Sex.
There. Now we’ve said it.
This ubiquitous biological process has remained among the least discussed in medicine.
But new medical research is exploring the implications of sexuality in everything from aging to cancer treatment. Two groundbreaking studies at the University of Chicago recently pointed out the importance of such considerations even when patients are being treated for other conditions.
In the first comprehensive national survey of sexual attitudes, behaviors and problems among older Americans, researchers from Chicago’s National Social Life, Health and Aging Project (NSHAP) found that sexuality remains an important part of life for most people ages 57 to 85.
Data reported in the Aug. 23, 2007, issue of the New England Journal of Medicine showed that the frequency of sexual activity among older adults—for those who remain active—declines only slightly from the 50s to the early 70s. Many men and women who remain sexually active continue to participate in vaginal intercourse, oral sex and masturbation well into their 70s and 80s, the researchers said.
“We found that older adults remain interested and engage in sex, yet many experience bothersome sexual problems that can compromise both health and relationships,” said lead author Stacy Tessler Lindau, MD, assistant professor of obstetrics and gynecology and of medicine.
With baby boomers now entering their 60s, older adults are the fastest growing segment of the U.S. population. Yet the “lack of reliable information about how sexual activity and function might change with age and illness, combined with taboos around discussing sex in later life, contributes to worry or even shame for many older adults,” Lindau said.
NSHAP, funded by the National Institutes of Health, was created to discover how social relationships, especially intimate relationships, influence health as people age. Between July 2005 and March 2006, the researchers interviewed 3,005 people ages 57 to 85 in their homes. They asked about social and marital history, sexual activity and function, and physical and mental health.
Many medical conditions and treatments can interfere with sexuality. American men spend more than $1 billion a year on medications to improve sexual function. Yet few older men (38 percent) and even fewer women (22 percent) had discussed sex with a physician since age 50, the researchers found. Men were more likely to do so, perhaps because effective drugs are available. Nearly one in seven men (14 percent) reported taking medication to improve sexual function.
The NSHAP team assessed participants’ vision, hearing, sense of touch, taste and smell and gathered data on how older adults perceive social relationships. In a departure from previous surveys, they also collected physiological specimens such as spots of blood, saliva and vaginal swabs. In follow-up studies, the researchers will use “biomarkers” from these specimens to obtain evidence about hormone levels, prevalence of diseases such as heart disease or diabetes, and the frequency of human papillomavirus, a sexually transmitted disease.
Despite the personal nature of many of the questions, study participants were very forthcoming. Seventy-five percent of those approached agreed to participate. Overall, only 2 to 7 percent declined to answer direct questions about sexual activities or problems. (Fourteen percent did not answer questions about masturbation on a self-administered questionnaire.) “Participants were more likely to refuse questions about income than they were about sex,” Lindau said.
Many of those who were sexually active found ways to remain active, despite worsening health. The proportion of sexually active couples that engage in oral sex, for example, hovered at around 50 percent for those under 75. More than half of men and a quarter of women, whether they had a sexual partner or not, acknowledged masturbating.
“Although sexuality has long been thought to deteriorate inevitably with age, we found that health is a more important indicator for many aspects of sexuality than is age alone,” Lindau said. “This suggests that older adults with medical problems, or those considering treatment that might affect sexuality, should be counseled based on health status rather than just their age.”

The most common reported reason for sexual inactivity among individuals with a spousal or other intimate relationship for men (55 percent) and women (64 percent) was the male partner’s physical health. Women, especially those who were not in a current relationship, were more likely than men to report lack of interest in sex.

“We hope our findings improve public health by countering harmful stereotypes and allowing older individuals to view their experience relative to others,” Lindau said. “It may comfort people to know that they are not alone in enjoying sexual activity as they age or in experiencing sexual problems, some of which could be alleviated with medical attention.”

Let’s talk about sex, cancer survivors say

In a separate study also conducted by Lindau, long-term survivors of genital-tract cancer reported they were pleased with the quality of their cancer care but less satisfied with the emotional support and information they received about dealing with the effects of the disease and treatment on sexuality.

Sixty-two percent of women who had undergone “severe compromise to their reproductive and sexual organs” said their physicians had never brought up the effects of their treatment on sexuality, even though 74 percent of the women in this study believed that physicians should initiate a discussion about sex.

“It seems unbelievable to me,” said one cancer survivor in the survey, “that a surgeon would remove one’s sexual organs and never talk about sex.”

Women who had not had such frank discussions with their doctors were three times as likely to suffer from multiple sexual problems at the time of the survey, the researchers reported in the August 2007 issue of Gynecologic Oncology.

“We found that these women valued sexuality and participated in sexual relationships and activities at a rate similar to women who had not been through cancer treatment, but they were not adequately prepared for the sexual issues that their cancer or its treatment introduced,” Lindau said.

“Discussions with a physician about sexual consequences of cancer and cancer treatment matter a great deal to many of these patients,” she said. “But survivors report that such conversations infrequently occurred. If such discussions are not happening in this context, we suspect that they are even less likely to occur when the connections between disease or treatment and sexual function are less apparent.”

Lindau and colleagues surveyed 219 women who had been treated for a rare form of vaginal or cervical cancer. The women were contacted through the Registry for Research on Hormonal Transplacental Carcinogenesis, established in 1971 by Arthur L. Herbst, MD, professor and former chairman of obstetrics and gynecology at Chicago. The registry tracks the medical history of patients with specific gynecologic cancers who may have been exposed to diethylstilbestrol or other synthetic hormones while still in their mother’s womb.

The researchers found that the cancer survivors—now in their late 40s and 50s—were just as likely as a control group to be married and to be sexually active, despite a remarkably higher prevalence of sexual problems. They were also four times as likely to have health problems that interfered with sex “all or most of the time” (17% vs. 4%).

More than one third complained that their treatment, though life-saving, had left them with surgical scars, frequent bladder infections or incontinence after sex that made them feel unattractive.

Those who reported a conversation with a physician about the sexual effects of cancer treatment were three times less likely to have “complex sexual problems” (defined as three or more concurrent sexual problems).

Previous studies found that patients typically will not initiate such a conversation. This study showed that although the vast majority of long-term cancer survivors believed physicians ought to initiate such a discussion, the majority of physicians did not do so.

“Strong evidence for the negative impact of medical illness and treatment on sexual functioning exists,” the authors note, “but concern for sexual matters remains largely on the margin of medical care, particularly for older women.”

—John Easton
Coelacanth fossil sheds light on fin-to-limb evolution

“Part of the reason why this is an interesting discovery is that people think of coelacanth animals as archetypal living fossils.”

—Matt Friedman, PhD student in evolutionary biology

A 400 million-year-old fossil of a coelacanth fin fills a shrinking evolutionary gap between fins and limbs, according to University of Chicago scientists whose paper was highlighted on the cover of the July/August 2007 issue of the journal Evolution & Development.

The first finding of its kind, the fossil shows that the ancestral pattern of lobed fins closely resembles the pattern in the fins of primitive living ray-finned fishes, the scientists said.

“This ends intense debate about the primitive pattern for lobed fins, which involves the ancestry of all limbs, including our own,” said author Michael Coates, PhD, associate professor of organismal biology and anatomy at Chicago.

The fossil’s pattern is similar to the branching arrangement still embedded in the fins of paddlefishes, sturgeons and sharks, Coates said.

“Part of the reason why this is an interesting discovery is that people think of coelacanth animals as archetypal living fossils,” said Matt Friedman, an evolutionary biology graduate student at Chicago and lead author of the paper. “But it’s a common misconception. If you look deep in the fossil record to the first members of that group, they are really different and very diverse.”

Until now, many biologists have looked at lungfish as a primitive model of the evolution of tetrapods, four-limbed vertebrates like ourselves. However, “to understand the developmental evolution of the limbs of tetrapods, we shouldn’t be looking at the fins of our nearest living fish relatives—lungfishes and coelacanths—because they’re far too specialized,” Coates said.

“If you’re going to figure out how limbs evolved, you need to have a good idea about pre-conditions,” Friedman said. “You need to know what the ancestral morphology was. With things like this [fossil], we’re beginning to hone in on the primitive conditions of fins that gave rise to limbs later on.”

Named Shoshonia arctopteryx after the Shoshoni people and the Shoshone National Forest, the fossil was excavated from Paleozoic sediments at Beartooth Butte in northern Wyoming.

Shoshonia also supports recent work by Chicago’s Neil Shubin, Marcus Davis and Randall Dahn that showed genetic expression of developmental patterns in fish fins and tetrapod limbs are conserved (Nature, May 24, 2007). “With this fossil, we have a conservative pattern in a close relative of tetrapods that is actually conserved in other fish groups outside of this immediate group,” Friedman said.

Not only does this fossil bridge the gap between primitive ray-finned fish and limbed animals like Tiktaalik roseae, the new data forces scientists to reassess the characteristics of the fossil, Friedman said.

Coelacanths were dubbed “Old Fourlegs,” because of their husky, limb-like fins.
Would you like fries with that?

“Simply by changing the timing, taking this medication with a meal instead of on an empty stomach, we could potentially use 40 percent—or even less—of the drug.”

—Mark Ratain, MD, professor of hematology and oncology

One man's trash is another man's treasure, the saying goes. And where high-priced, high-tech cancer treatments are concerned, one scientist's dosing problem could be another's opportunity.

Such is the argument presented by a pair of University of Chicago oncologists in the July 16, 2007, issue of the Journal of Clinical Oncology when they suggested that exploiting interactions between food and drugs could dramatically lower the cost of several anti-cancer drugs—and perhaps many other medications.

In a commentary, Mark Ratain, MD, and Ezra Cohen, MD, called attention to recent studies showing how certain foods can alter absorption or delay breakdown of precisely targeted anti-cancer drugs.

Instead of viewing such studies as highlighting a dosing problem, Ratain and Cohen argue they should point researchers toward a partial solution: a novel way to decrease medication costs while increasing benefits from these effective but expensive drugs.

The commentary was inspired by a study presented at the 2007 annual meeting of the American Society for Clinical Pharmacology and Therapeutics. Researchers from Dartmouth showed that taking the breast cancer drug lapatinib with food—instead of on an empty stomach as suggested on the label—resulted in more of the drug being absorbed and available to treat the cancer.

Patients currently take five 250 mg lapatinib tablets on an empty stomach. The study found that taking the drug with a meal increased the bioavailability of the drug by 167 percent. Taking the drug with a high-fat meal boosted levels by 325 percent.

“Simply by changing the timing, taking this medication with a meal instead of on an empty stomach, we could potentially use 40 percent—or even less—of the drug” to achieve the same result, Ratain said. “Since lapatinib costs about $2,900 a month, this could save each patient $1,740 or more a month.”

Topping off that meal with grapefruit juice, “which may also increase plasma concentrations” according to the package insert, could increase the savings to 80 percent, the authors suggested, “minus the cost of the food and juice.”

“We expect the one 250 mg lapatinib pill accompanied by food and washed down with a glass of grapefruit juice may yield plasma concentrations comparable to five 250 mg pills on an empty stomach,” Ratain said.

Such a “value meal,” the authors add, may have other benefits. The major toxicity associated with lapatinib is diarrhea, probably caused by unabsorbed drug. So taking a lower dose with food should “reduce the amount of unabsorbed drug, and therefore theoretically also reduce the frequency and severity of diarrhea.”

Ratain and Cohen are currently conducting a phase I trial of the combination of oral sirolimus (rapamycin) taken with grapefruit juice, which contains substances that delay the breakdown of many drugs.

Dozens, perhaps hundreds, of drugs should be studied in this way, the authors said. “If we understood the relationship between, say, grapefruit juice and common drugs, such as the statins, which are taken daily by millions of people to prevent heart disease, we could save a fortune in drug costs,” Cohen said. “And patients would get a little vitamin C to boot.”

“The rapidly escalating price of medications (especially for cancer and other life-threatening diseases) has provided incentives to explore pharmacological approaches to lower the costs of drugs,” the authors wrote. “As we enter an era of ‘targeted’ anti-cancer agents with a monthly cost measured in thousands of dollars, we should view drug-drug or drug-food interactions as opportunities to lower costs.”

—JE

Unpaired, vulnerable cell channels invite toxins

Scientists know that smoke and other toxins can seep into lung and heart cells, causing damage. But now they’ve pinpointed the spot where such toxins breach the cells. These small porholes, called hemichannels, normally function in pairs, helping cells exchange chemical signals. But some of these hemichannels are unpaired and vulnerable, according to a study by nano-microscopist Ratneshwarn Lal. “We were surprised to find out how little it took to cause such damage,” Lal said. “We expect that this mechanism could play a major role in the onset of diseases such as emphysema.” Researchers now are looking into creating drugs to protect those unpaired channels or even prevent them from being created in the first place.

Addiction: It may be all in your receptors

Addiction-prone people may have an especially sensitive receptor that triggers the brain’s reward center, according to neurobiologist Daniel McGehee. He found that rats with more responsive nicotinic acetylcholine receptors were more likely to self-administer addictive drugs than rats with less responsive ones. The same rats also were more likely to explore a new environment for a prolonged period of time, McGehee said. “This study raises the possibility that nicotinic receptors may be important targets for the treatment of multiple additions, not just nicotine. But blocking those receptors may also interfere with healthy behaviors that depend upon the same brain circuitry.”

NIH sows research harvest

A five-year, $23 million grant from the National Institutes of Health is part of an effort to “transform how clinical and translational research is conducted” by eliminating barriers among academic disciplines, between laboratory and clinical research, and among scientists. With the Clinical and Translational Science Award to the University of Chicago, scientists from the biological, physical, behavioral and social sciences, physician-scientists from the medical school, and faculty from the schools of public policy, social service administration and business will collaborate on translational and clinical research. Residents of the diverse neighborhoods surrounding the campus also will be brought into the program. The grant will speed the transition of new knowledge from laboratory bench to patient bedside and push the boundaries of personalized medicine.
Prostate cancer, the second leading cause of cancer death in American men, disproportionately strikes those of African descent. African Americans have a higher incidence rate, are diagnosed later, and have a higher mortality rate from the disease than those of other lineages.

Two recent University of Chicago studies examine the problem both from distinctly different angles: the patients’ genes and their points of view.

In one study, many African-American men radically underestimated the likelihood that having a needle biopsy for suspected prostate cancer would result in a cancer diagnosis, according to researchers who presented their findings at the American Society of Clinical Oncology annual meeting.

“A group that underestimates the risk of having cancer is likely to underestimate the value of early detection and thus skip the whole process,” said study author William Dale, MD, PhD, assistant professor of medicine, “which may explain, in part, why African-American men are so often diagnosed later and thus have worse outcomes.”

Dale and colleagues collected data on 243 patients waiting in a urology clinic. They asked what these patients expected from their biopsies and how anxious they were about the results.

In general, African Americans were less likely to believe they were at risk for cancer and less anxious about the possibility. In fact, even while awaiting a prostate biopsy, more than half the African-American patients said they believed they had a 0 percent chance of having the disease; only 20 percent of Caucasians gave the same response.

“These data suggest that, while men of both races underestimate their chances of having prostate cancer, African-American men are even more likely to do so. Such beliefs may cause these men at highest risk for prostate cancer to delay the pursuit of a diagnosis,” Dale said.

“With this data, we can’t say why the estimates are so low. We want to conduct more research to better understand the reasons for the overly low estimates,” he said. “That would hopefully lead to greater attention to prostate cancer for those at highest risk such as African Americans.”
Four Chicago faculty members have won National Institutes of Health grants to pursue biological sciences research crossing disciplinary boundaries. In the BSD, psychiatrist Kristen Jacobson and hematologist/oncologist Dorothy Sipkins each received $1.5 million grants. Jacobson will study the effects of individuals, family, peers and neighborhood on adolescent problem behavior. Sipkins will investigate molecular characteristics of microenvironments within bone marrow and how normal, healthy hematopoietic stem cells compete with malignant cells to occupy these coveted niches. Physicist Margaret Gardel and chemist Rustem Ismagilov were awarded $2.5 million each. Gardel will study differences between living, biological matter and inert, physical matter, which could lead to new therapies for cancer and other diseases. Ismagilov studies microfluidic technologies—the flow of fluids through channels thinner than a human hair—for aging and disease research.

A new genetic variant

Separate research at the university has uncovered two tiny genetic variations that may help scientists find more precise ways to estimate prostate cancer risk and improve screening and early detection for men of African descent.

Researchers from the University of Chicago and the Translational Genomics Research Institute (TGen) in Phoenix, Ariz., reported the results in the December 2007 issue of the journal Genome Research.

The researchers set out to determine whether results from four previous studies that linked genetic variations on one region of chromosome 8 to increased prostate cancer risk among Caucasians also were valid for men of African heritage. In the process, however, they found an additional genetic variation among African-American men that was an even stronger marker for cancer risk for these men. That variation is located within a gene that plays a role in DNA repair. A malfunction in DNA repair could contribute to cancer development.

“This finding emphasizes the importance of ancestry in studying genetics,” said study author Rick Kittles, PhD, associate professor of medicine.

Research groups led by Kittles and by John Carpten of TGen analyzed the region of chromosome 8 highlighted by the earlier studies done on Caucasian men. But this time they searched for tiny genetic differences between 490 African-American men who had been diagnosed with prostate cancer at Howard University Hospital in Washington, D.C., and 567 African-American men without cancer.

The researchers were able to replicate the link between one of the markers detected by previous studies and increased risk. More important, they found a new genetic marker, known as rs7008482, that was even more strongly associated with prostate cancer in African Americans. This marker was located within a gene that is involved in DNA replication, recombination and repair.

Altering this gene could confer an “inherited predisposition to genetic instability,” Kittles said. “This could lead to increased cancer risk. By studying this region, we may be able to develop molecular targets for improved screening, early detection and possibly treatment.”

—Scot Roskelley and JE

Gene mixing

In Greek mythology, the Chimera was a fire-breathing she-monster with a lion’s head, a goat’s body and a serpent’s tail. But the latest incarnation is much fuzzier—and smaller—than the original. University of Chicago researchers have teamed up with Chinese and British scientists to create hybrid offspring of a field mouse and a wood mouse. This chimera marks the first time researchers have used stem cells from two mammalian species to create a third, new species. Though both are rodents, the wood mouse and the house mouse have evolved separately for up to 20 million years. Their genes differ by as much as 18 percent—about 12 times the difference between human and chimpanzee.

“We’re going to continue with these animals for a while to see if we can understand the developmental cues and learn how to manipulate the system,” said geneticist Bruce Lahn. Researchers also plan to merge stem cells from mice and rats, which have vastly different body sizes and a 20 percent genetic difference.
For some diabetics, burden of care rivals complications of disease

“It is hard to convince some patients to invest their time and effort now in rigorous adherence to a complex regimen with no immediate reward, just the promise of better health years from now.”

—Elbert Huang, MD, assistant professor of medicine

Many patients with diabetes say that the inconvenience and discomfort of constant therapeutic vigilance—particularly multiple daily insulin injections—has as much impact on their quality of life as the burden of intermediate complications, researchers from the University of Chicago reported in the October 2007 issue of Diabetes Care.

A typical diabetes patient takes many medications each day: two or three different pills to control blood sugar levels, one or two to lower cholesterol, two or more to reduce blood pressure, a daily aspirin to prevent blood clots, plus diet and exercise. As the disease progresses, the drugs increase, often including insulin shots.

“The people who care for patients with a chronic disease like diabetes think about that disease and about preventing long-term complications. The people who have a chronic disease think about their immediate lives, which includes the day-to-day costs and inconvenience of a multi-drug regimen,” said study author Elbert Huang, MD, assistant professor of medicine. “The consequences are often poor compliance, which means long-term complications, which will then require more medications.”

Despite growing reliance on such complex multi-drug regimens, large proportions of patients with type 2 diabetes continue to have poorly controlled glucose (20 percent), blood pressure (33 percent) and cholesterol (40 percent).

“This tells us that we need to find better, more convenient ways to treat chronic illness,” Huang said. “It is hard to convince some patients to invest their time and effort now in rigorous adherence to a complex regimen with no immediate reward, just the promise of better health years from now.”

Huang and colleagues conducted hour-long, face-to-face interviews with a multi-ethnic sample of 701 adult, type 2 diabetes patients attending Chicago-area clinics between May 2004 and May 2006. They asked patients to rank the benefits of various treatments and the daily quality-of-life burdens of diabetes-associated complications.

Patients were asked to express their preferences in a series of trade-offs. The surveyors asked, for example: Would you rather have six years of life in perfect health, or 10 years with an amputation?

As expected, patients were most distressed by end-stage complications, especially kidney failure, a major stroke or blindness. They were slightly less concerned about amputations or diabetic retina damage, and still less about angina, diabetic nerve or kidney damage.

Patients also disliked intensive treatments, especially intensive glucose control, with multiple daily insulin injections, and what the authors called comprehensive diabetes care, which was intensive glucose control plus other medications.

On average, patients ranked the burden of comprehensive diabetes care and intensive glucose control as equal to the burden of angina, diabetic nerve damage or kidney damage.

Patients varied widely in how they ranked treatments and complications. Those who had experience with a specific medication or complication saw them as having less of an impact on quality of life than did those without such experience.

But many patients found both complications and treatment onerous. Between 12 and 50 percent were willing to give up eight of 10 years of life in perfect health to avoid life with complications. More surprising, between 10 and 18 percent of patients were willing to give up eight of 10 years of healthy life to avoid life with treatments.

“Our study results show that taking multiple medications on a routine basis represents a significant burden for many patients,” the authors conclude. “Quality of life related to treatments will be likely to improve if we can simplify or modify treatments.”

—JE
Internists prescribe placebos as treatment

“Placebos have been used in medicine since ancient times, and remain both clinically relevant and philosophically interesting.”
—Rachel Sherman, fourth-year medical student

Some doctors are putting the phrase "mind over matter" to use in their medical practices. Almost half of the Chicago internists who responded to a recent survey said they have given their patients prescriptions for placebos.

Of the 231 local physicians, 45 percent had prescribed placebos at some point during their practice.

"Placebos have been used in medicine since ancient times and remain both clinically relevant and philosophically interesting," said Rachel Sherman, a fourth year student at Pritzker Medical School who co-authored the study with John Hickner, MD, MSc, professor of family medicine at the University of Chicago. "In addition to their recognized use as controls in clinical trials, this study suggests that placebos themselves are viewed as therapeutic tools in medical practice."

Of the respondents who reported using placebos in clinical practice, 34 percent introduced the placebos to the patient as "a substance that may help and will not hurt." Nineteen percent told their patients that "it is medication," and 9 percent said "it is medicine with no specific effect." Only 4 percent explicitly said, "it is a placebo." In addition, 33 percent of the physicians reported they gave other information to patients, including "this may help you but I am not sure how it works."

The study, the first of its kind to examine American physicians’ use of placebos in clinical practice in the 21st century, was published in the January issue of the Journal of General Internal Medicine. It “indicates a need for greater recognition of the use of placebos and unproven therapies and discussion about its implications,” the authors said.

Only 12 percent of respondents said that placebo use should be categorically prohibited.

The authors acknowledge the controversy involving placebos. Some critics, citing informed consent, caution against their use. Others say placebos can be used in ways that don’t pose ethical dilemmas.

The study also revealed that many physicians believe a person’s mindset can impact the health and well-being of the body. Rather than using placebos to differentiate between patients who were faking their symptoms and those with genuine symptoms, as the majority of physicians did according to research several decades ago, 96 percent of physicians in the study said they believed placebos can have therapeutic benefits for patients.

The physicians most commonly defined a placebo as an intervention not expected to have an effect through a known or specific physiologic mechanism. Researchers then asked physicians about the possible benefits of other treatment and factors that may influence health according to this definition of a placebo. Physicians responded to questions about whether there might be psychological or physiological benefits to meditation, yoga or relaxation techniques; biofeedback; prayer or spirituality; a good social support system; having good doctor-patient rapport; and interior design of the health care environment. In most cases, the majority of physicians believed in both psychological and physiological benefits.

New hope in cancer care

Pediatric cancer patients have new options for treatment with the introduction of phase I clinical trials at the University of Chicago Medical Center. “Ultimately, these trials will deliver new pediatric cancer treatments more quickly,” said pharmacogeneticist Mark Ratain. The trials, available to adolescents age 14 or older with certain refractory or relapsed cancers, bring together the pediatric cancer specialists with the adult cancer research program. Physicians and scientists will compare pediatric and adult patients and monitor the effectiveness of the pharmacokinetics and the toxicity of the drugs. In phase I trials, physicians begin by using small doses and gradually increase to assess toxicity and determine the best dosage.

Religious doctors miss calling

Religious physicians may describe medicine as a calling, but many don’t answer the call to help the underserved, according to a study co-authored by internist Farr Curlin. “This came as both a surprise and a disappointment,” Curlin said. “We found that religious physicians were not more likely to report practice among the underserved than their secular colleagues.” Those who strongly agreed that religious beliefs influence their practices were more likely to practice among the underserved, he said. However, 35 percent who described themselves as non-religious practiced among the underserved, compared with 31 percent who were more “generally religious.” In a separate study, Curlin found that psychiatrists are the least religious of all medical specialties but take the most interest in their patients’ religions.
Self-described “country doc” named executive vice president, associate dean

“Eric Whitaker has an unrivaled track record for understanding the broader health care needs of the underserved and finding imaginative and remarkably effective ways to meet those needs.”

—James Madara, MD, dean of the Biological Sciences Division

Eric Whitaker, MD, MPH, a nationally recognized public health authority, expert on minority health issues and, in his own words, “country doc” for some of the city’s poorest communities, has been appointed executive vice president for strategic affiliations and associate dean for community-based research, a new position at the University of Chicago Medical Center.

Whitaker, 42, comes to Chicago from the Illinois Department of Public Health, where he has served as director since 2003, overseeing three state labs, seven regional offices, 200 programs, 1,200 employees and a $420 million budget. Under his direction, from 2003 to 2007, the agency placed special emphasis on emerging issues such as bioterrorism and emergency preparedness, as well as health disparities, patient safety and the creation of the Illinois Regenerative Medicine Institute to support stem cell research.

Prior to that, Whitaker was a senior attending physician at Cook County Hospital and founder and director of Project Brotherhood, an innovative, award-winning barbershop-based program designed to improve the often-neglected health of black men.

“Eric Whitaker has an unrivaled track record for understanding the broader health care needs of the underserved and finding imaginative and remarkably effective ways to meet those needs,” said James Madara, MD, chief executive officer of the medical center, dean of the Biological Sciences Division and vice president for medical affairs at Chicago. “He understands how people with fewer resources make decisions about their health, how to lead people toward better decisions and how to put programs in place—on the personal level as well as the state level—to make it all work.”

Whitaker will be a key player in implementing the Urban Health Initiative (UHI), the medical center’s long-range plan to build and maintain a network of community partnerships to provide patient care, conduct community-based clinical research and broaden medical education.

He will help set up strategic alliances to create and sustain the UHI, secure government and private sources of financing, and build patient confidence in and familiarity with the proposed network of independent health care providers—a system designed to improve access, quality, efficiency and coordination of health care services.

“The University of Chicago Medical Center has demonstrated an ongoing and increasing dedication to the rigorous intellectual pursuits of academic medicine, as well as an unfailing commitment to improving the health and well being of those who reside on the city’s South Side,” Whitaker said. “This position appealed to me as an opportunity

Goo-goo and ga-ga may not be exclusive to humans.

Dario Maestripieri, PhD, associate professor in comparative human development and on the committees on evolutionary biology and neurobiology, discovered that some female monkeys use special vocalizations to interact with infants, similar to human “motherese.” Maestripieri and a group of researchers analyzed the vocalizations among adult female macaques on an island near Puerto Rico and found that grunts and other specific sounds increased when a baby was present. “Adult females become highly aroused while observing the infants of other group members,” explained study researcher Jessica Whitham, a recent PhD graduate of Chicago. Unlike humans, the macaques did not direct such noises toward their own offspring. Researchers speculate they are familiar with their own offspring and use the sounds with others because they are excited about seeing a new infant.
to make a real and lasting difference in the lives of thousands of Chicagoans."

A graduate of Grinnell College and Chicago's Pritzker School of Medicine, Whitaker also earned a master's degree in health policy and management from the Harvard School of Public Health and studied health services management at Northwestern's Kellogg School of Management and corporate strategy at Chicago's Graduate School of Business.

He completed his residency in internal medicine at the University of California-San Francisco in 1996 and then served a two-year fellowship in the Robert Wood Johnson Clinical Scholars Program at Chicago. While an attending physician at Cook County Hospital, he joined the faculty at Rush Medical College in 1996 as an instructor in medicine and in 2000 became an assistant professor of medicine and then of preventive medicine. In 2003, he left Rush and joined the faculty at the University of Illinois-Chicago School of Public Health.

Whitaker gained national attention as founder and director of Project Brotherhood: A Black Men's Clinic. In 1998, he developed a new clinical model for that combined health care and disease prevention with vocational and spiritual guidance, all in the setting of a barbershop. Using the lure of free haircuts to bring in black men—who despite high rates of preventable disease and premature death tend not to seek regular medical care—this widely recognized South Side clinic brings primary care services, health advice, wellness programs, and emotional and spiritual support to thousands.

“In the United States, thanks to our world-renowned research centers, we have access to the best medical care in the world, but not everyone has the same access and not all of our health care resources are being used efficiently,” Whitaker said. “I see my role as trying to find new and innovative strategic ways to reduce health care disparities and inequities.”

He lives on Chicago’s South Side with his wife, Cheryl, their son, Caleb, and daughter, Caitlin. —JE

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**Dinosaurs and pre-dinosaurs** (called dinosaurmorphs) frolic on the Pangea land mass: Their bones were found together in the Hayden Quarry of North Mexico at the fossil-rich grounds of Ghost Ranch. This discovery challenges a long-held theory that dinosaurs diversified and replaced their predecessors relatively quickly in the late Triassic Period. The report in the July 2007 issue of the journal *Science* suggests that dinosaurs and dinosaurmorphs coexisted for at least 15 to 20 million years. Nathan Smith, a University of Chicago graduate student in evolutionary biology, was among the researchers who found the bones. The team also discovered a new species of dinosaurmorph and named it *Dromomeron romeri* after Alfred Sherwood Romer, the paleontologist who first described dinosaurmorphs in the early 1970s.

Illustration by Donna Braginetz for UC Berkeley—courtesy of *Science* magazine

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**Therapy fails broken hearts**

Therapy may help a broken heart, but it won’t improve them all, according to a study of cardiac resynchronization therapy, or CRT. “This is a valuable therapy for carefully selected patients,” said John Beshai, study leader and director of pacemaker and defibrillator services, “but further research will be necessary to determine which additional groups might benefit.” CRT devices are surgically implanted and deliver electrical impulses that improve the heart’s pumping efficiency. The therapy benefits the 10 to 15 percent of patients with moderate to severe heart failure, but failed to improve peak oxygen uptake during exercise testing for patients with moderate heart failure. This larger group of heart patients—about 40 to 50 percent of the 550,000 new cases diagnosed each year—experienced increased activity levels and decreased discomfort, but reported no improvement in the other parameters.

**Two-in-one PhD program**

Typical graduate programs involve long nights in one lab, working with one adviser in a specific field of study. But a new Chicago program will give PhD candidates the chance to study with two mentors, in two labs, and earn a dual degree in biological and physical sciences. “We’re training students who will be able to walk in both worlds,” said Tobin Sosnick, director of the PhD program in biophysics and synthetic biology. Four students entered the first class this past fall. Eventually the program will house about 55 PhD candidates, or about 12 new students a year. Forty-seven faculty from a variety of departments—including biology, physics, chemistry and medicine—will teach classes, mentor students, supervise research and act as thesis advisers.

**Unclogging medical procedures**

Standards for the use of ultrasound as a screening tool to measure narrowing of the carotid artery may be too aggressive, resulting in some needless follow-up tests and procedures according to a recent study. Vascular surgeon Hisham Bassiouny found that ultrasound produced similar results to CT angiography and nearly identical measurements of the arteries. The findings allow doctors to consider eliminating an ultrasound after the patient has a CT angiography, which would save money and reduce unnecessary procedures. “As a result, we’ve changed the standards in our vascular lab,” Bassiouny said. “We hope these new standards will be adopted everywhere.”
Recurrent genetic deletion tied to autism

“By disturbing the network of affected genes, this loss of selected genes may underlie the development of autism.”

—Susan Christian, PhD, associate professor of human genetics

The loss of a small portion of chromosome 16 is significantly associated with autism, according to a study published Dec. 21, 2007, online by the journal Human Molecular Genetics by University of Chicago researchers working with the colleagues at the University of Illinois-Chicago and the Roswell Park Cancer Institute.

The genetic “microdeletion,” which occurred in only four of 712 study subjects with autism, is the second most common recurrent genomic disorder associated with autism. The deletion, called 16p11.2, results in the loss of about 25 known genes.

“Twelve of those genes appear to be part of a single genetic network that includes genes involved in cell-to-cell signaling and interaction,” said first author Ravinesh Kumar, PhD, postdoctoral scientist in human genetics at the University of Chicago. “At least three of the deleted genes are primarily expressed in the brain and are thought to influence behavior, which makes them very promising candidates for autism.”

The authors suspect the lost or damaged genes also may be involved in other cognitive, language and social impairments.

“We suspect that 16p11.2 microdeletions are a risk factor for autism spectrum disorders generally and may cause mild autism in some families,” said study author Susan Christian, PhD, associate professor of human genetics at Chicago. “By disturbing the network of affected genes, this loss of selected genes may underlie the development of autism.”

To find genes linked to autism, the researchers scanned the entire genomes of 180 subjects with autism searching for submicroscopic pieces of DNA that either were lost or mistakenly duplicated in patients diagnosed with autism. They first found that two out of those 180 (1.1 percent) had a deletion in region 16p11.2, on the short arm of chromosome 16. None of the 372 control subjects had the same deletion.

For confirmation, the researchers screened DNA from 532 additional subjects with autism. They found two more with the same deletion (0.4 percent), which was seen in none of the 465 controls. Combining the two samples produced a total prevalence of 16p11.2 deletions of 0.6 percent.

The 16p11.2 region is flanked on both sides by bands of segmental duplications, short strings of nearly identical DNA that predispose to the loss, shuffling or amplification of this region during genetic recombination. “Many human diseases are caused by these types of chromosomal rearrangements, however, this is the first recurrent microdeletion in autism too small to be seen under a microscope,” Christian said.

The most common known genetic cause of autism, linked to about 1 to 3 percent of cases, is a much larger duplication of part of chromosome 15, involving about a dozen genes. The chromosome 15 abnormality is associated with autism as well as intellectual disability (www.idic15.org). The chromosome 16 deletion, by contrast, is not consistently associated with intellectual disability.

“Although this only explains about one-half of 1 percent of autism, it provides the best clues yet for finding the specific genetic changes that lead to the disease,” said co-author William Dobyns, professor of human genetics and pediatrics at Chicago. “This is a small region with a limited number of genes, including several strong candidates, each of which merits a closer look. The next step is to find the specific gene or genes involved. There may be one gene within that deletion that is at the core of the problem.”

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Trials yield hope for thyroid cancer drug

“This is exciting. Until now we really didn’t have anything to offer thyroid cancer patients with advanced disease that was refractory to standard measures.”
—Ezra Cohen, MD, PhD, assistant professor of medicine

A new drug shows promise in the treatment of advanced thyroid cancer, a disease that the American Cancer Society accounts for more than 1,500 deaths in the United States each year, University of Chicago researchers report.

The investigational drug axitinib produced tumor regression or stable disease in almost three of four patients with advanced thyroid cancer, the research team reported at the annual meeting of the American Society for Clinical Oncology in Chicago.

In an exploratory phase II trial, 18 of 60 patients (30 percent) had their tumors shrink by 31 to 83 percent. Another 25 patients (42 percent) had stable disease, with no tumor progression or slight reduction in size, when measured at four months. Many of those patients still have stable disease.

“This is exciting,” said study presenter Ezra Cohen, MD, PhD, assistant professor of medicine. “Until now we really didn’t have anything to offer thyroid cancer patients with advanced disease that was refractory to standard measures.”

Although the drug did not produce complete responses, it appears to have caused “significant tumor reduction in most subjects,” Cohen said. “Axitinib has prevented the disease from progressing in most patients, and in a lasting way.”

In this trial, which began nearly three years ago, “the median duration of stable disease has not been reached,” he said. “Twenty-four patients are still in treatment.”

Axitinib is a small molecule designed to prevent tumors from acquiring the blood supply they need to grow. It blocks all three known receptors for a substance that tumors release in order to grow new blood vessels. The study confirmed that the drug significantly reduced the presence of these receptors.

More importantly, it prevented tumor growth. In only 10 of 60 patients (17 percent) did the tumors continue to grow. Another 18 patients left the trial for other reasons, including toxicity. Five of them withdrew because of treatment-related adverse events.

The most common side effect was fatigue, affecting 50 percent of patients, but only 5 percent had severe fatigue and only one patient left the trial for this reason. Axitinib also caused hypertension in about 28 percent of patients and a range of digestive disorders, including diarrhea (47 percent), nausea (32 percent), consequent weight loss (23 percent) and vomiting (13 percent). Several patients complained of headaches or rash.

All patients in this trial had advanced thyroid cancer. Many had already been given standard therapy—such as surgery or treatment with radioactive iodine. Others, because of their advanced disease, were not candidates for standard treatments.

“It’s a relief to have a real option for these patients,” Cohen said. “The standard chemotherapy for refractory thyroid cancer is not very effective and can have multiple significant side effects. It appears, in this early study, to keep the cancer from growing for a significant period for the majority of patients without doing any real damage to their quality of life.”

A follow-up trial testing axitinib in patients who have not responded to standard chemotherapy is ongoing. Pfizer, the maker of axitinib, funded this trial.

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Axitinib blocks all three known receptors for a substance that tumors release in order to grow new blood vessels.

Diabetes cost-benefit analysis improves

An ounce of prevention isn’t just better than a pound of cure. It’s also cheaper and better for you. A new Chicago-based study of 34 community health centers in 17 states found several initiatives—including the federal Health Disparities Collaborative—enhanced processes for managing diabetes, such as testing for blood glucose, and improved patients’ health. Quality improvements at the clinics cost less than $500 per patient each year, the study found, and reduced the incidence of diabetes complications that can cost $44,000 per patient each year. “A small investment in upgrading the delivery of health care brought about a substantial improvement in health that justified the costs of the program,” said Chicago’s Elbert Huang, MD, study leader. Studies show poorly managed type 2 diabetes costs the U.S. health system an extra $22.9 billion a year in direct medical costs.

Super molecule fights cancer

There’s a small but powerful RNA molecule you want to keep in your anti-cancer arsenal. Called let-7, this microRNA molecule targets a particular gene—HMGA2—in a variety of cancers. HMGA2 is less prevalent in people with higher amounts of let-7, said cancer researcher Marcus Peter. Let-7 puts the brakes on expression of selected genes, appearing to prevent human cancer cells from reasserting their prenatal capacity to divide rapidly, travel and spread. “Expression levels of let-7 can discriminate more effectively between more and less advanced stages of cancer than any other microRNA,” Peter said. “We suspect that loss of members of the let-7 family may be a major determinant of cancer progression.”

Pulling teeth

All it took was a tooth to name a new species in honor of Leigh Van Valen, a University of Chicago evolutionary biologist. Researchers from India identified the hoofed mammal, which they named Kharmerungulatum vanvaleni, after finding a single lower molar interbedded in lava in Central India. The fossil is the only one of its kind in India and possibly the Old World. Van Valen said. Paleontologist Ashok Sahni was among the fossil finders and said the species name is a nod to Van Valen’s groundbreaking work with cretaceous mammal teeth in the 1960s. “In view of Leigh’s continuing romance with early mammals and the whole process of evolution,” Sahni said, “we decided to name the species after him.”
Gene mutations can cause neonatal diabetes

“If we could detect the disease early enough and somehow silence the abnormal gene or just protect insulin-producing cells from the damage caused by misfolding, we might be able to preserve or restore the patient’s own insulin production.”

—Louis Philipson, MD, PhD, professor of medicine

Mutations in the insulin gene can cause permanent neonatal diabetes, an unusual form of diabetes that affects very young children and results in lifelong dependence on insulin injections, researchers from the University of Chicago and Peninsula University (Exeter, UK) reported in the Sept. 18, 2007, issue of the Proceedings of the National Academy of Sciences.

This is the first time that an insulin mutation has been connected to severe diabetes with onset early in life.

The researchers describe 10 mutations, found in 21 patients from 16 families. They suspect that the mutations alter the way insulin folds during its synthesis. They suggest that these improperly folded proteins interfere with other cellular processes in ways that eventually kill the cells that produce insulin.

“This is a novel and potentially treatable cause of diabetes in infants,” said study author Louis Philipson, MD, PhD, professor of medicine at Chicago. “It’s exciting because each of these patients has one normal insulin gene as well as one mutated gene. If we could detect the disease early enough and somehow silence the abnormal gene or just protect insulin-producing cells from the damage caused by misfolding, we might be able to preserve or restore the patient’s own insulin production.”

The effort to learn more about possible genetic causes of neonatal diabetes followed a flurry of publicity last September.

Philipson and colleagues at Chicago—using a protocol developed by co-author Andrew Hattersley, MD, professor of molecular medicine at Peninsula—were able to wean a young diabetes patient with a known, treatable mutation in an ion channel protein essential for insulin secretion, off of insulin. This was one of the first such cases in the United States.

Media coverage of that case and outreach by the Juvenile Diabetes Research Foundation stimulated parents of other children diagnosed as infants with type 1 diabetes to contact one of the two centers to request genetic testing. These tests uncovered more than a dozen patients with the same treatable mutation.

The publicity also brought calls from the families of more than 70 patients who had been diagnosed with diabetes at less than one year of age but who, as it turned out, did not have a known mutation.

In one family with four affected individuals, tests for known mutations were negative. A combination of linkage studies and candidate-gene testing, however, traced the problem to an abnormal insulin gene. Further tests identified 10 different insulin-gene mutations in patients from 15 other families.

All 10 are “missense” mutations: They code for a different amino acid than the one normally found at that position. Such mutations can prevent a protein from folding into its customary shape.

“Insulin mutations are an important cause of neonatal diabetes,” accounting for about 20 percent of cases of this rare disorder, the authors said. Most cases tied to insulin mutation were diagnosed in the first six months of life, with an average age at diagnosis of only 13 weeks. Three of the cases were diagnosed between six months and one year after birth.

Neonatal diabetes is considered a genetic disorder by many, Philipson said. Mutations in known genes explain 50 to 60 percent of cases and research teams in the United States and Europe are trying to identify a genetic cause of diabetes in the remaining patients.

Even though neonatal diabetes is rare, identification of genes causing it has led to important knowledge about pancreatic development and function, as well as to more precise diagnosis and improved management of patients.

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Even though neonatal diabetes is rare, identification of genes causing it has led to important knowledge about pancreatic development and function, as well as to more precise diagnosis and improved management of patients.
Your Brain on Cubs: Inside the Heads of Players and Fans
Dan Gordon, ed.
Dana Press, 2008
How can a batter hit a 90-mile-per-hour fastball that has barely enough time to register visually? Why are there more left-handers on baseball teams than in the general population? What makes a sports fan remain loyal year after year? Finally, a book examines the brains of fans and players alike, probing the science of talent, the depths of fan loyalty and the neurology behind hitting a home run. Even those who aren’t Cubs fans should enjoy the authors’ approach to understanding America’s favorite pastime. University of Chicago neurologists Steven Small, MD, PhD, and Ana Soloedkin, PhD, co-authored the book’s third chapter: “Why Did Casey Strike Out? The Neuroscience of Hitting,” with computational neuroscientist John Milton, MD, PhD. They claim a hitter’s decisions begin even before the ball leaves the pitcher’s hand. The batter’s brain must prepare the neuronal program for the movement involved in swinging the bat and then interpret the movement of the pitcher in order to predict where the ball will go.

Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human Body
Neil Shubin, PhD
Pantheon, 2008
What does the human hand have in common with a fly’s wing? Can we trace the evolutionary origin of ailments as varied as cancer and hiccups? Neil Shubin answers such questions in a new chronicle of evolutionary history that helps us discover our “inner fish.” His new book demonstrates how worms, fish and even flies hold secrets to the inner workings of our own bodies and the origins of many of today’s common diseases. Shubin explores the ancient origins of teeth, head, ears, eyes and how just a few cells containing a creature’s DNA can assemble a complete individual. Scientists and people with only a layperson’s knowledge of evolution can learn from this book that shows us how the distant past is deep within our DNA. Shubin is professor and associate dean for organizational and evolutionary biology at the University of Chicago and provost of the Field Museum. (See excerpt from book on page 47.)

Speciation in Birds
Trevor Price, PhD
Roberts and Co., 2008
The mysteries of large numbers of tropical bird species—including the roles of geography, ecology and sexual selection—are explored in this beautifully illustrated book by one of the leading experts in the field. Trevor Price has created an authoritative and modern synthesis on the subject of bird speciation, exploring the integration of behavior, ecology and genetics. This text is recommended reading for bird lovers or anyone interested in natural history, evolution and biology. Price is a professor of ecology and evolution at the University of Chicago.

Teaching Atlas of Vascular and Non-Vascular Interventional Radiology
Brian Funaki, Jonathan Lorenz, AB ’87, MD ’93, and Thuong Van Ha
Thieme Medical Publishers, 2008
A resource for residents as well as experienced radiologists and endovascular surgery experts, this comprehensive atlas covers the full range of nonvascular and vascular interventional procedures performed in clinical practice. Its 75 cases are organized with brief summaries of clinical presentation, radiologic studies, diagnosis and treatment, and guide the reader through each stage of management. The authors, all from the University of Chicago, provide essential background for each case on the etiology of the problem, and offer lists of noninvasive imaging workup, therapeutic options and possible complications. Brian Funaki is associate professor and section chief of vascular and interventional radiology; Jonathan Lorenz directs the vascular and interventional radiology fellowship program; and Thuong Van Ha is assistant professor of interventional and vascular radiology.

Thoracic Surgery Atlas
Mark K. Ferguson, MD ‘77
Saunders, 2007
Highly illustrated and comprehensive, this 325-page review of general thoracic surgery guides the practitioner through details of complex procedures, demonstrating ways to avoid common problems and to manage complications when they occur. Each chapter is illustrated with original line drawings that depict relevant anatomy and steps associated with each procedure. Mark Ferguson is a cardiothoracic surgeon and professor of surgery at the University of Chicago.

Dialysis without Fear: A Guide to Living Well on Dialysis for Patients & Their Families
Daniel Offer, MD ’57, Marjorie Kaiz Offer, Susan Offer Szafir
Oxford University Press, 2007
Written by a psychiatrist and dialysis patient and his wife and daughter, this book offers advice on how to live well on dialysis. Drawing on his long experience in the medical profession and with kidney disease, Daniel Offer dispels many misconceptions surrounding this treatment. He explains how to adapt to the new diet and continue to travel, work and participate fully in life’s celebrations and joys. Daniel Offer is a professor of psychiatry and behavior sciences at Northwestern University. The author of 16 books and 200 scientific articles, he has been on dialysis since 1999. His wife, Marjorie Kaiz Offer, is a research assistant in Northwestern’s Department of Psychiatry and Behavior Sciences. Their daughter, Susan Offer Szafir, is a freelance writer and marketer.

Robbins Basic Pathology
Vinay Kumar, MBBS, MD; Abul K. Abbas, MBBS; Nelson Fausto, MD; and Richard Mitchell, MD
Elsevier Science, 2007
Now in its 8th edition, this 960-page hard-cover classic pathology text comes with Student Consult online access (www.studentconsult.com). Current, succinct and user-friendly, this primer is written for medical students and course directors, or anyone interested in studying pathology. The text includes state-of-the-art gross and photomicrographic illustrations to help readers understand complex principles, and provides clinicopathologic correlations that highlight the relationships between basic science and clinical medicine. Its authors are all practicing pathologists: Vinay Kumar, at the University of Chicago; Abul Abbas, at the University of California-San Francisco; Nelson Fausto, at the University of Washington; and Richard Mitchell, at Brigham and Women’s Hospital.