and avoiding inappropriate medications in the elderly, but as the authors combed through these, with their frail older patients in mind, they noticed that none considered when medications that might have previously been appropriate should be discontinued.

"Most drug studies tell you how to treat the chart, how to treat the numbers," said co-author Caleb Alexander, MD, assistant professor of medicine and a member of the
Center for Clinical Medical Ethics at the University of Chicago. “But they don’t always help you treat the patient. We set out to fill some of those gaps.”

One of those gaps was prognosis. Drugs with long-term benefits, such as those for high blood pressure or elevated cholesterol, provide no immediate relief, are seldom entirely without side effects and can be quite expensive, especially for the elderly, who often take many different drugs. Such medications may be appropriate for a 65-year-old with mild heart disease but at some point in the next 25 years patient and physician may have to overcome what the authors refer to as “clinical inertia” and rethink that initial decision.

The authors suggest four criteria for doctors considering adding—or subtracting—a drug from an elderly patient’s therapeutic arsenal:

- Calculate the patient’s life expectancy, based on actuarial charts and modified by the patient’s current health status and history.
- Weigh the time to benefit. Pain relief may be immediate but some preventive medications, such as a statin, may not provide any benefit for years.
- Work with the patient and family to determine the goals of care, a shifting balance of prevention, treatment and palliation.
- Define treatment targets, such as relief of specific symptoms, that agree with the goals of care.

Even when it makes clinical sense to take patients off of a medicine, the authors note, it can be emotionally challenging. Sixty-five percent of all office visits end with the granting of a prescription. “It’s often the closing moment of a caring interaction,” Holmes said. “It seals the deal. It’s not the same when you have to take it away.”

Nonetheless, the authors say, it is necessary. “Medication discontinuation, when done right, can decrease costs, simplify prescription regimens, decrease adverse drug events and focus therapy for maximum benefit,” Alexander said.

“Evidence-based medicine has changed the way physicians practice, but it seems to have had tunnel vision when it comes to withdrawing drugs,” Holmes said. “The discontinuation of medications is a neglected science. It’s not an area that the pharmaceutical companies are looking to fund.”

“Medication discontinuation, when done right, can decrease costs, simplify prescription regimens, decrease adverse drug events and focus therapy for maximum benefit.”

—Caleb Alexander, Assistant Professor of Medicine

Liver recipient graduates
The world’s first successful living-donor liver transplant recipient, Alyssa Smith, marked another milestone in May when she graduated from high school. Nearly two decades ago, on Nov. 27, 1989, a surgical team at the University of Chicago Hospitals transplanted a portion of liver tissue—donated from her 29-year-old mother, Teresa Smith—into then 21-month-old Alyssa. Weighing just 25 pounds at the time, Alyssa suffered from biliary atresia, the most common fatal liver disease in childhood. The medical event was the subject of national attention: First Lady Barbara Bush even called Alyssa’s mom to congratulate her and to wish her well. Alyssa, who has been off her anti-rejection medications for three years, leads a normal life, is active in several school groups and studies ballet. This fall she enrolled at Meredith College in Raleigh, N.C., and plans to become a medical social worker.

Measured hope for Type 1 diabetics
Recent attempts to manipulate the immune system of mice that have Type 1 diabetes have shown measured success. In three separate studies at the University of Chicago, Harvard and Washington University in St. Louis, researchers successfully reversed Type 1 diabetes in 32 percent of the 22 mice in the experiments. However, the scientists found no evidence of insulin-producing beta cells derived from donated spleen cells, which initially had been thought to be a crucial component of the therapy, transplant immunologist Anita Chong said. The study offers hope for reversal of the disease for recently diagnosed patients, but may disappoint those who hoped to cure established diabetes by using stem cells from donor spleens to help patients grow new pancreatic islets. The three studies sought to confirm the results of a high-profile 2003 study in which those hurdles appeared to have been overcome.

New surgery chief at Chicago
Gastrointestinal surgeon Jeffrey Matthews, MD, has been named chairman of surgery at the University of Chicago, effective Oct. 1, 2006. Matthews, 47, is an authority on the surgical treatment of diseases of the pancreas, bile ducts and liver, and is known for his fundamental research on defects in chloride transport in epithelial tissue. He comes to the University of Chicago from the University of Cincinnati College of Medicine where he was the Christian R. Holmes Professor and Chairman of the Department of Surgery and a professor of molecular and cellular physiology.

Jeffrey Matthews joined the University of Chicago in July as the new chairman of surgery.
“We are enormously pleased to bring in Jeff Matthews as chairman of surgery,” said James Madara, MD, dean of the Biological Sciences Division and the Pritzker School of Medicine, vice president for medical affairs and chief executive officer of the Medical Center at the University of Chicago. “He combines a sterling reputation as a physician, international renown as a bench scientist and widespread recognition as an inspirational teacher with an established track record as an imaginative and efficient administrator, having run a large academic surgery department for five years. He is the model of a University of Chicago faculty member and leader and exactly the sort of rare person we had hoped to find.”

In his five years as chairman of surgery at Cincinnati, Matthews more than doubled research funding and doubled clinical revenue. He recruited 35 new clinical and research faculty and developed programs in minimally invasive and robotic surgery. He expanded multidisciplinary programs in pancreas and liver disease and in vascular, weight-loss and cosmetic surgery, and rebuilt the division of cardiac surgery.

He also launched an interdisciplinary program in emerging technologies and extreme-environment research that brought together academic, industrial and military resources to “create a platform for developing, validating and disseminating new technologies for surgical care in military and civilian settings,” he said. His efforts to improve teaching throughout the department resulted in a four-fold increase in Cincinnati in the number of medical students who chose a surgical career. Deeply committed to cultural and gender diversity in the discipline of surgery, he launched a successful initiative to attract women and underrepresented minorities into the specialty.

An active clinical surgeon, Matthews has special expertise in pancreatitis, bile duct reconstruction and complex reoperative gastrointestinal surgery. His laboratory research, with long-term support from the National Institutes of Health, focuses on the fundamental mechanisms used by epithelial tissues to regulate salt secretion, which goes awry in several diseases, including cystic fibrosis and many forms of diarrhea.

Born in New Rochelle, N.Y., Matthews graduated summa cum laude from Harvard College in 1981 and from Harvard Medical School in 1985. He began his residency at Harvard’s Beth Israel Hospital in 1985, spent a year as a fellow in hepatobiliary surgery at the University of Bern, Switzerland, then returned to serve as chief resident at Beth Israel from 1990 to 1991. He joined the Harvard faculty as an assistant professor of surgery in 1992. In 2001, he was appointed professor and chairman of surgery at Cincinnati and surgeon-in-chief at Cincinnati’s University Hospital.

Author of nearly 100 articles in research journals, 30 reviews and book chapters, and several instructional videos, Matthews is active at the national level in many professional organizations and has served on editorial boards of numerous surgical and scientific journals. A recent past-president of the Society of University Surgeons, he is currently a director of the American Board of Surgery and treasurer of the Society for Surgery of the Alimentary Tract. He is also a member of the American Surgical Association, the American Society for Clinical Investigation and the Society of Clinical Surgery. He has been both member and chair of review committees for the NIH, Veteran’s Administration, the National Pancreas Foundation and has won many awards for his research and teaching.

—JE

Zimmer inducted as president
On July 1, 2006, Robert Zimmer began his tenure as the 13th president of the University of Chicago, and on Oct. 27, he was inducted in Rockefeller Memorial Chapel. James Crown, chairman of the board of trustees, performed the induction, after which Zimmer shared his vision for his presidency during an inaugural address.

He acknowledged the long series of convocations leading to his own and observed that despite changes in society and scholarly agendas “at any time since its inception, we would know unmistakably that we were at the University of Chicago.” The Field Museum hosted his inaugural celebration (at right) the evening prior to Zimmer’s official inauguration.
Chicago’s new team to manage Argonne

A new team assembled by the University of Chicago has been selected to manage Argonne National Laboratory, the U.S. Department of Energy has announced.

Through UChicago Argonne, LLC, the University of Chicago has established partnerships with Jacobs Engineering Group Inc. and BWX Technologies Inc. (BWXT) to manage the lab. Chicago is the sole member of the LLC.

Northwestern University and the University of Illinois also will be involved in the lab’s management through membership on the Argonne National Laboratory Board of Governors.

“We are very pleased to lead this strong team in managing Argonne for the Department of Energy,” said Robert Zimmer, PhD, president of the University of Chicago. “Argonne’s unique facilities and scientific and engineering expertise are vital resources for the development of science and technology and enhancing the energy, economic and national security of the nation.”

Argonne National Laboratory is one of the nation’s leading federally funded research and development centers. Its 2,900 employees include approximately 1,000 scientists and engineers, of whom about 600 hold doctoral degrees. Argonne’s annual operating budget of approximately $475 million supports about 200 research projects in energy, science, technology, biomedicine and national security.

“The university’s open-minded approach and strong intellectual traditions have fostered an effective and symbiotic relationship that will continue to produce future scientific and engineering dividends,” said Robert Rosner, PhD, president of UChicago Argonne, LLC, and director of Argonne National Laboratory. “This new team combines individual strengths to forge a unique and powerful partnership on behalf of the DOE and the nation.”

Among Argonne’s missions is the design, construction and operation of major national user facilities—large, unique facilities used for cutting-edge research by the scientific community. Researchers on site collaborate with scientists and engineers from universities, research laboratories and corporations. Collaborative efforts extend beyond science to include the university’s economics, social science and public policy programs, thereby bringing multiple perspectives to science, energy and national security issues.

“Working with the DOE, we are bringing together world-class talent to tackle the most pressing problems facing our nation,” said Thomas Rosenbaum, PhD, CEO of UChicago Argonne, LLC, and vice president for Research and Argonne National Laboratory at Chicago. “Our team has responded to the competition by and scientific and engineering expertise are vital resources for the development of science and technology and enhancing the energy, economic and national security of the nation.”

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The new partnership brings proven resources to lab management. Jacobs Engineering is one of the world’s largest and most diverse providers of technical, professional and construction services. BWXT is one of the nation’s premier managers of laboratory operations and high-consequence facilities with significant experience within the DOE.

—Steven Kopper

Novel technique to remove tumor in infant’s liver

On June 28, infant Chloe Lobins got a new chance at life after receiving a liver resection—removal of part of the organ—at the University of Chicago Comer Children’s Hospital. Born prematurely and diagnosed

High in the rankings

The University of Chicago’s Pritzker School of Medicine and the University of Chicago Hospitals received high rankings in two new U.S. News & World Report surveys. Pritzker rose from 19th to 17th place in the magazine’s ranking of research medical schools. Its graduate programs climbed one notch from 20th to 19th, with paleontology ranking first nationally and ecology and evolution fourth. Pritzker and the Biological Sciences Division ranked higher than any other Illinois biomedical program. Pritzker was the highest ranked medical school in Illinois.

In the 2006 “Best Hospitals” issue of the report, UCH is ranked among the best in the country in 11 specialty areas, more than any other Illinois hospital. Two programs—digestive disorders (#6) and cancer (#6)—were ranked in the top 10 nationally. Ranked in the top 25 are endocrinology (#13), neurology & neurosurgery (#16), respiratory disorders (#22), orthopedics (#22), and ear, nose & throat (#25). Four other programs—kidney disease (#26), gynecology (#32), urology (#41) and heart & heart surgery (#45)—scored in the top 50. Only 176 of the country’s 5,189 hospitals (about 3 percent) made at least one of the specialty lists. The magazine noted that many of these hospitals are referral centers that see sicker patients and conduct more difficult procedures, often following or pioneering advanced treatment guidelines while utilizing advances in imaging, surgical devices and other technologies.

The University of Chicago’s geriatric program has been ranked in the top 20 every year since 1993, but the magazine dropped the category for 2006 because the field is oriented more toward primary care than to specialized hospital treatment. The rankings are based on such factors as available technology, patient/community services, procedure volume, nursing care and reputation.
Born prematurely and diagnosed with hepatoblastoma, Lobins is believed to be the smallest infant ever to undergo massive liver resection for a primary liver cancer.

noticed eating problems, they performed a CAT scan. They found a fast-growing, cancerous tumor and quickly transferred her to Comer Children’s Hospital.

Born April 26 at 29 weeks, Lobins’s size presented a challenge for pediatric surgeon Donald Liu, MD, surgeon-in-chief at Comer Children’s Hospital. At the time of surgery, she was 63 days old and weighed approximately 4 lbs, 6 oz.

“Her small blood volume was a significant operative risk,” said Mindy Statter, MD, director of pediatric trauma, who assisted Liu with the operation.

An infant that tiny has about a teacup of blood, Liu said. Because of the great number of blood vessels, the liver is a fragile organ, especially in babies. “If you can’t stop the bleeding, then they die on the operating table,” he said.

Liu knew he needed to work quickly to keep blood loss low and to preserve the remaining liver. The catch: The liver cannot endure long without blood flow. An adult liver can survive without permanent damage for about an hour. “The length of time a baby’s liver can go without blood flow is anyone’s guess,” Liu said.

Liu reviewed all possible types of resection and chose a new method. Using a linear stapler, a device that looks like a vise, he simultaneously cut out the tumor and minimized the bleeding. In one action, the stapler sliced and sealed the liver by firing four rows of staples and cutting in between them, leaving two rows in the remaining liver and two rows in the removed portion. The operation took about 40 minutes, the resection about 30 seconds.

For many children with hepatoblastoma, doctors use chemotherapy to shrink the tumor before removing it. In Lobins’s case, her doctors felt it was too risky to wait.

“Did surgery because such tumors are very aggressive, and without expeditious resection, it could fast become unresectable,” Liu said. “It is hard to give [infants] chemo.”

The tumor turned out to be one-tenth of the baby’s body weight.

Attending physician William Meadow, MD, co-section chief of Neonatology, said, “It looks like they saved her life.”

A biopsy of the removed mass revealed that the infant had embryonal hepatoblastoma, which is more aggressive than fetal hepatoblastoma. Because of this discovery, “Chloe will be receiving some chemotherapy to insure that the tumor will not come back elsewhere in the body,” said Charles Rubin, MD, a pediatrician at Comer Children’s Hospital and an authority on childhood cancers.

Today, tests show the remaining liver is cancer-free, Liu said. Since enough healthy tissue remained, Lobin’s liver eventually should regain its normal size.

—Theresa Carson

Small naps are big help for young docs on long shifts

Creating “protected times” when interns can sleep during a night on-call significantly reduced fatigue among medical residents during extended shifts, according to a study published in the June 10, 2006, issue of the Annals of Internal Medicine.

Researchers from the University of Chicago reported that although average sleep time for interns in the study increased only modestly—by about one hour—the interns felt that even small gains in sleep led to substantial reduction in fatigue and improvement in sleep quality and ability to care for their patients. It was the first study to assess the benefits of naps for first-year medical residents, also known as interns.

“This is a proven method of alleviating fatigue in industries that combine high intensity with long shifts,” said study director Vineet Arora, MD, instructor of medicine at the University of Chicago. “Yet it has been neglected by the one industry that studies sleep. Our results show that a well-timed nap can provide a significant boost in physician concentration and take away some of the burden of chronic sleep deprivation.”

The researchers studied 38 first-year medical residents on the general medicine service at the University of Chicago from July 2003 to June 2004. For several month-long periods during that year, the interns were on-call every fourth night. Interns on-call often work a 30-hour shift, consisting of a full day, then a night on-call, followed by a shorter day. Each intern wore an “Activwatch” for a month that recorded his or her movements around the hospital, time in bed and time asleep.

For two weeks out of each month on-call, interns followed the standard schedule,
grabbing a little sleep whenever they could during the night shift. For the other two weeks they had access to protected time, allowing them to nap. Those on the nap schedule were strongly encouraged to forward the care of their patients to a designated “night-float” resident who would cover for them between midnight and 7 a.m.

During 119 total months on service, interns on the nap schedule increased average sleep time by 41 minutes, from 144 minutes a night up to 185 minutes. Interns on the nap schedule who forwarded their pages to the “night-float” resident increased their sleep times even more, from 142 up to 210 minutes. Sleep efficiency—the ratio between time in bed and time asleep—also improved for those on the nap schedule, from 73 percent, considered abnormal, up to 80 percent.

The 38 interns were randomly prompted during on-call and post-call days (but not between midnight and 7 a.m.) to report their fatigue using the seven-point Stanford Sleepiness Scale. One point indicates “feeling active and vital, alert, wide awake”; seven points indicate “losing struggle to remain awake.”

When prompted, interns on the nap schedule reported far less fatigue. They logged an overall sleepiness rating of 1.74 compared with 2.26 for those on the standard schedule. They had lower scores while on call, 1.59 vs. 2.06, and much lower scores the day after being on call, 2.23 vs. 3.16.

“A rating of one or even two is consistent with peak performance,” Arora said, “but people may start to get “sluggish,” she said, at three. Anything above three is “clinically relevant.”

The researchers found, however, that despite mounting fatigue and the allure of protected sleep time, interns were reluctant to rely on the night-float residents, forwarding their pages in just 22 percent of available opportunities. When interviewed, interns emphasized the importance of caring for their own patients and concerns about losing important information when responsibility is transferred back and forth with another physician.

“Our study,” the authors wrote, “suggests that these young physicians are choosing to care for their patients over their own immediate welfare.”

Although interns did not mind sacrificing sleep for their own patients, they did not feel the same allegiance when, to help other physicians, they tended patients they did not know. Many found ways to retain the pages for their own patients but were happy to transfer others to the night-float resident.

At a time when newly imposed restrictions on resident hours result in more frequent cross-coverage, “this finding is concerning,” the authors wrote.

As hospitals nationwide search for ways to reduce resident sleep deprivation, many have considered shorter shifts. This study suggests that an extended long shift, punctuated by a substantial nap, may be more effective, reducing levels of resident fatigue but also limiting the amount of time that

“This is a proven method of alleviating fatigue in industries that combine high intensity with long shifts.”

—Vineet Arora, Instructor of Medicine
Distinguished educators named during Medical Education Day

Clinical medicine is a high-stakes profession, one that requires great teachers who embody professional mastery in all its complexity.

That’s the message Molly Cooke, MD, director of University of California-San Francisco’s Haile T. Debas Academy of Medical Educators, delivered at the Pritzker School of Medicine’s first Medical Education Day this past April. The crowd, some 200 strong, included physicians, residents, professors and students, among others.

In her keynote address, Cooke emphasized how important it is for medical educators and teachers to draw learners into the “community of practice” and to do the work of making that community of practice visible.

Cooke congratulated the six inaugural members of the Academy of Distinguished Medical Educators in the Biological Sciences Division and the Pritzker School of Medicine. Chosen for their contributions to the field of medical education, they are:

- organismal biologist Eric Lombard, PhD
- pathologist Stephen Meredith, MD/PhD
- medical ethicist Mark Siegler, MD
- internist Scott Stern, MD
- pathologist Ting-Wa Wong, MD
- longtime medical educator Lawrence D.H. Wood, MD/PhD

To further honor Wood’s legacy as an educator, the academy created the L.D.H. Wood Teaching Scholar Award to honor a senior faculty member for outstanding contributions to medical education at Pritzker. Bruce Gewertz, MD, the Dallas B. Phemister Professor and Chairman of Surgery, was selected as the first recipient of this award.

Establishing such an academy elevates the division’s level of awareness and support for medical education, said Halina Brukner, MD, associate dean of medical school education and the academy’s director. “It creates a cadre of collaborating faculty who can lead curricular evaluation and innovation,” she said.

The new emphasis on medical education resonates with the university and the division’s tripartite mission of patient care, research and education, said Holly Humphrey, MD, Pritzker’s dean of medical education. “The University of Chicago has a long history of being the teacher of teachers, and so this is the perfect setting in which to establish an academy of distinguished medical educators. Our inaugural members represent the kind of lifetime excellence in teaching that befits membership in such an academy.”

Workshops and a poster session demonstrating research in medical education followed Cooke’s address. An oral plenary session highlighted five posters, two of them by students in Pritzker. Medical student Sam Seiden’s poster, titled “Effect of a Student Duty Hours Policy on the Teaching and Satisfaction of Third-Year Medical Students,” illustrated the effects of Pritzker’s 2003 decision to restrict duty hours in an effort to eliminate sleep deprivation, which affects both learning and safety.

Medical student Cynthia Galvan collaborated with other students and with Benjamin Abella, MD, assistant professor of medicine, on a research poster that described how students have developed, implemented and maintained a basic life-support training program that is now a mandatory requirement in the medical education curriculum. The program, begun in 2002, is based on the idea that all medical students should be proficient in basic life support to prepare for the clinical wards.

—Susan Soric

University recruits for exclusive partnership

At the Janelia Farm Research Campus, faculty rarely write grant proposals. They hardly ever deliver lectures. And they seldom perform administrative duties.

Instead, they conduct research.

The Howard Hughes Medical Institute opened the Janelia Farm campus in early September, and researchers already have moved into the space. By this time next year, the University of Chicago, England’s Cambridge University and Janelia—a 281-acre campus in Virginia—collectively will have welcomed a few carefully selected, highly motivated students from around the world into the unique research program in a remarkable new setting.

Currently, Chicago is recruiting students throughout the Americas while Cambridge

The Howard Hughes Medical Institute’s new Janelia Farm Research Campus in Loudoun County, Va., opened its doors in September. The campus includes a three-story Landscape Building (top) and a winding corridor leading to the main entrance.
recruits students elsewhere. The two schools are the only entrance points for study at Janelia, where students will complete PhD degrees during their research.

Students will come from a variety of scientific backgrounds. They will spend one year at their partner university and the remainder of their time at Janelia. Each student will have two mentors—one at Janelia and one at the university.

Two senior fellows have been recruited so far: Sydney Brenner, a molecular biologist and Nobel laureate, and Charles Shank, former director of the Lawrence Berkeley National Laboratory.

“Janelia opens up a whole new set of resources for our students and provides new opportunities for scientific imagination and collaboration,” said James Madara, MD, dean of the Biological Sciences Division at Chicago.

Because HHMI will completely fund the 20 to 30 group leaders and 300 researchers who eventually will work there, research at Janelia Farm will differ from that at traditional institutions. Without the constraints that accompany most grant funding, researchers will have greater opportunity to follow new leads and the surprising twists and turns that arise in their investigations.

The idea for the campus was sketched out on the back of a napkin during a lunch seven years ago. Thomas Cech, current HHMI president, and HHMI vice presidents David Clayton and Gerald Rubin sought a place, like England’s Medical Research Council Laboratory of Molecular Biology or AT&T’s Bell Laboratories, where researchers from various disciplines could come together in research and discussion to answer complicated biological questions that require more time and attention than most federal grants allow.

Proposed projects at Janelia reflect that multidisciplinary ambition. Students will build new types of microscopes capable of magnifying living cells to unprecedented detail. They’ll study adaptations the brain makes in response to new experiences. They’ll interpret neurons in the fruit fly’s brain, and use protein design and computation techniques to create nanosensors for living cells.

The first students will begin in fall 2007.

—KSB

“Uniquely human” component of language found in songbirds

Although linguists have argued that certain patterns of language organization are the exclusive province of humans—perhaps the only uniquely human component of language—researchers from the University of Chicago and the University of California-San Diego have discovered the same capacity to recognize and distinguish such patterns in *Sturnus vulgaris*, the common European starling.

In the April 27, 2006, issue of *Nature*, the researchers show that these starlings—long known as virtuoso songbirds and expert mimics—can be trained to reliably discriminate between two different patterns of organizing the sounds they use to communicate.

“Our research is a refutation of the canonical position that what makes human language unique is a singular ability to comprehend these kinds of patterns,” said Timothy Gentner, PhD, assistant professor of psychology at UCSD and lead author of the study. “If birds can learn these patterning rules, then their use does not explain the uniqueness of human language.”

The researchers focused on recursion, or center-embedding, a characteristic found in all human languages. Recursion is one

### NOTEWORTHY

**Morton F. Arnsdorf, MD**, a professor of medicine, won the American Heart Association’s 2006 Women in Cardiology Mentoring Award, designed to recognize individuals effective at mentoring women cardiologists. He received the award during the annual Clinical Cardiology Council Dinner at the AHA’s Scientific Sessions this November.

**Elliot S. Gershon, MD**, professor of psychiatry, won the 2006 Lifetime Achievement Award from the International Society for Psychiatric Genetics.

**Arthur Herbst, MD**, a professor emeritus of obstetrics/gynecology who exposed the dangers of diethylstilbestrol (DES), a hormone that doctors prescribed for the prevention of miscarriages between 1938 and 1971, received the University of Arizona Alumni Association’s College Alumni Council Award for Excellence.

**Ken Kasza, PhD**, a research associate in emergency medicine at the University of Chicago and a senior mechanical engineer at Argonne National Laboratory, won a R&D 100 Award for “one of the year’s most innovative ideas” from *R&D* magazine. His work revolves around ice slurries—a mixture of ice and salt water that, when injected into the lungs, may sustain the heart and brain cells after heart attack.

**Raymond Roos, MD/PhD**, professor and former chair of neurology, has been elected to the Johns Hopkins University Society of Scholars as one of 15 esteemed scientists and clinicians honored during the society’s 37th induction ceremony. Roos is a nationally recognized researcher and leading clinician in the field of neurodegenerative disorders, particularly amyotrophic lateral sclerosis, multiple sclerosis and prion diseases.
A way of creating new and grammatically correct meanings by inserting words and clauses within sentences—so-called center-embedded constructions—may not be unique to human language. "Linguists have developed a mathematically rigorous system of rules, a hierarchy of syntactic complexity, that governs the process of how humans create and understand utterances," said Daniel Margolis, professor of anatomy and organismal biology at the University of Chicago and coauthor of the study. "These rules govern how to properly express yourself—how to structure your phrases and sentences.

Language experts have used properties of these rules, whose complexity is described by the Chomsky hierarchy, to define the boundaries between humans and other creatures," Margolis said. "Now we find that we have been joined on this side of that boundary by the starling. It should no longer be considered an insult to be called a bird brain."

One previous study, however, suggested that even non-human primates are incapable of recognizing anything beyond the simplest syntax. A paper published in Science in 2004 by scientists at Harvard and MIT found that cotton-top tamarin monkeys were not able to master higher-level grammar patterns. "The acquisition of hierarchical processing ability," the authors concluded, "may have represented a critical juncture in the evolution of the human language faculty." They also noted that vocal learners, such as songbirds, might have produced different results.

"When I saw that study I was not convinced of the significance of the failure of the monkeys," said Howard Nusbaum, chairman and professor of psychology at the University of Chicago and senior author of the Nature study. "There are many ways for an experiment to fail and most failures are not scientifically interesting. I immediately thought: We could do that in starlings."

Although they are not known for the lilting beauty of their songs, starlings produce an amazing array of complex sounds, combining chirps, warbles, trills and whistles with rattling sounds. They also have a talent for mimicry.

Nusbaum, Margolis and psychologist Kimberly Fenn had collaborated previously on studies of the role of sleep in speech perception. Centner, a neuropsychologist, expert on starlings and, at the time, a postdoctoral fellow at the University of Chicago, was an essential addition.

To assess the birds' syntactical skills, the research team exploited the diverse sounds in starling songs. They recorded eight different 'rattles' and eight 'warbles' from a single male starling and combined them to construct a total of 16 artificial songs. These songs followed two different grammars, or patterning rules.

Eight songs followed the "finite-state" rule, the simplest sort, thought to account for all non-human communication. A finite-state grammar allows for sounds to be appended only at the beginning or end of a string. These songs were built up from a rattle-warble base by adding rattle-warble pairs at the end. The simplest song (ab) was one rattle followed by one warble; the next simplest a rattle, then a warble, followed by a different Rattle and Warble (abAB).

The other eight songs followed the "context-free" rule, which allows sounds to be inserted in the middle of an acoustic string, the simplest form of recursive center-embedding. So a context-free sequence also began with rattle-warble base (ab) but built up by inserting new sounds in the middle, such as rattle-Rattle-Warble-warble (aABB).

Eleven adult birds were given lessons on distinguishing between these two sets of songs using classic reinforcement techniques. The birds were rewarded with food when they heard a song from the context-free set and for refraining when they heard one from the finite-state set.

After 10,000 to 50,000 trials over several months, nine of 11 tested starlings learned to distinguish the patterns. The birds were not simply memorizing particular sequences of rattles and warbles; they could distinguish between different patterns even when presented with entirely new sequences of rattles and warbles. They were applying rules to solve the task.

The finding that starlings can grasp these grammatical rules shows that other animals share basic levels of pattern recognition with humans. "There might be no single property or processing capacity," the authors wrote, "that marks the many ways in which the complexity and detail of human language differs from non-human communication systems."

"When I describe our results to linguists and psycholinguists, they are amazed," Nusbaum said. "When I mention them to people who study animal behavior," Margolis countered, "they are not surprised. They are well aware of the cognitive abilities of many animals."


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