AN ENEMY IN OUR MIDST
New approach to asthma

The University of Chicago Hospitals is the site for the first U.S. trial of bronchial thermoplasty, an experimental treatment for patients with moderate to severe asthma. UCH is one of about 30 centers worldwide, and the only one in Illinois, to participate in the Asthma Intervventional Research 2 (AIR2) clinical trial.

“This is an entirely novel and exciting approach to treating asthma, unlike anything else available,” said pulmonologist Imre Noth, MD, assistant professor of medicine at the University of Chicago and director of the study. “Early reports from three human trials in Canada, Brazil and Europe have attracted a lot of attention, but this will be the first big human trial.”

This study will evaluate the safety and effectiveness of an experimental device—the Alair System, manufactured by Asthmatx Inc. The device is designed to prevent airway constriction, the hallmark of asthma, by eliminating some smooth muscle that surrounds the breathing passages. When irritated or inflamed, this smooth muscle contracts and narrows the breathing passages. The resulting wheezing and reduced breathing capacity can be severe, even life-threatening.

Fewer than 100 patients have been treated with bronchial thermoplasty, none in the United States. In a Canadian trial involving 16 asthma patients, the procedure improved average air-flow rates; about 75 percent of them reported they were “less limited” in their daily activities one to three years after therapy.

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Bronchial thermoplasty involves inserting a flexible tube, called a bronchoscope, into the lungs’ major airways and passing a catheter with a small heat source at its tip through that tube. Using radiofrequency energy, surgeons heat the tip to the temperature of a hot cup of coffee for 10 seconds, killing about half the smooth-muscle cells that line that portion of the airway. Then they repeat the procedure for all accessible airways in one lobe of the lung. Patients in this study will undergo three thermoplasty procedures, separated by three-week intervals, to treat the lower lobe of the right lung, the lower left lobe and then both upper lobes. The right middle lobe, about 15 percent of the total lung volume, will be left untreated.

Smooth muscle is uniquely heat sensitive and can be eliminated without lasting damage to the cell layers that line the inner surface of the airways. After thermoplasty, epithelial re-growth is quick and complete. Smooth muscle at the treatment site is replaced by loose connective tissue.

The smooth muscle that lines the human airway “is a lot like the appendix,” Noth said. “It serves no known purpose other than to cause serious medical problems.

“Even if this works as we imagine, it is not a cure for asthma. Our fondest hope is that it may reduce the severity and frequency of asthma symptoms, especially for those with severe asthma, and perhaps improve the quality of life for people with moderate to severe asthma,” said Noth, who has no financial interest in Asthmatx Inc., the study’s sponsor.

Asthma specialist Alan Leff, MD, professor of medicine at Chicago and a consultant to Asthmatx, said the procedure is intended “for patients who are inadequately controlled on current drug therapy.”

—John Easton

Time of transitions

More than the latest crop of residents will take on new responsibilities this summer. On July 1, Robert J. Zimmer will become the 13th president of the University of Chicago. Zimmer, 58, who has been serving as provost of Brown University, succeeds Don Michael Randel, who has served as president since 2000. Randel will become president of the Andrew W. Mellon Foundation.

A mathematician who was a faculty member at Chicago for more than two decades, Zimmer served as chair of the mathematics department, deputy provost and then vice president for research for Argonne National Laboratory before leaving in 2002 to become the provost at Brown.

The University of Chicago Hospitals also is preparing for a change in leadership. Mike Riordan, who has served as president and chief executive officer of UCH since 2001, has announced his decision not to seek reappointment. At the same time, Paula Wolff will hand over the gavel as chairwoman of the hospital trustees to Valerie Jarrett, currently vice chairwoman of the hospital trustees.
of the hospital board of trustees and a university trustee.

During this period of transitions, a small group of trustees will reexamine the hospital governance structure. A second group of trustees, chaired by Jarrett, will direct the search for Riordan’s successor.

While the search gets underway, Kenneth P. Kates has been appointed interim president and CEO of UCH. Kates, 51, joined the medical center in 1988 and has served as executive vice president and chief operating officer since July 2001.

During Riordan’s tenure, UCH built and opened the new state-of-the-art Comer Children’s Hospital, remodeled other parts of the medical center to upgrade and expand capacity, and completed the conceptual design for a new hospital pavilion. In the past five years, UCH has been listed in various surveys as one of the nation’s top hospitals.

“The Institute for Genomic & Systems Biology also will gain a new director. Kevin P. White, PhD, is a pioneer in combining experimental and computational techniques to understand the networks of factors that control gene expression during development and evolution. In addition to institute director, he has been appointed professor in the departments of human genetics and of ecology and evolution, both effective July 1, 2006. He also will have an appointment at Argonne National Laboratory.

White, 35, comes to Chicago from Yale University School of Medicine, where he is an associate professor in the departments of genetics and of ecology and evolutionary biology, and director of applied genomics in the Yale Center for RNAi and Therapeutic Chemical Genetics.

“Getting Kevin was a real coup,” said Conrad Gilliam, chairman of human genetics at Chicago. Seven university departments, plus Argonne and the Chicago Biomedical Consortium, pooled their resources to attract him. In the end, Gilliam said, “I think our enthusiasm plus the range of collaborative potential we assembled made the difference.”

“Chicago seems to have an institution-wide commitment to interdisciplinary research that’s going to be key to the development of our genome-to-medicine concept.”

—Kevin White, PhD, Incoming Director of the Institute for Genomic & Systems Biology

“It all came down to structure,” White said. “Chicago has lots of assets, including arguably the best molecular evolution and statistical genetics in the world, but Yale also has real strengths. Both places were eager to invest in systems biology, but Chicago seems to have an institution-wide commitment to interdisciplinary research that’s going to be key to the development of our genome-to-medicine concept. It also offers a close connection to the proteomics, computation and engineering talents at Argonne.”

White studies how the networks of genes and proteins that control development produce differences between individuals or between species. Some of his more
recent work has applied approaches developed and tested in fruit flies to the study of human evolution and disease.

At Chicago, White will partner with several biological science departments and Argonne to create the Institute for Genomic & Systems Biology. This institute eventually will house nine core faculty members in genomics and computational biology at Chicago, as well as several scientists at Argonne. It will move to a permanent home in the Center for Biomedical Discovery when it opens in 2008.

While 2008 remains slightly distant, another recent change took place at Chicago when Christopher Gomez, AB ’77, PhD ’81, MD ’83, a leading authority on the molecular and cellular mechanisms of neurodegenerative disease, was appointed professor and chairman of the neurology department in January 2006.

Gomez came to Chicago from the University of Minnesota, where he was a professor of neurology, director of the laboratory of ion channel disorders and neurodegeneration, and associate head for research affairs in neurology.

Gomez is widely recognized for his clinical expertise in the treatment of ataxia and his research on the molecular and genetic causes of these disorders. He established the University of Minnesota Ataxia Clinic, a nationally recognized specialty clinic for patients with these rare degenerative diseases, and is a founding member of the Cooperative Ataxia Group, a national consortium of ataxia specialists.

In his laboratory, Gomez studies how mutations in ion channels or other essential proteins lead to neurodegeneration. By understanding these mutations, he hopes to identify new therapies, such as selective channel-blocking agents, that might help patients with neurodegenerative disorders.

Gomez earned a bachelor’s degree in biology from Chicago in 1977, followed by a PhD from the Committee on Immunology in 1981 and an MD from the Pritzker School of Medicine in 1983. He completed an internship at Michael Reese Hospital and residency training in neurology at UCH.

With the influx of new faces, Chicago employees also must bid farewell to their departing peers, including Bruce Gewertz, the Dallas B. Phemister Professor and chairman of the department of surgery. Gewertz is leaving Chicago to serve at Cedars-Sinai Medical Center in Los Angeles—a major teaching affiliate of the University of California—Los Angeles—as chairman of the department, surgeon-in-chief and vice president for interventional services.

Gewertz joined the surgery department at Chicago as an associate in 1981 and subsequently was promoted to professor in 1988. During his 25 years of service, and 14 years as chairman, Gewertz became both a nationally acclaimed vascular surgeon and served in leadership positions in virtually every major national surgical society. He also distinguished himself as a medical educator, a fact borne out by a multitude of awards for excellence in teaching from Pritzker.

Erectile dysfunction and heart disease

Erectile dysfunction may warn of significant coronary heart disease, according to University of Chicago research published in the Archives of Internal Medicine in January. Other studies have suggested an association between ED and atherosclerotic vascular disease, but this is the first to link ED with abnormal results on cardiac stress testing. It also provides evidence of severe coronary artery blockages and markers of a poor cardiovascular prognosis.

University cardiologists reported that ED is a stronger predictor of significant coronary heart disease than traditional office-assessed risk factors, such as family history, cholesterol levels or blood pressure. ED also was associated with reduced exercise endurance and decreased pumping capacity of the heart.

“This suggests we may need to ask male patients a new set of sensitive questions as part of the evaluation for heart disease,” said study director Parker Ward, MD, assistant professor of medicine and director of the cardiology clinic. “The good news is that a decrease in sexual function could provide an additional warning sign for the presence of heart disease.”

This paper suggests that communication about this topic between patients and physicians may lead to increased treatments and better quality of life for patients. It also may help identify men at risk for significant heart disease.

The study, supported in part by a Pfizer Pharmaceuticals grant, involved 221 men who underwent nuclear stress testing, a widely used noninvasive way to detect the extent, severity and reversibility of coronary heart disease. Before testing began, the men filled out a questionnaire that assessed erectile function.

Almost 55 percent had erectile dysfunction and, on average, they scored less well on exercise tests and measures of coronary heart disease. They also exhibited greater evidence of significant coronary artery blockages. Forty-three percent of men with ED and 17 percent of men without ED had stress scores “strongly associated with clinically significant obstructive coronary artery disease,” the authors wrote.

Risk factors for ED and coronary artery disease are similar, including obesity, diabetes, hypertension, smoking and hyperlipidemia. While ED does
Families get extra help

A new March of Dimes support service will boost assistance for families of premature or critically ill newborns in the Neonatal Intensive Care Unit (NICU) at the University of Chicago Comer Children’s Hospital. Cathy Gray, Hospital perinatal network administrator and nine-year March of Dimes volunteer, said the program’s purpose is to make the experience less traumatic for parents. The three-year NICU Family Support Project will encourage family involvement, provide Spanish-speaking assistance and customize such services as sibling and extended family support, and ante-partum aid and preparation. NICU families will receive the March of Dimes Parent Care Kit, which includes a guide to unit staff, equipment, procedures and conditions. The program also will offer more training and preparation for taking the baby home, which strengthens Comer’s “Transition to Home” program. Comer, the first Illinois hospital chosen for the program, was one of 23 nationwide.

Trans-catheter replacement of a pulmonary valve

The first U.S. trans-catheter pulmonary-valve replacement was performed at the University of Chicago in December. The three-hour minimally invasive procedure went smoothly, said Ziyad Hijazi, MD, the George M. Eisenberg Professor of Pediatrics and chief of pediatric cardiology, who led the medical team.

The patient, 16-year-old Justin Reaves, was discharged from the University of Chicago Comer Children’s Hospital the next day. That afternoon he and his parents began their drive home to the family farm in South Dakota.

Surgically replacing a leaky or damaged heart valve is a complicated procedure. For patients like Reaves who already have undergone multiple cardiac surgeries, the risks increase substantially because scar tissue at the incision site and around the heart can make access extremely difficult and impair healing.

Born with a narrowing of the aortic valve, Reaves underwent valvuloplasty to open the narrowing at age 18 months and again at age 5. That kept him going until he turned 14, when his constricted, leaky aortic valve had to be replaced. Then he came to the University of Chicago, where surgeons performed the Ross procedure. They removed the pulmonary valve, used it to replace the aortic valve and replaced the pulmonary valve with one from a cadaver. But post-operative complications, including an infection around the surgical incision, required several trips to the operating room. Eventually both valves were again replaced.

By the summer of 2004, Reaves had developed a new narrowing, this time in his transplanted pulmonary valve. The problem got worse over time. This past fall he was so short of breath that “he even got tired just talking,” said his mother, Jeanine Reaves.

Because of Reaves’ previous heart operations, Hijazi’s team began searching for alternatives to surgery. Traditional valve-replacement surgery requires opening the patient’s chest, stopping the heart and maintaining circulation with cardiopulmonary bypass.

Hijazi has a personal consulting relationship with Edwards Lifesciences,
assisting the company in testing and developing devices in pre-clinical studies. One of those devices, the Cribier-Edwards percutaneous heart valve, is designed to be an alternative to open-heart surgery. Last year, clinical trials began in the United States to determine whether this replacement heart valve could be delivered via a catheter inserted into a blood vessel in the groin and snaked up into the heart.

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Chicago cardiologists replaced a patient’s pulmonary valve with a Cribier-Edwards percutaneous heart valve via a catheter.

But the feasibility trial focused only on aortic valve replacement, not the pulmonary valve. So Hijazi and Edwards Lifesciences got special “compassionate-use” permission from the FDA to insert the experimental device into Reaves. More than 75 patients have received an aortic heart valve as part of U.S. and European feasibility studies to test catheter delivery of the valve. Reaves is the first U.S. case involving the technology for pulmonary valve replacement.

Within a few minutes after the procedure, Reaves was awake, alert and talking with his parents and nurses. “Mom, I can actually take a deep breath,” he said when he awoke. His hands and fingers were “pink, actually pink,” right after the procedure, instead of their customary pale gray, his mother said.

“Ongoing trials will tell us what we can expect in the long term from this percutaneous approach for replacing aortic valves,” Hijazi said. “The jury is still out. We don’t expect this to be a substitute for traditional surgical valve replacement in most cases. But, for now, we appear to have fixed Justin’s immediate problem.”

—John Easton

Youngest patient receives sunken-chest procedure

Weighing in at 19 pounds, 17-month-old Coreon Kelly of Joliet, Ill., became the youngest and smallest patient ever treated with the minimally invasive “Nuss” procedure last March at the University of Chicago Comer Children’s Hospital. The procedure repaired a congenital chest-wall deformity called pectus excavatum, also known as sunken or funnel chest. The next youngest patient on record is a 5-year-old.

Most children never need surgery for this disorder, however, many families elect to correct it when children are between the ages of 8 and 12.

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The minimally invasive surgery requires a one-inch incision on each side of the chest and takes less than an hour.

Kelly experienced increasing shortness of breath, frequent respiratory infections and was falling behind on developmental milestones. He needed surgical repair “as soon as possible,” said Darrel Waggoner, MD, an assistant professor of human genetics, who helped care for the toddler.

“He was slow to crawl,” his mother said, “because he couldn’t lie on his stomach, and that made him slow to walk.”

Kelly also has Marfan syndrome, a genetic disorder that causes heart and aorta abnormalities. He had an enlarged heart and high blood pressure requiring daily doses of adult anti-hypertensive, making surgical correction more urgent.

At such a tender age, the risks of major surgery, compounded by severe cardiac disease, are traditionally prohibitive, said Donald Liu, MD, chief of surgery at Comer.

Conventional surgery for pectus excavatum includes cutting through the breastbone and several ribs and repositioning them. Recovery can take weeks and post-operative complications are common.

Since 2002, however, Liu has used the newer Nuss procedure, named for Donald Nuss, a Norfolk, Va., pediatric surgeon who developed the technique in 1987.

The minimally invasive surgery requires a one-inch incision on each side of the chest and takes less than an hour. A tiny camera and a curved surgical steel bar are threaded underneath the rib cage. The bar
is then rotated 180 degrees to move the chest wall into the normal position. Within three months patients return to normal activities, even playing sports.

For Kelly, the bar will be removed in about two years, after the normal curve of the chest has been established and the underlying bone structure solidified. Kelly will still have Marfan’s, which can cause other heart complications, learning problems and connective tissue disease, but “thanks to this novel surgical intervention,” Liu said, “he should soon be living a more normal life.”

—John Easton

**Gene variation increases SIDS risk in African Americans**

Sudden infant death syndrome claims nearly one-third of U.S. infants who die between 1- to 12-months of age. African-American infants have a three times greater risk of SIDS than Caucasians and six times the risk of Hispanics or Asians, suggesting genetics play an important role.

Now a research team based at the University of Chicago has traced about 5 percent of SIDS cases among African-American infants to variations in the gene SCN5A, which is associated with abnormal heart rhythms. In half of these SCN5A-associated deaths, infants had two copies of a common variation of the gene, called Y1103, which translated into a 24-fold increased risk of SIDS. Yet infants with one copy of Y1103 did not appear to have an increased risk.

The team’s findings were published in February in the *Journal of Clinical Investigation.*

One of nine African Americans carries one copy of Y1103, which confers an eight-fold risk of cardiac arrhythmia in African-American adults. “The common polymorphism alone does not cause SIDS,” said Steven Goldstein, MD, PhD, professor and chairman of pediatrics and director of the study. “Our findings suggest, however, that it renders infants vulnerable to environmental challenges—such as a long pause in respiration—that are tolerated by children without the mutation.

“The hope is that findings like this may one day allow us to intervene,” he said. “We might screen to identify children at high risk and teach parents how to lessen the likelihood of secondary challenges. We have already begun to evaluate drugs that may mitigate the risk.”

Supported by Goldstein’s grants from the National Institutes of Health and the Doris Duke Foundation, the researchers studied genes from 133 African-American infants with a diagnosis of SIDS after autopsy. They compared results with tissue samples from 1,056 African-American adults with no known health problems.

Three of the 133 African-American SIDS cases had two copies of Y1103 (2.3% of all deaths), compared with only one individual of 1,056 controls (0.1%). Four other SIDS cases had other damaging mutations in one copy of the gene. How, the researchers asked, might this variation contribute to SIDS?

The SCN5A gene codes for a sodium channel essential to the heartbeat. Mutations in SCN5A have been linked to a condition called long QT syndrome, which can cause abnormal heart rhythms and sudden death.

Goldstein said his team’s findings indicate that Y1103 is a risk factor for SIDS. “We need to find other genes that are related to SIDS,” he said. “We might screen to identify children at high risk and teach parents how to lessen the likelihood of secondary challenges.”

The researchers are now working to identify other genes that may contribute to SIDS and are exploring the possibility of genetic testing to identify high-risk infants.

**Leading 100**

Solucient, the Evanston, Ill.-based health care information company, has named the University of Chicago Hospitals one of the top 100 in the country. The study, now in its 13th year, examines changing performance levels in U.S. hospitals across five critical performance areas: outcome of care, patient safety, efficiency, financial performance and growing community service. In general, the winners of the 100 Top Hospitals National Award also experienced less adverse outcomes than their competitors. According to Solucient, winning hospitals display “balanced organizational performance—an ability to provide sustainable and reliable health care services to their communities.”

UCH was the only Chicago hospital named to any list in any category. From the metropolitan area, Evanston Northwestern and Advocate Lutheran General (Park Ridge) made the major teaching hospitals list.
**BOOKMARK**

*The Physician’s Guide to Investing: A Practical Approach to Building Wealth*

Robert M. Doroghazi, MD ’77, and Dan W. French, PhD
Humana Press, 2005

This guide to investing is tailored to the needs of medical students and physicians. It offers advice on how health professionals can manage and invest money. The guide covers all aspects of investing and financial planning, including stocks, bonds, mutual funds and real estate. It includes information on retirement planning and funding children’s education. Doroghazi is a specialist with Missouri Cardiovascular Specialists in Columbia, Mo.

*Symptom to Diagnosis*

Diane Atkorn, MD ’82, Adam Cifu, MD, and Scott Stern, MD ’84
McGraw-Hill Medical, 2005

This textbook offers a step-by-step process for evaluating a patient’s clinical complaints, diagnosing and establishing a treatment regimen. Medical students may find it helpful in making appropriate judgments about diagnosis and treatment and in prescribing optimal therapies. It also includes diagnosis tables and treatment decision-making flow charts, as well as chapters on specific ailments ranging from abdominal pain to wheezing and stridor. All three authors are associate professors of medicine at the University of Chicago.

*Exploring the Thalamus and its Role in Cortical Function, 2nd ed.*

S. Murray Sherman, PhD, and R.W. Guillery, PhD
MIT Press, 2005

The authors of this second edition challenge readers to rethink current assumptions about the cortex and its interactions with the rest of the brain. They present a counter approach to the dominant “corticocentric” way of understanding the cerebral cortex, which does not acknowledge the influence of the thalamus on neocortical areas as well as lower motor centers. In this edition, Sherman and Guillery include a new chapter that suggests perception and action have a structural link in the brain, an observation often overlooked in current understanding of perceptual processing. Co-author Sherman is professor and chairman of neurobiology, pharmacology and physiology at the University of Chicago.

*Managing Failed Anti-Reflux Therapy*

Mark K. Ferguson, MD ’77, and M. Brian Fennerty, MD, eds.
Springer, 2006

Written for any physician who treats patients with gastro-esophageal reflux disease, this multi-authored work covers standard and new therapeutic options, touching on the pathophysiology of the disease, appropriate medical management and indications for the performance of surgical and endoscopic procedures. Topics include tissue susceptibility, cyclical changes in the lower esophageal sphincter tone and the roles of bile and digestive enzymes. The text offers information on newer endoscopic treatments, including Endocinch and Stretta. It also examines injection of bulking agents along with surgical remedies. Ferguson is professor of surgery at the University of Chicago.

*Children in Medical Research: Access versus Protection*

Lainie Friedman Ross, MD, PhD
Oxford University Press, 2006

Ross presents a critical investigation of policy development governing the involvement of children in medical research. She examines the shift in focus from protection of medical research subjects to the current emphasis of access assuming a greater precedence. Ross explores infamous studies as evidence that before the policy shift, protection for the most vulnerable groups was not always adequate. She also examines the validity and fairness of the safeguards and she offers specific recommendations to modify current policies and guidelines. Ross is an associate professor of pediatrics and associate director for the MacLean Center for Clinical Medical Ethics at the University of Chicago.
African-American infants have a three times greater risk of SIDS than Caucasians and six times the risk of Hispanics or Asians, suggesting genetics plays an important role.

channel, a pore found in cardiac muscle cells that controls the passage of sodium ions in and out of the cell.

“This seemed like a good candidate for a genetic difference that could contribute to SIDS,” Goldstein said, “but we had no clear idea how it increased risk since the Y1103 variant did not affect channel operation under normal conditions.”

Cellular activity, particularly that of nerve and muscle cells, is controlled by the flow of ions like sodium and potassium. A change in an ion channel, if it disrupts ion flow, can alter the cell’s activity. So Goldstein’s team concentrated on how Y1103 might change a cell’s behavior.

On first look, it appeared to make no difference. Cells with either normal or Y1103 channels “were found to function indistinguishably,” the authors wrote.

But SIDS is not purely genetic; it appears to require multiple “hits” from altered genes and the environment. The environment’s role was demonstrated by the “Back to Sleep” campaign, begun in 1994, which cut SIDS’ prevalence in half by teaching parents to put babies to sleep lying on their backs. The campaign was based, in part, on the assumption that babies sleeping on their tummies had more spells of interrupted breathing or apnea.

An immediate consequence of apnea is a slight increase in acid levels inside oxygen-hungry muscle cells. When the researchers compared cells with the Y1103 mutation against normal cells in a slightly more acidic environment, the cells with the abnormal channels began to misbehave.

In normal cells, these sodium channels are closed at rest. In response to electrical signals they open briefly, allowing ions to flow through, then rapidly close again. When the pH levels fall, however, the mutant sodium ion channels tend to pop back open, delaying the cells’ recovery after a burst of activity. In the heart, changes like this are known to increase the risk for abnormal rhythms and sudden death.

The drug mexiletine, which is prescribed for patients with arrhythmias, blocks late re-openings of sodium channels. Goldstein and his colleagues at Chicago, as well as Yale, Howard and Ohio State universities, found that the drug restored normal function in cells with two copies of the Y1103 channels even under acid conditions.

The authors stress the need for additional studies that could “lead us

Abdominal chemo extends life

Women with stage III ovarian cancer should be treated with a combination of two types of chemotherapy to extend their longevity, according to the National Cancer Institute. The NCI based its advice on a study of 429 women with stage III ovarian cancer who were given chemotherapy after tumor removal. Those who received a combination of intravenous (into a vein, or IV) and intraperitoneal (directly into the abdomen or peritoneal cavity, or IP) chemotherapy survived nearly 16 months longer than patients who received IV chemotherapy alone. The IP chemo group also experienced more relapse-free months—23.8 compared with 18.3 for the IV group. The Johns Hopkins-directed study built upon evidence from eight clinical trials, including one conducted at the University of Chicago. Although the IP group suffered more severe side effects during treatment, the effects were temporary. Gynecologic oncologist and principal investigator Diane Yamada said the hospital will continue to offer patients as many pre- and post-operative treatments as possible.

The brain’s visual map

To convey spatial information to the brain, the eyes require cooperation between two chemical signaling systems, according to University of Chicago neurobiologists. A research team led by Yimin Zou found that a gradient of a molecule known as Wnt3 counterbalances another force provided by the EphrinB1-EphB signaling system. Together, these forces create a kind of neural connection called a “topographic mapping,” or literally a “copying” of one part of the nervous system onto another. Light-sensitive cells in the retina use this grid of censors to transfer information to the structures in the brain that interpret information from the eyes. Zou said the study is the first biological validation of a computational model developed in the early 1980s, which suggested “that two such forces would be necessary to guide axons as they establish the connections that relay spatial information from one part of the nervous system to another.” Zou’s lab also studies a family of proteins known as the Wnts and their role in nerve growth.
to consider genetic screening in African Americans in at least three situations: infants with acute life-threatening events, siblings of SIDS victims and couples that experience infertility or fetal demise.”

—John Easton

**Lung transplant program approved**

The University of Chicago Hospitals’ new lung transplant and heart/lung transplant programs won approval from the United Network for Organ Sharing earlier this year. In February, the lung transplant program began placing patients on its waiting list.

In November, five physicians and eight other team members moved to Chicago from Loyola University Medical Center in Maywood. They include medical director Edward Garrity, MD; associate medical director Sangeeta Bhorade, MD; and surgical director, Wickii Vigneswaran, MD, plus an anesthesiologist, an infectious disease specialist and six nurses. Among the nation’s most experienced teams, they have performed more than 480 lung transplants, about 35 transplants a year, with a one-year survival rate well above the median at 85 percent.

The lung team joins the medical center’s nationally recognized teams in heart, liver, kidney, pancreas, multi-organ and islet-cell transplantation, making Chicago one of the region’s most comprehensive transplant programs. Organ transplantation began at the university in 1904 when Alexis Carrel, MD, who won the Nobel Prize for his pioneering work in cardiac surgery, developed the surgical techniques and performed the first organ transplant—a heart transplant in a dog.

—John Easton

**New GI-oncology center opens**

Two top-ranked medical specialties at the University of Chicago are joining forces in a new, interdisciplinary gastrointestinal-oncology center.

“We are bringing together the enormous strengths of both the GI and oncology programs in a ‘center’ concept to provide efficient, top-notch care for our patients and innovative approaches to disease,” said Mitchell Posner, MD, professor and section chief of general surgery.

Nationally, Chicago’s gastroenterology and oncology services placed sixth and seventh, respectively, in the 2005 U.S. News & World Report Honor Roll rankings of medical specialty services. The GI-oncology center, which includes general surgery, hematology/oncology and gastroenterology, will take on complex gastroenterological cancer cases. It is funded with a $2 million grant, the largest of seven awards from the Practice Plan’s Dean’s Initiative.

Center oncologist Hedy Kindler, MD, associate professor of medicine, designs and conducts clinical trials of novel agents, including angiogenesis inhibitors and other targeted drugs for patients with gastrointestinal malignancies, such as advanced pancreatic cancer.

“We have superb, cutting-edge clinical trials to offer our patients, and we bring together an excellent team in a way that allows us closer interchange among the different specialties,” she said.

“By acting as a group,” said gastroenterologist Irving Waxman, MD, professor of medicine, “we offer our patients assistance in navigating the system, coordinated visits and better follow-up with referring physicians for optimal long-term care.”

—Susan Soric

**Genes reveal rapid evolution, separate humans from apes**

One of the first comprehensive scans of the human genome shows widespread evidence of recent evolution. A University of Chicago team has found that, during the past 100 centuries of human evolution, more than 700 genetic variants may have been targets of natural positive selection.

“There have been a lot of recent changes—the advent of agriculture, shifts in diet, new habitats, climatic conditions—over the past 10,000 years. We’re using these data to look for those signals of very recent adaptation,” said Jonathan Pritchard, professor of human
strongest signal in the genome hunt. A metabolism, such as the lactase gene, the reproductive processes and carbohydrate metabolism genes may be specific to modern human adaptation, the body’s ability to store extra resources was important; in today’s environment, those genes have been linked to obesity.

Other processes that show signals of selection include genes related to metabolism of foreign compounds, brain development, morphology, and hair formation and patterning. For instance, the researchers found five genes involved in skin pigmentation and all show evidence of positive selection in Europeans. “The idea that skin pigmentation is under strong selection in general is sort of accepted,” Pritchard said, “but only one of these five signals was known before.”

In a separate study of much older evolutionary events, another research team has found that vast differences in the human genome.

Human geneticist Jonathan Pritchard found widespread evidence of recent evolution in the human genome.

genetics and corresponding author of the paper published March 7, 2006, in the online Public Library of Science-Biology.

With data from the International HapMap Project and funding from the National Institutes of Health, the researchers classified all genes in the human genome into 222 categories based on biological function. They then examined what kinds of biological systems are undergoing adaptation. The data represented 209 unrelated individuals from three distinct populations: 89 East Asians, 60 Europeans and 60 Yorubas from Nigeria. The researchers found that the number of signals of positive selection is roughly the same within each population, and that each group shares about one-fifth of the signals with one or both other groups.

“Many of the signals seem to be more specific to modern human adaptation, like metabolism genes, which may respond to changes in agriculture, or skin pigmentation, which may respond to changes in habitat,” Pritchard said.

The researchers listed the top 16 categories that had the strongest signals, which included previously known sites of recent adaptation, such as the salt-sensitive hypertension gene. Other such categories were the sense of smell, reproductive processes and carbohydrate metabolism, such as the lactase gene, the strongest signal in the genome hunt. A mutation in the lactase gene that enables adults to digest milk was present in about 90 percent of the Europeans.

“Presumably, a few thousand years from now, if selection pressure remains the same, everyone will have [this mutation],” Pritchard said.

Modern diets and how food is used and stored in the body are important facets of human evolution. The “thrifty gene” theory suggests some genes encourage efficient food storage, leading to rapid weight gain in times of abundant supply. The researchers found signals of selection in several of these genes. Prior to modern agriculture, the body’s ability to store extra resources was important; in today’s environment, those genes have been linked to obesity.

Children at risk

Children who live in households with one or more unrelated adults are 50 times more likely to die from an inflicted injury than children who live with two biological parents, according to a recent study. Researchers Bernard Ewigman from the University of Chicago and Patricia Schnitzer from the University of Missouri-Columbia discovered that while 72 percent of children in their study lived in two-parent households, only 37 percent who died of inflicted injuries came from such a household. Risk was just as low in households with a single parent and no other adults. The researchers used data from the Missouri Child Fatality Review Program, which Ewigman, chairman of family medicine, developed in 1991. They examined 149 children under age 5 who died from injuries inflicted by a parent or caregiver in Missouri between 1992 and 1999. They found 21 percent who died from inflicted injuries lived in homes with a parent and an unrelated adult compared with only 1 percent of 289 controls, a random selection of similarly aged children who died of natural causes. Children who died from inflicted injuries were more likely to be born to young, unmarried women with less than a high-school education and limited income.

Food more powerful than pain

University of Chicago neurobiologists Peggy Mason and Hayley Foo recently proved a theory that the vertebrate brain is wired to subdue pain signals temporarily in order to accomplish crucial survival tasks such as eating, drinking and urinating. Earlier studies with food-deprived rats demonstrated similar results. However, this study shows that feeding also suppresses pain in well-fed animals, further demonstrating that eating activates pain-related “off” cells and shuts down “on” cells in the ventromedial medulla, a small region in the brain stem, duplicating the effects of morphine. Mason and Foo studied male rats in containers with wire-mesh floors, delivering enough radiant heat to one hind paw that the animal withdrew from the heat in seconds. Researchers also inserted electrodes to monitor brain activity in the feeding rats. When the rats ate, they postponed retracting the heated paw for six to eight seconds and continued to eat. The study is a major step in understanding the neurobiological mechanisms of decision making in the face of conflict.
between humans and other primates are due more to changes in gene regulation than to differences in individual genes themselves. The new finding builds on the 1975 work of Mary-Claire King and Allan Wilson, who documented a 99 percent similarity among human and chimp genes.

Scientists from Yale, the University of Chicago and Australia's Hall Institute provided powerful new evidence that altered gene regulation, rather than changes in coding, might explain how so few genetic changes could produce the wide anatomic and behavioral differences between humans and other primates. They published their findings this past March in the journal *Nature*.

They simultaneously measured the extent of gene expression in thousands of genes, providing new evidence that humans diverged from their ape ancestors in the past five million years. The team also found that transcription-factor genes —those that control the expression of other genes—were four times as likely to have changed their own expression patterns compared with the genes they regulate.

For 30 years scientists have suspected that gene regulation has played a central role in human evolution, said senior author Kevin White, PhD, associate professor of genetics and ecology and evolution at Yale. (This July, White will join the University of Chicago as the new director of the Institute for Genomic & Systems Biology and professor in the departments of human genetics and of ecology and evolution. See *Time* story, page 2.)

“These new results help to define exactly which regulatory factors may be important, at least in certain tissues,” he said. “This helps open the door to a functional dissection of the role of gene regulation during the evolution of modern humans.”

Transcription-factor genes influence the activity of many “downstream” genetic targets, so small changes in how these regulatory genes are expressed can have an enormous impact.

“When we looked at gene expression [on these specific groups of genes], we found fairly small changes in 65 million years of the macaque, orangutan and chimpanzee evolution, followed by rapid change along the five million years of the human lineage,” said study author Yoav Gilad, PhD, assistant professor of human genetics at Chicago. “This rapid evolution in transcription factors occurred only in humans.”

Liver tissue from five adult males from each species was analyzed for expression levels of two sets of genes. One set remained largely unchanged across all four species while the other changed more dramatically—usually in the human lineage—indicating powerful incentives to adapt to a changing environment.

Sixty percent of the 1,056 examined genes showed fairly consistent expression levels across all four species. This indicates that fundamental and ancient genes, many of which are involved in basic cellular processes, have remained seemingly constant for 70 million years. The authors suggest that regulation of these conserved genes is under evolutionary constraint and that altering their regulation may be harmful.

Only 10 percent of the genes in the total array were transcription factors, but among humans they represented 42 percent, a pattern consistent with “directional selection.”

Previous studies have found that many of these same genes also have evolved rapidly in humans, accumulating changes in their coding sequence and expression rates. “Together, these findings raise the possibility that the function and regulation of transcription factors have been substantially modified in the human lineage,” the authors wrote.

This is a very efficient way to make big changes with very little effort, Gilad said. By altering transcription factors, the entire
regulatory network can change with very few mutations, increasing the impact and minimizing the risk.

“The big question,” Gilad said, “is why are humans so different? What sort of changes in the environment or lifestyle would drive such a rapid shift in the expression of genes in humans and in no other primate?”

Part of the answer, he suspects, is rapid alteration in diet, probably related to the acquisition of fire and the emerging preference for cooked food. “No other animal relies on cooked food,” he said. “Perhaps the cooking process altered the biochemical requirements for maximal access to nutrients as well as the need to process the natural toxins found in plant and animal foods.”

—Catherine Gianaro and John Easton

Philanthropic encore
Let’s hope it’s a leading economic indicator. During the first four months of 2006, the University of Chicago Biological Sciences Division and Hospitals received four consecutive eight-figure donations, adding up to more than $100 million.

Gary C. Comer, founder of the Lands’ End clothing-catalogue company, led the parade. On Jan. 25, he and his wife, Frances, announced a $42 million gift to create the Comer Center for Children and Specialty Care—a four-story, 122,500-square-foot facility adjoining the recently opened Comer Children’s Hospital. This largest single donation ever made to Chicago also will help recruit leading physician-scientists and build programs in pediatric medicine.

The new Comer Center will add 50 percent to the space of the Comer Children’s Hospital. It will include a new pediatric emergency room, on the first floor, which will open this year, followed in phases by space dedicated to specialty ambulatory care, advanced operating rooms and procedural areas, and expansion of inpatient units.

The donation brings total support from the Comers for children’s services at Chicago to more than $84 million. That includes a $21 million donation in 2001 to build the children’s hospital, a $20 million gift in 2003 to add a pediatric emergency room, and support for other programs such as a mobile

Sudafed vs. Singulair
Over-the-counter Sudafed performs as well in treating hay fever as the prescription medicine Singulair, according to a University of Chicago study. Surgeon Fuad Baroody conducted the study during Chicago’s 2003 ragweed allergy season. He found that daily doses of 240 mg of pseudoephedrine hydrochloride (Sudafed 24 Hour) were just as effective as 10 mg daily of montelukast sodium (Singulair) at relieving symptoms such as nasal congestion, runny nose, sneezing and itching, and at improving the quality of life for those with hay fever—without any additional side effects. Despite similar results, the drugs work in different ways. Pseudoephedrine, designed to treat nasal congestion, constricts vessels within the nasal mucosa without any anti-inflammatory effects. Montelukast, originally designed to treat asthma, antagonizes leukotrienes, substances released during the allergic response with inflammatory effects that likely cause nasal congestion. The study found that pseudoephedrine was slightly more effective in reducing congestion and costs about 80 cents a day while montelukast costs $3.20.

Fertility clinic moves to the West Loop
The University of Chicago’s reproductive endocrinology and infertility services have moved to a new state-of-the-art facility: the Center for Reproductive Medicine and Fertility at 333 S. Desplaines St. in Chicago’s West Loop. The nearly 9,000-square-foot center combines a comforting environment with the latest in medical technology to provide a comprehensive range of services. Specialists gear services toward individuals and couples with complicated fertility and reproductive disorders, including problems caused by age-related changes in fertility, cancer-associated damage to fertility potential, and genetic and surgical problems that diminish the ability to conceive or sustain a pregnancy. Among the services is oocyte cryopreservation—egg freezing and storage that helps preserve fertility for cancer patients and others, including women who are taking medications known to decrease fertility or who wish to delay pregnancy.
primary care van for South Side schools.

Comer was born and raised on the South Side of Chicago and graduated from the Paul Revere School. An avid sailor, he gave up his career as an advertising copywriter in 1962 to start his own mail-order sailing equipment business. By 1986, that company, Lands' End, was the world's second largest apparel-only mail-order business. In 2002, it was purchased by Sears.

Comer asked that this gift not be the end of the story. “I’m tapped out,” he said. Now, it’s up to others “to dig into their pockets, to come up with the programs, to do the funding—to keep this thing going.”

Two weeks later, Jules and Gwen Knapp kept it going. Their $25 million donation will support construction of the Jules and Gwen Knapp Center for Biomedical Discovery, a 330,760-square-foot, 10-story, state-of-the-art facility that will provide a new home for translational research programs in children's health, cancer, genomics and other medical specialties.

Soon to be the tallest building on campus, the Knapp Center will provide a focal point for researchers who work at the interface between basic science and medicine. It will house up to 50 research teams from the Institute for Molecular Pediatric Science and will provide a central office for the Cancer Research Center and the newly created Ludwig Center for Metastasis Research. It also will house the Institute for Genomics and Systems Biology, which will provide genomics technologies to support research.

Like Gary Comer, Jules Knapp grew up in modest circumstances on the South Side of Chicago. He began his business purchasing Grisham Manufacturing, a maker of steel security and storm doors, in 2000 and turned that ailing company around.

The Knapps, like the Comers, are philanthropic recidivists. They previously donated $10 million to establish the Jules F. Knapp Research Center and the Gwen Knapp Center for Lupus and Immunology Research. Now, in honor of the Knapps' longstanding support, the university has named one section of campus the Knapp Research Complex. This includes the towering Knapp Center, to open in 2008, plus the existing Jules F. Knapp Research Center and the adjoining Donnelley Biological Sciences Learning Center.

After a few quiet weeks, on April 26, Ellen Gordon, the president of Tootsie Roll Industries, and Melvin Gordon, chairman of the board, announced the third big gift: $25 million dedicated to Chicago's largest science building, the 400,000-square-foot Ellen and Melvin Gordon Center for Integrative Science.

The Gordon Center, designed to support research that crosses the boundaries between physics, chemistry and biology, will bring together 100 senior scientists, along with 700 additional researchers and students. It provides desperately needed and drastically modernized space for the biochemistry and molecular biology department, the Howard Hughes Medical Institute, the Ben May Cancer Research Institute, the chemistry department and the James Frank Institute. Occupying the heart of the building is the Institute for Biophysical Dynamics, which was

The University of Chicago Biological Sciences Division and Hospitals received four consecutive eight-figure donations, adding up to more than $100 million.
jointly founded in 1998 by the divisions of Biological Sciences and Physical Sciences. “We all dream of a day,” Mrs. Gordon said, “when there is less suffering and pain in the world. Thanks to institutions like the University of Chicago, we have made enormous progress toward that day, but there is still much more to do. In business, Melvin and I look for the best return on our investment. In philanthropy, we also look for the best return and are therefore pleased to be a part of this wondrous collaborative research that can make life better for many people.”

Soon after receiving the Gordon gift, the university announced a fourth donation: $10 million for cancer research from Janet and Craig Duchossois—bringing the spring total for major gifts to $102 million. This donation, again from a family with a distinguished history of giving at Chicago, will support laboratories devoted to cancer and metastasis research, as well as cancer-related efforts in radiology and genetics.

These magnanimous gifts played a major role in driving the university’s capital campaign, the Chicago Initiative, launched in 2002, past the $1.5 billion mark toward its goal of raising $2 billion by June 2008. In honor of this extraordinary success, “Spark Discovery, Illuminate Life,” the BSD’s segment of the campaign, has been expanded to $700 million from its initial goal of $550 million.

—John Easton

Breathing problems in Rett syndrome and SIDS

Multi-institutional teams, led by University of Chicago researcher Jan-Marino Ramirez, PhD, have taken crucial steps toward understanding and treating Rett syndrome and SIDS (sudden infant death syndrome) by identifying how breathing disorders may play a part in their origin.

Rett syndrome (RS), a rare, often misdiagnosed neurodevelopmental disorder, affects one in 10,000 children, mostly female. Many die before adolescence. Breathing abnormalities are thought to be the leading cause of RS, which also slows brain and head growth, and causes mental retardation, seizures, gait abnormalities and handwringing.

“It’s a progressive disease that shows no mercy, and it’s absolutely tragic for the family,” said Ramirez, professor of organismal biology and anatomy.

One hypothesis that has dominated the thinking of many clinicians is that erratic breathing arises from problems in the brain cortex, Ramirez said. Using a

Chicago test goes nationwide

The University of Chicago has licensed a genetics test to the Mayo Clinic so that patients nationwide with colon or rectal cancer can access the technology. The test, called UGT1A1, is one of a growing number of pharmacogenomic tests, and indicates an individual’s risk for toxicity from irinotecan, an anti-cancer drug. UGT1A1 reveals whether patients have one of two common versions of a gene that encodes for a protein involved in the metabolism of the drug commonly known as Campostar. Developed by hematologist/ oncologist Mark Ratain and his colleagues, UGT1A1 previously was available only to patients enrolled in university studies. Precise dosing is extremely important for cancer chemotherapy, Ratain said, because “many of these drugs are most effective at the highest possible dose, yet they are quite toxic.” In response, the Food and Drug Administration has ordered alterations to Campostar’s package insert, advising that patients with a particular UGT1A1 genotype receive a lower starting dose. Ratain also leads the Pharmacogenetics of Anticancer Agents Research Group, which received an $18 million grant in 2005 to continue research on the connections between genetics and response to anti-cancer therapies. Funding comes from the National Institute of General Medical Sciences and the National Cancer Institute. The group includes investigators from St. Jude Children’s Research Hospital in Memphis, the University of Texas MD Anderson Cancer Center in Houston and the University of Pittsburgh.

A boon for biology

The Searle Fund at the Chicago Community Trust has granted the first $5 million of a $25 million, five-year donation to the Chicago Biomedical Consortium (CBC), a collaboration of Northwestern University, the University of Chicago and the University of Illinois at Chicago. The grant will support and stimulate innovative multi-institutional collaborations in research and education to help the Chicago area become a leader in biomedical sciences. The CBC focuses on the field of emerging systems biology—the study of protein networks, cells, tissues, entire organisms and other biological systems as integrated “wholes.” The new funds will enable the consortium to expand faculty support and further develop its infrastructure. If the program progresses as planned, the Searle Fund may provide an additional $25 million for a five-year extension, bringing the 10-year total to $50 million.
mouse model for RS, researchers instead traced the source of erratic breathing to the medulla, in the breathing center itself. Many neurons that arise in the medulla project to other targets in the brain, which may explain why many other functions are affected. Funded by the Rett Syndrome Research Foundation, the research was published Dec. 14, 2005, in the Journal of Neuroscience, with Ramirez as lead author.

Ramirez’s team also found a significantly decreased amount of the neuromodulator norepinephrine in the breathing center. When his team added norepinephrine to the isolated breathing center, the breathing pattern normalized. “It became exactly as regular as the control. This was amazing,” he said. “This experiment shows that the breathing problem can potentially be treated because you can compensate for the missing neuromodulatory drive.”

The researchers also suggest that the nervous system initially may compensate for the loss of norepinephrine, which may explain why breathing appears normal at the behavioral level. However, the norepinephrine deficiency eventually disturbs other neuromodulators, including serotonin and substance P. Other systems become disrupted, setting off a cascade of physiological problems in the developmental and autonomic systems.

The team included scientists from Centre National de la Recherche Scientifique, Université de la Méditerranée, Instituto Politécnico Nacional, Northwestern University, Hôpital d’Enfants de la Timone and the Medical College of Wisconsin. While some researchers worked with brain tissue, others worked with the RS mouse model.

In 1999, a team of scientists in Texas, led by Huda Zoghbi, located the mutated RS gene MECP2 on the X chromosome. Exploring how this gene leads to disturbance of norepinephrine is “obviously one of the next issues that needs to be addressed in our experiments,” Ramirez said.

Using the animal model, Ramirez and his colleagues plan to start screening commercially available medications for erratic breathing, looking at drugs that affect norepinephrine and serotonin. For example, Prozac, which treats depression, boosts serotonin levels, while prescription drugs for attention deficit hyperactivity disorder boost serotonin and norepinephrine levels. (Substance P, located in the same nerve cells as serotonin, also will be affected.)

Ramirez said he is eager to discover whether treating erratic breathing will affect other problems associated with RS. “Norepinephrine, serotonin and substance P are involved in many other functions, including motor control, which may help with handwringing or, if we are lucky, possibly also walking. And by understanding any of these neuromodulators, we’ll better understand a lot of childhood disorders,” he said.

That includes SIDS, another focus of Ramirez’s research. Working with mouse tissue slices, he and colleagues discovered that pacemaker cells, a type of neuron, control gasping. These findings were published last year in the journal Neuron. Recently, University of Bristol researchers got the same results using rats.
“Gasping is an important arousal or auto-resuscitation mechanism,” Ramirez said. “It resets a baby’s normal breathing rhythm and also alerts infant and mother that something is wrong.”

Now Ramirez and colleagues at the Medical College of Wisconsin and the Departamento de Farmacobiologia, Cinvestav-Coapa, Mexico, have found evidence that disturbed serotonin levels in pacemaker cells may lead to SIDS. The results of their recent study, funded by a National Institutes of Health grant, were published in March in the Journal of Neuroscience.

Serotonin regulates the sodium channels in pacemaker cells, so Ramirez’s team examined serotonin levels in pacemaker neurons in the breathing center. When the body senses a lack of oxygen, known as hypoxia, it shuts down most of the cellular respiratory network and focuses its energy on gasping, which is modulated solely by sodium-driven pacemaker neurons. If pacemaker neurons are blocked, for whatever reason, the body cannot gasp.

If a baby goes into hypoxia—from a blocked airway or insufficient oxygen while sleeping on the tummy—the child needs those sodium-driven pacemakers in order to gasp, which then wakes the baby and initiates movement or crying.

When the researchers removed serotonin from pacemaker cells, the gasping decreased drastically, from about 20 gasps to just two or three gasps—not enough to awaken the baby.

“During normal breathing, it’s a complicated network,” Ramirez said. “However, the network becomes more vulnerable to situations like hypoxia, because under these conditions, respiration relies on only one group of pacemakers that become the critical drivers of [breathing] rhythm.”

Disturbed serotonin levels also are implicated in psychiatric conditions, including depression, bipolar disorder and attention deficit disorder. Adults with such conditions may be SIDS survivors, Ramirez said.

Now Ramirez and his colleagues are looking closely at the effects of different levels of serotonin and norepinephrine to gain a better idea of exactly how much of each is necessary to keep auto-resuscitation intact.

If there’s a problem with serotonin, the gasping is gone, he said. “And when these children don’t gasp, they don’t wake up.”

—Catherine Gianaro

### Little help for obese poor

Lower-income obese people are the least likely to undergo weight-loss surgery, an increasingly popular obesity remedy, according to researchers at the University of Chicago and the University of California-Irvine. In 1998, U.S. surgeons performed an estimated 13,365 bariatric procedures, primarily gastric bypass operations. In four years, that number quadrupled to 72,177. The study’s authors project as many as 218,000 procedures by 2010. However, the group most in need of the surgery is not the one driving the increase. Along with this trend is a slower but substantial shift toward patients from wealthier households with private insurance. This shift, which the study authors describe as “worrisome,” coincides with the American population’s increase in obesity. In 1986, one in 200 American adults had a body mass index of 40 or above, indicating morbid obesity. By 2002, that number had risen to one in 20, with even higher rates among those with lower income and education levels.

### Minorities gain little from genetic testing

Women with a family history of breast and/or ovarian cancer should meet with a genetics counselor to assess their own risk, consider genetic testing and take appropriate precautions, according to authors of a University of Chicago study on minority women and cancer risk. Hematologist/oncologist Funmi Olopade and colleagues discovered that some ethnic minorities are getting left behind in the push to find breast cancer susceptibility genes. In fact, so few high-risk minority women have received genetic counseling or testing that the standard methods of calculating risk remain unvalidated in these groups, leaving room for surprises in genetic test results. The researchers found that predicting risk based on family history and age of diagnosis works just as well for families of African ancestry. However, the spectrum of genetic mutations that occurs in African Americans with breast cancer is vastly different. “Irrespective of ancestry,” Olopade said, “early age of diagnosis and family history of breast and ovarian cancer are the most powerful predictors of mutation status.”