Illinois public schools fall short in sex ed

“Uninformed teens often become uninformed young adults.”

—Adjoa Tetteh, research assistant and a college peer sex educator

Only two-thirds of Illinois public school teachers provide comprehensive sex education, University of Chicago researchers report in the February 2008 issue of the journal Obstetrics and Gynecology.

Sixty-five percent of teachers who responded to the researchers’ survey covered the four basic topics required to be rated “comprehensive”: abstinence until older or until marriage, HIV/AIDS, other sexually transmitted diseases and contraception. When the researchers added a widely recommended fifth topic—where to get condoms, birth control and health-related services—only 42 percent of sex education teachers passed the comprehensive test.

The survey also found that 30 percent of the state’s sex-education teachers had never received training in the subject, well above the national average of 18 percent. Although most teachers with training reported that they felt “very comfortable” teaching adolescents about sex, only 56 percent of those who lacked such training said they felt comfortable.

“For this study, we set the bar for comprehensiveness fairly low relative to what most medical and public health organizations recommend,” said senior author Stacy Tesler Lindau, MD, assistant professor of obstetrics and gynecology and medicine, “and one out of three programs failed to clear it.”

“Our children learn many of the skills they need to be healthy citizens and to take responsibility for their own health in school,” she said. “That should include information about sexual aspects of health. Physicians who care for adolescents need to know what students are or are not learning in school in order to fill gaps caused by deficits in program content, quality and teacher training.”

Previous studies showed that nearly two-thirds of 12th-graders have engaged in sexual intercourse and that accurate knowledge can delay sexual debut and increase the use of condoms or other forms of contraception when adolescents do become sexually active.

“Most parents support school-based sex education, and teens regard it as an important source of information,” Lindau said. “Yet we found that several important health topics and skills are omitted, more often than not, from most Illinois public school sex-education criteria.”

“Uninformed teens often become uninformed young adults,” said second author Adjoa Tetteh, research assistant and a college peer sex educator. “Working with college students, I have witnessed this firsthand. Many students come to college with years of sexual experience but are learning for the first time about effective ways to prevent [sexually transmitted infections] and unintended pregnancy.”

The researchers used data collected by the National Opinion Research Center (NORC), a survey research firm at the University of Chicago. NORC mailed self-administered questionnaires to 335 sex education teachers from 201 public middle and high schools in 112 Illinois school districts during the 2003–04 school year. Sixty-two percent of the teachers, representing 91 percent of schools, responded.

Teachers were asked which of 17 possible topics they taught and, if they omitted certain topics, to explain why. They also were asked about their training and how they would grade the sex education curriculum.

Of the responding schools, 93 percent offered sex education, 7 percent did not.

The most frequently taught topics, covered by 96 percent of teachers, were HIV/AIDS and other sexually transmitted diseases. Almost 90 percent of teachers covered abstinence. Among those who taught abstinence, 57 percent emphasized it was the “best alternative,” 39 percent said it was the “only alternative” and 4 percent described it as “one alternative.”

Practical skills—such as contraception, condom use, decision-making and communicating with a partner—and morally debated topics, such as abortion and sexual orientation, were among the least frequently taught. Teachers who had not received sex-education training were less likely to spend time on practical or morally debated topics.

Of the 17 topics, emergency contraception was mentioned least, taught by only 30 percent of teachers. Only 32 percent of teachers brought up homosexuality or sexual orientation, 34 percent taught how to use condoms, 37 percent taught how to use other forms of birth control, 39 percent discussed abortion and 47 percent taught students where to get contraception and sexual health services.

The most common reason for omitting a topic was “not part of the curriculum.” Those who omitted condom use, however, most often cited “school or district policy.”

Teachers gave themselves the highest grades for instruction on reproductive basics and abstinence, with nearly four out of five ranking that part of the curriculum as good or excellent. About two-thirds gave themselves comparable grades for teaching their students about the emotional consequences of sex, dealing with pressures to have sex, or where to access contraception or services.

Though about half rated their instruction on how to use condoms or other forms of birth control as good or excellent, a quarter rated instruction on these topics as average and another quarter rated them as poor or very poor.

“Although a recent study has called into question the effectiveness of abstinence-only sex education, the trend over the last 10 years, supported by federal incentives, has been to emphasize abstinence and exclude information about contraception,” Lindau said. “Given that a large number of young people are sexually active, we worry that such restrictive approaches leave students unprepared to prevent pregnancy and/or sexually transmitted diseases.”

“In most cases,” she added, “they are not even given access to information about how to talk about these issues or where to get help should they need it. Doctors need to be aware of this and should be proactive in initiating discussion about sexuality with parents and adolescents. Doctors may also be an important resource for providing teachers with medically accurate information and training.”

“Our study provides important new data from the teachers’ perspective,” said study co-author Melissa Gilliam, associate professor and section chief of family planning and contraceptive research. “It supports other recent studies showing that large numbers of teens, especially low-income and youth of color, received no instruction about birth control methods before they first had sex.”

—John Easton
Lack of deep sleep may increase risk of type 2 diabetes

“A decrease in slow-wave sleep resembles the changes in sleep patterns caused by 40 years of aging.”

—Esra Tasali, MD, assistant professor of medicine

Suppression of slow-wave sleep in healthy young adults significantly decreases their ability to regulate blood-sugar levels and increases the risk of type 2 diabetes, University of Chicago scientists reported in the Early Edition of the Proceedings of the National Academy of Science in December.

Deep sleep, also called “slow-wave sleep,” is thought to be the most restorative sleep stage, but its significance for physical well-being has not been demonstrated. This study found that after only three nights of selective slow-wave sleep suppression, young healthy subjects became less sensitive to insulin. Though they needed more insulin to dispose of the same amount of glucose, their insulin secretion did not increase to compensate for the reduced sensitivity, resulting in an increased risk for type 2 diabetes. The decrease in insulin sensitivity was comparable to that caused by gaining 20 to 30 pounds.

Previous studies have demonstrated that reduced sleep quantity can impair glucose metabolism and appetite regulation resulting in increased risk of obesity and diabetes. This current study provides the first evidence linking poor sleep quality to increased diabetes risk.

“Those findings demonstrate a clear role for slow-wave sleep in maintaining normal glucose control,” said lead author Esra Tasali, MD, assistant professor of medicine. “A profound decrease in slow-wave sleep had an immediate and significant adverse effect on insulin sensitivity and glucose tolerance.”

“Since reduced amounts of deep sleep are typical of aging and of common obesity-related sleep disorders such as obstructive sleep apnea, these results suggest that strategies to improve sleep quality, as well as quantity, may help to prevent or delay the onset of type 2 diabetes in populations at risk,” said Eve Van Cauter, PhD, professor of medicine at Chicago and senior author of the study.

“These findings shed light on a problem faced by many elderly, that of fragmented sleep and less time spent in restorative sleep,” said Andrew Monjan, PhD, chief of the neurobiology of aging branch at the National Institute on Aging, which partially funded the research. “More research is needed into the link between insufficient sleep and common metabolic disturbances of later life, such as type 2 diabetes and obesity.”

The researchers studied nine lean, healthy volunteers, five men and four women between the ages of 20 and 31. The subjects spent two consecutive nights in the sleep laboratory, where they went to bed at 11 p.m., slept undisturbed but carefully monitored, and got out of bed 8.5 hours later, at 7:30 a.m. The same subjects also were studied for three consecutive nights during which they followed identical nighttime routines. During this session, however, when their brain waves indicated that they were drifting into slow-wave sleep, they were subtly disturbed by sounds administered through speakers beside the bed.

These sounds were loud enough to disrupt deep sleep but not so loud as to cause a full awakening. This technique enabled the researchers to decrease slow-wave sleep by about 90 percent, shifting the subjects from the onset of deep sleep (stage 3 or 4) to a lighter sleep (stage 2) without altering total sleep time.

“The system proved quite effective,” Tasali said. When asked about the sounds the next morning, study subjects vaguely recalled hearing a noise “three or four times” during the night. Some recalled as many as 10 to 15. On average, however, subjects required about 250 to 300 interventions each night, fewer the first night but more on subsequent nights as “slow-wave pressure,” the body’s need for deep sleep, accumulated night after night.

“This decrease in slow-wave sleep resembles the changes in sleep patterns caused by 40 years of aging,” Tasali said. Young adults spend 80 to 100 minutes per night in slow-wave sleep, while people over age 60 generally have less than 20 minutes. “In this experiment,” she said, “we gave people in their 20s the sleep of those in their 60s.”

At the end of each study, the researchers gave intravenous glucose (a sugar solution) to each subject, then took blood samples every few minutes to measure the levels of glucose and insulin, the hormone that controls glucose uptake.

They found that when slow-wave sleep was suppressed for only three nights, young healthy subjects became about 25 percent less sensitive to insulin. As insulin sensitivity decreased, subjects needed more insulin to dispose of the same amount of glucose. But for eight of the nine subjects, insulin secretion did not go up to compensate for reduced effects. The result was a 23 percent increase in blood-glucose levels, comparable to older adults with impaired glucose tolerance.

“The alarming rise in the prevalence of type 2 diabetes is generally attributed to the epidemic of obesity combined with the aging of the population,” Tasali said. “Previous studies from our lab have demonstrated many connections between chronic and partial sleep deprivation, changes in appetite, metabolic abnormalities, obesity and diabetes risk.”

“Chronic shallow non-REM sleep, decreased insulin sensitivity and elevated diabetes risk are typical of aging,” the authors conclude. “Our findings raise the question of whether age-related changes in sleep quality contribute to the development of these metabolic alterations.”

—JE

Helping pain meds

Thirty years after it was discovered, methylnaltrexone, a drug developed to relieve a major side effect of pain therapy for cancer patients, received marketing approval April 24 from the U.S. Food and Drug Administration. The FDA’s European equivalent rendered a “positive opinion” for methylnaltrexone on the same day. Health Canada approved the drug March 28. The drug, to be marketed as Relistor, “will be helpful to patients who experience severe constipation associated with the continuous use of morphine or other opioids, which are an important part of care for patients with late-stage, advanced illness,” said FDA’s Joyce Korvick, deputy director for the Division of Gastroenterology Products. More than 1.5 million Americans who suffer from advanced illnesses such as cancer take powerful opioid-based pain relievers such as Percocet, OxyContin or morphine. Methylnaltrexone, invented in 1979 by the late University of Chicago pharmacistologist Lon Goldberg, blocks the side effects without disrupting pain relief.

E paper meets better breathing

Imagine discovering a principle of physics with the potential to create electronic paper and to help people with respiratory distress syndrome. A team of researchers, including University of Chicago MD-PhD student Lukas Pociusavicius, entered such territory when they documented the dynamics of wrinkling and folding in different materials during a study on a lung surfactant called dipalmitoylphosphatidylcholine, or DPPC. Lung surfactant has the ability to wrinkle and fold under pressure and then gracefully pop back into a stiff configuration when relaxed, like a thin elastic sheet. When first compressed, an elastic material begins to form a trough or peak. Lung surfactant has the ability to reverse this stress, allowing the folding that occurs on exhalation to smoothly stretch back into its previous state with inhalation. This principle means it is possible, Pociusavicius said, “to create a polymer composite that would never wrinkle.”
Impact of free drug samples, Medicare Part D

“Physicians should use caution in assuming that the use of free samples ultimately reduces patients’ out-of-pocket prescription cost.”

—G. Caleb Alexander, MD, assistant professor of medicine

Prescription drug programs have significant effects on how patients use their medication and on the prices they pay, but those effects may not always be the expected ones, according to a pair of studies headed by a University of Chicago researcher.

G. Caleb Alexander, MD, assistant professor of medicine, examined both the Medicare Prescription Drug Benefit (Part D) and the practice of providing free samples of prescription drugs to certain patients.

In the latter study, published in the March 24, 2008, issue of *Medical Care*, Alexander discovered that patients who receive these samples have significantly higher prescription costs than those who don’t.

“Out our findings suggest that physicians should use caution in assuming that the use of free samples ultimately reduces patients’ out-of-pocket prescription costs,” Alexander said. “However, all too often, physicians and patients end up continuing the medicines initially begun as samples, even though older, less expensive alternatives may exist.”

Previous surveys have found that free samples can lead to overuse of newer drugs over their older counterparts, but the prior studies usually examined just one clinical setting and not the costs associated with samples.

Alexander’s team used the Medical Expenditure Panel Survey, conducted by the Agency for Healthcare Research and Quality, to examine the characteristics of those receiving samples, as well the relationship between sample receipt and out-of-pocket prescription costs. They followed 5,709 patients from the national survey for up to two years.

The authors found there were important differences in the characteristics of patients who received samples and those who did not. The odds of sample receipt were lower among those who were older and also among those who had Medicaid as their source of insurance coverage.

Alexander said further research is needed to examine patient-physician communication about samples “as well as how physicians decide who needs samples and how samples are distributed across different types of physician practices.”

The study was supported by the Robert Wood Johnson Foundation. Additional authors of the paper include James Zhang, PhD, of Virginia Commonwealth University, and Anirban Basu, PhD, of Chicago.

In a separate study published in the Feb. 5, 2008, edition of the *Annals of Internal Medicine*, Alexander reported that Medicare Part D benefit led to a 13.1 percent decrease in out-of-pocket costs for patients and a 5.9 percent increase in prescription use. The most thorough study to date of the impact of Medicare Part D, the research involved 117,000 patients. Researchers from Chicago, Harvard University and Virginia Commonwealth University compared out-of-pocket costs and the number of pills purchased by those who were eligible for Part D with patients who were not. They also compared Part D enrollees to patients who were eligible, but did not enroll in, Part D.

“Despite extensive debate, it was not clear to what extent Part D would save money,” Alexander said. “We found that it had a modest but significant effect on both savings and drug use.”

Using data from customers who filled prescriptions in 2005 and 2006 through the Chicago-based Walgreens pharmacy chain, the researchers found that the program saved people who enrolled before the May 15, 2006, deadline about $6 a month and gave them, on average, an extra three to four days worth of one medicine per month. After the enrollment deadline, average savings among all eligible seniors in the study increased to about $9 a month and 14 extra days of medicine per month.

Although the sample group may not be nationally representative of all beneficiaries, “our report represents one of the first analyses of the impact of Part D,” said co-author Wesley Yin, PhD, an assistant professor in the Harris School of Public Policy at Chicago and a Robert Wood Johnson Foundation Scholar at Harvard. “It reflects the experiences of millions of Americans accounting for approximately 15 percent of the market share in the United States.”

The authors also found that patients who enrolled early in the Part D program had higher rates of utilization and out-of-pocket costs prior to the Part D period and stood to benefit most from enrollment.

They conclude that Medicare Part D has, indeed, led to savings and increases in prescription drug use by older people. However, “more research is needed to see whether these effects have any influence on people’s health,” Alexander said.

—Maja Fiket

The 1.2 million-square-foot new hospital pavilion, approved this spring by both the University of Chicago, Medical Center and University of Chicago Boards of Trustees, will span two city blocks and rise 10 floors. Construction on the $700 million project is slated to begin in 2009, with a 2012 open date. As the largest single health care investment in South Side Chicago’s history, the new building will house 210 private inpatient and intensive care beds, 24 state-of-the-art operating rooms; 12 rooms for gastrointestinal and pulmonary procedures; seven interventional radiology suites; and advanced diagnostic tools including high-resolution, high-speed MR and CT scanners. “The new hospital pavilion is more than a building,” said James Madara, MD, dean of the biological sciences and Pritzker School of Medicine, and chief executive officer of the University of Chicago Medical Center. “It embodies our commitment to provide the finest medical care, to train the next generation of physicians, and to serve the community with even the most challenging illnesses. It also is a model of flexibility, which will enable physicians to leverage advances in medical science for the benefit of our patients for decades to come.”

IN BRIEF

Pritchard named HHMI investigator

Human geneticist Jonathan Pritchard was named a Howard Hughes Medical Institute investigator. Pritchard has studied “a wider range of topics than most biologists cover in a lifetime,” according to HHMI, which commits more than $400 million to 56 of the nation’s top scientists over their first terms of appointment. Pritchard has analyzed the patterns in human DNA created by historical migrations, the consequences of natural selection, and the question of whether modern humans and Neanderthals interbred. Since joining the University in 2001, Pritchard has worked to understand the links between genetic variation and human traits. He plans to determine how common variations in human DNA are and link them to disease and other traits.

Hope for peripheral neuropathy

Mutations in a protein called dynedin, required for proper sensory nerve cell function, can cause defects in mice that may provide crucial clues leading to better treatments for peripheral neuropathy. A prevalent disease with no known cause or effective treatment, peripheral neuropathy results from damage to nerves and nerve processes that are located outside the brain and spinal cord. Symptoms include pain in the hands, arms and legs—sometimes constant and quite severe—as well as progressive numbness and weakness in the arms and legs. Neurologist Brian Popko showed that mice with mutations in only one copy of a gene coding for one part of dynedin protein had severe defects and a significant reduction in sensory nerve cells.
Location matters, even for genes

“This could be tremendously important . . . for understanding the underlying cause of some diseases that result from mutations in genes encoding inner nuclear membrane proteins.” —Karen Reddy, PhD, post-doctoral fellow

Moving an active gene from the interior of the nucleus to its periphery can inactivate that gene, University of Chicago scientists reported in an article published in the journal Nature in February. Attachment to the inner nuclear membrane, they showed, can silence genes, preventing their transcription—a novel form of gene regulation.

“Several years ago, we and others described the correlation between nuclear positioning and gene activation,” said study author Hatinder Singh, PhD, professor of molecular genetics and cell biology and an investigator in the Howard Hughes Medical Institute at Chicago. “With that in mind, we wanted to take the next step, to design an experiment that could test causality. Could we move a gene from the center of the nucleus to the periphery and then measure the consequences of such repositioning?”

In mammalian nuclei, chromatin—a complex of DNA and associated proteins—is organized into structural domains through interactions with distinct nuclear compartments. In this study, the authors developed the molecular tools to take specific genes from these interior compartments, move them to the periphery and then attach them to the nuclear membrane—which turned those genes off. Not only were selected “test” genes that served as markers turned off after being attached to the inner nuclear membrane, but so were nearby “real” genes.

Singh’s team became interested in studying the role of nuclear positioning in the control of gene activity based on work analyzing immunoglobulin heavy-chain genes. These genes are assembled by DNA recombination and code for proteins that are a crucial part of antibodies, produced in antibody-secreting lymphocytes or are a crucial part of antibodies, produced in antibody-secreting lymphocytes or are a crucial part of antibodies, produced in antibody-secreting lymphocytes or are a crucial part of antibodies, produced in antibody-secreting lymphocytes or are a crucial part of antibodies, produced in antibody-secreting lymphocytes.

In B-cells that don’t produce antibodies, like fibroblasts or T-cells, these antibody genes are attached to the inner nuclear membrane and are not recombined or expressed, ‘Singh said.

The reorganizing of chromosomes occurs when cells divide. “This suggests that cell division is used not only to transmit the genetic information into daughter cells and create two equivalent cells,” Singh said, “but it is also an opportunity for cells to reorganize their genomes in 3-D space, sequestering parts of the genome at the nuclear periphery and rendering it inaccessible to transcription.”

Singh and colleagues are now looking for examples of striking reorganization of the genome separated by one cell division—in which active genes, that will not be active after the cell divides, get pushed away from the interior to the periphery.

The lead author, Karen Reddy, PhD, a post-doctoral fellow in the Singh laboratory, proposes that such compartmentalization “implies the existence of DNA segments that encode for ‘nuclear addresses’ acting like a nuclear zip code to direct or predispose genes to associate with specific regions within the nucleus. This could be tremendously important,” she said, “for understanding the underlying cause of some diseases that result from mutations in genes encoding inner nuclear membrane proteins.” —MF

Ancestral differences affect response to drugs and infections

“We want to understand why different populations experience different degrees of toxicity when taking certain drugs.” —Eileen Dolan, PhD, professor of medicine

Differences in gene expression levels between people of European versus African ancestry can affect how each group responds to certain drugs or fights off specific infections, according to researchers from the University of Chicago and the Expression Research Laboratory at Affymetrix Inc. of Santa Clara, Calif. Using Affymetrix exon arrays, the scientists found expression levels for nearly 5 percent of the 9,146 human genes studied vary significantly between individuals of European and African ancestry. The results were published in the March 7, 2008, issue of American Journal of Human Genetics. The research team took an unbiased, whole-genome approach and found significant differences in several unrelated processes, especially among genes involved in producing antibodies to potential microbial invaders.

The researchers used lymphoblastoid cell lines derived from blood from 180 healthy individuals. They studied 60 nuclear families, including mother, father and child. Thirty of the families were Caucasians from Utah, and 30 were Yorubans from Ibadan, Nigeria.

One of the genes that regulate how people respond to medicines, such as cancer chemotherapies, is ESR1, said cancer specialist Eileen Dolan, PhD, professor of medicine at Chicago and senior author of the study. “We want to understand why different populations experience different degrees of toxicity when taking certain drugs and learn how to predict who might be most at risk for drug side effects.”

In the process the research team saw several other differences. Some, including variation in the immune system’s response to microbial invaders, were expected. Previous studies have found that African-Americans may be more susceptible than Caucasians to infection by certain bacteria, such as Propionobacterium gingivalis that causes periodontitis. Other differences were unanticipated, including significant differences in expression levels among genes involved in fundamental cellular processes, such as ribosomal biosynthesis, transfer RNA processing, and Notch-signaling—a part of a complex system of communication that governs basic cellular activities and coordinates cell actions. “Population differences in gene expression have only recently begun to be investigated,” Dolan said. “We believe they play a significant role in susceptibility to disease and in regulating drug response. Our current research focuses on how these genetic and expression differences play a role in sensitivity to adverse effects associated with chemotherapy.”

Understanding at the genetic level how individuals within and among populations vary in their response to drugs could improve treatment. The research team worked closely with Affymetrix on new technology that enabled them to perform a very comprehensive study including evaluation of expression levels of every known gene. —MF

Malaria drug attacks toxoplasmosis

A new drug that will soon enter clinical trials for malaria treatment also appears to be 10 times more effective than current treatments for toxoplasmosis, a disease caused by a related parasite that infects more than 2 billion people worldwide. Research based at the University of Chicago shows that the drug, known as JPC-2066, is extremely effective against Toxoplasma gondii, the parasite that causes toxoplasmosis. “JPC-2066 has the potential to replace the standard treatment of pyrimethamine and sulfadiazine,” said infectious disease specialist Bima McIntosh, senior author of the study. “The drug, taken by mouth, is easily absorbable, biosoluble and relatively nontoxic. In tissue culture and in mice, it was rapidly effective, markedly reducing numbers of parasites within just a few days.”

Even moderate drinking elevates women’s cancer risk

The more a woman drinks, the higher her cancer risk. Even moderate alcohol consumption—defined as one or two drinks per day—increased risk of developing tumors classified as positive for both estrogen and progesterone receptors, according to research by Jasmin Q. Lew, a fourth-year student at the Pritzker School of Medicine. Lew received a Howard Hughes Medical Institute-National Institutes of Health Research Scholarship to spend a year doing research at the National Cancer Institute’s Division of Cancer Epidemiology and Genetics. She presented her results on “Alcohol consumption and risk of breast cancer in postmenopausal women: the NIH-AARP Diet and Health Study,” at the American Association for Cancer Research annual meeting in San Diego.

Computation helps locate drug targets

Using a novel computational approach, researchers have produced helpful new guidelines for efficient target screening for new drugs, said professor of medicine Andrey Rzhetsky at the University of Chicago. With colleagues at Chicago and Columbia University, Rzhetsky analyzed properties of human genes and proteins that serve as targets for nearly a thousand FDA-approved drugs. They identified a number of characteristics that were common among successful drug targets, especially among high-revenue drugs. “When a drug company must decide which target to pursue among pathologic pathways, this could provide useful estimates of each target’s expected success rate,” Rzhetsky said. Because the cost of developing a new drug can reach more than $1 billion, “information that helps only a little bit,” he said, “can still be quite valuable.”
Metabolic syndrome linked to cold tolerance

“All these genes are likely to be involved in metabolic adaptations to cold climates.”

—Anna Di Rienzo, PhD, professor of human genetics

Researchers from the University of Chicago have discovered that many of the genetic variations that enable human populations to tolerate colder climates also may affect their susceptibility to metabolic syndrome, a cluster of related abnormalities including obesity, elevated cholesterol levels, heart disease and diabetes.

More than 100 years ago, scientists noted that humans inhabiting colder regions were bulkier and had relatively shorter arms and legs. In the 1950s, researchers found correlations between colder climates and increased body mass index (BMI), a measure of body fat, based on height and weight.

In a study published in the February issue of the open-access journal PLoS Genet, scientists show a strong correlation between climate and several of the genetic variations that appear to influence the risk of metabolic syndrome. This correlation is consistent with the idea that these variants played a crucial role in adaptations to the cold. The researchers report that some genes associated with cold tolerance have a protective effect against the disease, while others increase the risk.

“Our earliest human ancestors lived in a hot, humid climate that placed a premium on dispersing heat,” said Anna Di Rienzo, PhD, professor of human genetics at Chicago. “As some populations migrated out of Africa to much cooler climates, those who had been better adapted to hot environments would have been at a disadvantage, so to speak. Those populations that developed the appropriate adaptations were better at surviving and reproducing in these cold environments.”

They selected 82 genes associated with energy metabolism—many of them previously implicated in disease risk—and looked for climate-related variations. They studied genetic variation in 1,034 people from 54 populations, finding widespread correlations between the frequencies of certain genetic variations and colder climates, as measured by latitude, as well as summer and winter temperatures.

One of the strongest signals of selection came from the leptin receptor, a gene involved in the regulation of appetite and energy balance. One version of this gene is increasingly common in locales with colder winters. This version of the leptin receptor is associated with increased respiratory quotient—the ability to take up oxygen and release carbon dioxide—which plays an important role in heat production. The allele also has been linked to lower BMI, less habitual fat and lower blood pressure, and is thus protective against metabolic syndrome.

Other genes that vary according to climate included several involved in heat production, cholesterol metabolism, energy use and blood glucose regulation. Not all cold-tolerance-related gene variants protect against metabolic syndrome. Increased blood glucose levels, for example, could protect someone from the cold by making fuel more readily available for heat production, yet it raises the risk of type 2 diabetes. The version of a gene known as FARKP7 that becomes more common as temperatures fall causes increased BMI, promotes fat storage and elevates cholesterol levels. This genetic variant would protect against the cold but increase susceptibility to heart disease and diabetes.

“All these genes are likely to be involved in metabolic adaptations to cold climates,” Dr. Rienzo said, “but they have opposing effects on metabolic syndrome risk. We suspect they spread rapidly as populations settled into colder and colder climates at higher latitudes, but in the modern era they have taken on a whole new significance, as the supply of calories from food has mushroomed, and the survival advantage of generating more heat has been minimized by technology.”

The researchers say their search for genes that vary according to climate could provide additional clues about the onset of metabolism-related diseases.

Opiates, nicotine addiction show similarities

“Research . . . reinforces the fact that these addictions are very physiological in nature and that breaking away from the habit is certainly more than just mind over matter.”

Daniel McGhee, PhD, associate Professor of anesthesia and critical care

This research is important to scientists because it demonstrates overlap in the way the two drugs work, complementing previous studies that showed overlapping effects on physiology of the ventral tegmental area, another key part of the brain’s reward circuitry. The hope is that this study will help identify new methods for treating addiction—and not just for one drug type.

“It also demonstrates the seriousness of tobacco addiction, equating its grip on the individual to that of heroin,” McGhee said. “It reinforces the fact that these addictions are very physiological in nature and that breaking away from the habit is certainly more than just mind over matter.”

—Scott Rokosky

Protein expression predicts breast cancer risk

A novel systems-based approach—combining comprehensive gene expression profiling with genome-wide transcription factor analysis and protein-protein interaction—has led researchers to a gene marker that can help physicians know which breast cancer patients are at highest risk and require more aggressive treatment, a research team based at the University of Chicago Medical Center reports. They found that high expression of a protein known as H2A.Z, associated with the expression of genes within the nucleus, can help physicians predict which patients are most at risk for disease spread and death. It also could serve as a new target for therapy. “Elevated H2A. Z expression is significantly associated with metastasis and shorter survival, and it could quickly help doctors make better predictions and treatment choices for patients.”

In Brief

Only Caucasian women helped by stopping hormone therapy

A recent decrease in invasive breast cancer in the United States did not extend to women of African ancestry, University of Chicago researchers report. U.S. breast cancer rates in women over 50 fell sharply during 2002 and 2003, but the decline was confined to Caucasians. For Caucasian women aged 50 to 69, the rate of invasive breast cancer decreased by more than 2 percent during that period, then stabilized in 2004. For African-Americans, there was virtually no change. Much of the disparity may result from differences in biology. In mid-2003, many women who had been taking replacement hormones stopped taking them in response to a Women’s Health Initiative trial that showed increased rates of coronary heart disease and breast cancer risk related to hormone replacement therapy. “African-Americans are less likely to use hormone replacement therapy and less likely to develop breast cancers that are responsive to estrogen,” said health studies researcher Dacheng Huo. “So they were harmed less by taking hormones and benefited less by discontinuing them.”

Fall 2008
‘Making a model, in reverse’

“When you actually find something, it’s rewarding.”
—Barrett Boody, first-year medical student

Clad in scrubs and hunched over stainless steel tables, a group of first-year medical students began to explore the intricacies of anatomy as more than two dozen cadavers lay waiting.

This school year, students plunged into a class called “The Human Body” on the first day of orientation—weeks before most other courses began.

“They can focus just on anatomy,” said instructor Betty Katsaros, who has taught the subject for 25 years, 15 of them at the University of Chicago.

Lectures and labs began with the development of the body, radiology and embryology, and progressed to specific body parts and organ systems with each passing week.

With diagrams sketched on white boards and anatomy books strewn across nearby stools, first-year students wrapped the bodies in cloth soaked in an antifungal solution. Each day, as they studied a new part of the body, they peeled away damp fabric to unveil the skin, arteries and organs underneath. They were discovering the patient’s health ailments along the way: Pacemakers, gallstones and cancer had all been revealed during the first month of work.

In late August, students examined the abdomen, the intestines and the blood supply to abdominal organs. The pungent odor of formaldehyde pervaded the room as students looked at livers, pale or bright green gallbladders, arteries, veins and intestines. Teams of first-years carefully separated fat and muscle tissue looking for arteries. They traded terms such as “superior mesenteric artery” and “hepatic artery” while exploring the abdominal networks of blood vessels.

“It’s really hard to disentangle everything,” said medical student Dana Sun, while she looked for vasculature surrounding the intestines and abdominal organs.

Students paged through anatomy books with nitrile gloves, seeking roadmaps for the body. Student David Voce scribbled a diagram of the arteries of the liver on his pants for easy reference while he worked.

Manuel Diaz and his lab partners called the cadaver a gift: an invaluable way to examine the body as a whole. “It’s like making a model in reverse,” Diaz said. “All the detail is there. You have to reveal it.”

But they also recognized the relationships they were building with each other. “This is a cool experience. We get to bond. We really do absorb a lot,” Diaz said.

Barrett Boody, who was working with Diaz, said the learning experience was unlike anything he had before. Though some students had taken other anatomy classes, the work with the cadavers brought more depth and emotion. “Ethically, morally, there’s a lot more involved,” he said.

Ellen Rebman was studying a cadaver with a herniated stomach, gallstone and pacemaker. Students knew the elderly patient died of cardiac arrest, Rebman said, but other details of her health were not revealed until they began studying the body. “It makes you wonder if she was in pain,” she said.

Such study led to discovery. Students excitedly spread the news when they found an artery or vein.

“When you actually find something,” Boody said, “it’s so rewarding.”
—Suzanne Wilder
Gene-shuffling patterns uncovered

"Genetic recombination is a fundamental process at the core of reproduction and evolution."
—Graham Coop, PhD, post-doctoral fellow in human genetics

The first large-scale, high-resolution study of human genetic recombination has found remarkably high levels of individual variation in genetic exchange, the process by which parents pass on a mosaic-like mixture of their genes.

University of Chicago researchers located nearly 25,000 recombination events that occurred in the transmission of the parental genomes to 384 offspring, described in the March 7, 2008 issue of Science. The high-resolution maps allowed the researchers to precisely locate where these genetic exchanges occur and to assess the differences in recombination rates between individuals.

"Genetic recombination is a fundamental process at the core of reproduction and evolution," said study author Graham Coop, PhD, post-doctoral fellow in human genetics at Chicago, "yet we know very little about where it occurs or why there is so much variation among individuals in this important process."

"Now, Coop said, "we know where it occurs. Understanding where it happens provides us with important clues as to how it happens, how it is regulated and what mechanisms control this essential biological phenomenon." Recombination occurs during meiosis, a special kind of cell division that takes place only in the testicles and ovaries. In the process of making sperm or egg cells, the parent-to-be takes the chromosomes from each parent, but shuffled together into entirely new combinations.

This process leads to offspring having different combinations of genes than their parents and is thought to have many advantages. The research team focused on the Hutterites, a genetically similar population of European immigrants who settled in the Dakotas in the 19th century and have maintained a communal agricultural lifestyle. One member of the research team, Carole Ober, PhD, professor of human genetics and of gynecology, has been working closely with this group for many years on health and inheritance issues. (See cover story, Spring 2008 Medicine on the Midway.)

The researchers collected DNA from 725 volunteers representing 82 overlapping nuclear families, most of whom had four or more children. They are part of a 1,650-person, 13-generation pedigree of the Hutterites in the United States. The scientists used 300,000 markers of genetic variation (SNPs) to determine, along each chromosome, whether the genetic material came from the child’s maternal or paternal grandmother or grandfather. The large number of markers allowed the researchers to map out the high-resolution recombination events in the genome where ancestry shifts from one grandparent to another, known as recombination events.

Chromosomes from the mother (not including the X chromosome) averaged around 40 recombination events per gamete. Those from the father had only 26. The authors confirmed a previous finding that older mothers have more recombination events in the transmission of their genome to their offspring, while the father’s age has no such effect. For both sexes, the majority of crossovers occur at genetic “hotspots,” small regions where genetic exchanges are unusually common. Although the overall rate of hotspot use was similar between the two sexes, a subset of hotspots, "seems to be used mainly by one sex or the other.”

NorthShore University HealthSystem and the University of Chicago Pritzker School of Medicine have created an academic affiliation that will place medical students, residents and fellows from the University of Chicago Medical Center at the three NorthShore hospital locations for a portion of their educational experience. Located in Chicago’s northern suburbs, NorthShore is an integrated health care system that includes Evanston, Glenbrook and Highland Park hospitals, NorthShore Medical Group (comprising 65 medical offices and facilities), NorthShore Home Services, NorthShore Research Institute and NorthShore Foundation.

Although students and residents participate in several small programs for clinical training off campus, the majority of medical student training has always been centered at the University of Chicago Medical Center. That will not change. This new affiliation, however, will make the NorthShore hospital locations the primary off-site learning environment for Pritzker students and UCMC residents.

Leaders at both organizations believe the fit is natural, bringing together Pritzker, one of the premier medical schools in the country, and NorthShore, one of the nation’s leading teaching hospitals. Both share a commitment to the highest levels of patient care and medical research, yet they expose students and residents to different patient populations, operational systems and an urban-academic-medical-center vs. a suburban-community-teaching-hospital patient care setting.

The affiliation became effective July 1, 2008, and includes a one-year transition period. In July 2009, UCMC residents and medical students from Pritzker-sponsored training programs will begin to gain clinical experience at NorthShore, working closely with physicians who are part of the NorthShore-based faculty.

"Health care takes place in a variety of different settings," said Holly J. Humphrey, MD, professor of medicine and dean for medical education at Pritzker. "Medical schools achieve a diversity of settings by linking up with affiliates, in addition to their own teaching hospitals, to give students a richer variety of patient care experiences. That kind of broad educational exposure is incredibly robust.”

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The earlier, the better

The early stages of ovarian cancer—when the tumour is still confined to the ovary—is the best time to administer marimastat or prinomastat, a new study shows. These drugs inhibit an enzyme called MMP-2 that is necessary for ovarian cancer to attach itself to other sites, such as the peritoneal cavity, where it can spread. Though MMP-2 inhibitors can dramatically reduce a tumor’s ability to establish itself beyond the ovary, they were abandoned after they failed to extend survival in earlier clinical trials. It was not known then that the drug had to be given before the cancer had spread, according to obstetrician and gynecologist Ernst Lengyel. By inhibiting MMP-2 activity early in the disease, the University of Chicago team was able to prevent injected ovarian cancer cells in mice from attaching to tissues in the peritoneum and omentum. This reduced growth of new tumors in mice by 68 percent, when measured four weeks after treatment.

Organizational biology and anatomy professor Michael Lubberhah, teaching students in a lab session. (Photo by Dan Dry)

Among the best, again

In the 2008 “Best Hospitals” issue of U.S. News & World Report, the University of Chicago Medical Center is ranked among the best in the country in 10 specialty areas. Seven programs ranked in the top 25 nationally: digestive disorders (#6), endocrinology (#11), cancer (#18), neurology and neurosurgery (#19), heart and heart surgery (#20), kidney disease (#22), and ear, nose and throat (#22). Geriatrics (#29), respiratory disorders (#31) and gynecology (#34) also scored in the top 35. Only 170 of the country’s 5,000-plus hospitals (about 3 percent) made at least one of the specialty lists. The only Illinois hospital ever to be included in the honor roll, the Medical Center has appeared on this sought-after list 11 times since 1995. Adding to that, the magazine’s annual survey of children’s hospitals selected the University of Chicago Comer Children’s Hospital as one of the top 20 in the United States for neonatal care (the care of critically ill or very premature newborns). The 2008 America’s Best Children’s Hospitals list ranked the top 10 hospitals in general pediatrics and six specialties based on a combination of reputation, outcomes and care-related measures such as nursing care, advanced technology, credentialing and other factors. “Neonatal care is a difficult field,” said Michael Schreiber, Comer Children’s Hospital’s chief physician, “in terms of its technical demands, the constant medical and ethical decision-making it requires, and the need for caregivers to manage their tiny, complex, fragile patients as well as the emotional roller coaster faced by the infants’ parents.” This is the first time Comer hospital, which opened in 2005, has appeared in the U.S. News survey.
Pritzker transforms its curriculum

"During an era of fragmented health care delivery systems, it is increasingly urgent that future physicians develop mastery in these fundamental areas. These are the kinds of doctors our patients deserve."
—Holly J. Humphrey, MD, dean for medical education

In an effort to inspire the next generation of physicians, the University of Chicago Pritzker School of Medicine is launching the Pritzker Initiative, a new curriculum designed to transform medical education at the school. (See Perspective on page 48.) The initiative will increase student-faculty interaction, reduce the number of large lecture classes and replace them with small-group, hands-on learning under the direct mentorship of faculty physicians, researchers and clinical educators.

"Students will learn medicine at the cutting edge of biomedical science, translate that science into direct patient care and acquire the moral foundation of the profession as they prepare to become future doctors and leaders," said Holly J. Humphrey, MD, professor of medicine and dean for medical education at Pritzker. "During an era of fragmented health care delivery systems, it is increasingly urgent that future physicians develop mastery in these fundamental areas. These are the kinds of doctors our patients deserve."

The goal of the Pritzker Initiative is to improve education for the next generation of leaders in all aspects of medicine, preparing aspiring physicians for careers that combine scholarly inquiry with clinical practice on improving health care. It also aims to increase the number of physicians overall. Physician supply in the United States is already at an all-time high, having risen from 200 doctors per 100,000 people in 1980 to a predicted 293 by 2015.

"Our goal is to train physicians who will change medicine by bringing new knowledge to the field and passing it on." In response to the renewed emphasis on mentorship, the school will reduce the average class size from 104 new students each year to 88 by fall 2009. This will enable faculty to increase interaction and clinical insights from surgeons as well as experts on medical imaging. (See story on page 12.) All incoming students also participate in a course devoted to understanding health care disparities in the United States. (See story on page 22.)

Pritzker has risen faster than any other medical school in the country during the past five years. It is ranked fourth in the country—behind only Harvard, Johns Hopkins and Yale—for the percentage of graduates who go on to careers in academic medicine. Nearly 24 percent of Pritzker students who graduated from medical school between 1989 and 1998 are now on the faculty at academic medical centers, about twice the national average.

As a new home away from home, Ronald McDonald House Charities of Chicagoland and Northwest Indiana celebrated the recent grand opening of a new Ronald McDonald House facility near the University of Chicago Comer Children's Hospital in Hyde Park. For families of children who require prolonged hospitalization, the new 22-bedroom, 30,000-square-foot Victorian-style home holds nearly twice as many families as the original home in Hyde Park that opened in 1986. Within a year, that facility—the second to open in Chicago—was filled to capacity with long waiting lists. Eventually six more bedrooms were added. In 2004, in partnership with the University of Chicago Medical Center, the facility moved to a temporary location pending completion of the new building. The new house is one of four in the Chicago area now operated by the charity.

The average class size for Pritzker students will be reduced, countering national trends. (Photo by Glenn Foyt)

The University of Chicago Medical Center in the mid-20th century. (Archival photo)

Taking the life out of tumors

University of Chicago researchers are finding novel ways to stop the growth of cancerous tumors. In pathologist Hans Schreiber's lab, researchers discovered ways to target and kill the non-malignant cells that surround a tumor. The death of those surrounding cells stops tumor growth in mice. The stroma, the layers of cells that surround a tumor, can accumulate tumor antigens and present them on their surface, which make them cancer-specific targets for killer T lymphocytes and therefore cannot escape destruction. These genetically stable surrounding cells retain the molecules that present tumor antigens.

"We already knew that targeting the stroma is essential for eradicating established large tumors, because the stroma is like the root of the tumor," said Schreiber, MD, PhD. "However, effects of current treatments that target stroma are usually transient and not cancer-specific." Cancer scientist Marcus Peter, PhD, also has found an innovative way to treat advanced tumors. One group of small, non-coding RNA molecules could serve as a marker to improve cancer staging and may be able to convert some advanced tumors to more treatable stages. When normal cells are transformed into cancer cells, epithelial tissue lining internal and external body surfaces can adapt the characteristics of embryonic tissue. This process can produce invasive and mobile cells that can pass through membranes and travel to distant sites, where they seed new tumors. Peter and his colleagues found that a certain family of RNA helped regulate this transition. His team also showed that these microRNA molecules could convert tumors into a less invasive form.

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In June, the University of Chicago Medical Center closed the books on the Spark Discovery, Illuminate Life campaign, after raising $811 million and exceeding the original goal by more than $250 million. Gifts to the Medical Center through Spark Discovery accounted for more than a third of the University-wide Chicago Initiative, which raised $2.3 billion.

A sharp increase in giving delivered record-breaking results for the Medical Center. In each of the past three years, donors contributed more than $100 million, up from an annual average of $75 million earlier in the nine-year campaign, during which more than 22,000 donors made contributions.

More than $500 million in campaign philanthropy has been invested in research. The Medical Center landscape has been transformed by new facilities including the Comer Children’s Hospital, Emergency Department and Center for Children and Specialty Care; the Gordon Center for Integrative Science; and the Knapp Center for Biomedical Discovery, set to open in 2009.

The campaign provided funding for 14 new professorships, held by distinguished faculty. There are now 73 endowed professorships in the biological sciences, with a goal of reaching 100 such positions. More than $45 million was contributed for student aid. Almost $200 million was added to the endowment.

Key programs, including cancer, genomics, personalized medicine and neuroscience, gained a strong foundation from the campaign. In early 2009, construction will begin on the new hospital pavilion (see story on page 7), designed to accommodate emerging technologies and provide state-of-the-art care far into the future for patients with complex disease.

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To enable young, community-oriented physicians to build a better network of care in the underserved areas where they learned their profession, the University of Chicago Medical Center is initiating the REACH (Repayment for Education to Alumni in Community Health) program, which will encourage graduates of the Pritzker School of Medicine to return to the South Side of Chicago to practice medicine in underserved communities.

The program will provide up to four years of financial support for Pritzker graduates who complete a residency in primary care or much-needed specialties and then return to practice medicine at a Federally Qualified Health Center (FQHC) or a community hospital in the Medical Center’s primary service area.

“The high cost of college and medical education often prevents even the most altruistic young doctors from practicing in underserved areas such as Chicago’s South Side,” said James Madara, MD, dean of the biological sciences.

“is to increase the number of medical careers the opportunity to contribute to the care of people the burdens of 12 million people across the United States who serve on hospital ethics committees. Written specifically for educational purposes, this book draws on experts in such fields as bioethics, health law, social psychology and clinical consultation, and topics that include education, ethics consultation and policy development. It addresses such concerns as developing cultural and spiritual awareness, promoting just and ethical organizations, and preparing for the forces of group dynamics in committee discussions and consensus building. One of the chapters in which the authors, ‘Ethics and Pediatrics,’ is written by Tracy Koegler, MD, assistant professor of obstetrics and gynecology and pediatrics at the University of Chicago.

Dismantling Discontent: Buddha’s Way Through Darwin’s World
Charles Fisher, SB ’89, SM ’90, MD "Fisher draws up data on animal and human societies, and neuroscientific findings to explore the existential dilemma defined by the Buddha: illness, old age, death, and the transcendence of all of these. A meditator, teacher and Chicago alumna, Fisher said that early hominids lived in harmony with nature and free from existential suffering so familiar to Homo sapiens. As our ancestors’ brains and bodies evolved, our species became more capable of creative productivity and the discontent of being disconnected from our environment. Our most profound spiritual and intellectual yearnings emerged from this evolution, he suggests. Fisher shuttles between these relationships reveal about the world. His portrayals of Rhesus monkey and humans—have survived in a complex and sometimes hostile world. His portraits of Rhesus monkey and humans—have survived in a complex and sometimes hostile world. His portrayal of how the production of food on land and in oceans, the emergence and spread of infectious disease, human medicines and biomedical research are dependent on biodiversity. More than 100 scientists contributed to 10 chapters that cover everything from how human activity threatens biodiversity to how we can help conserve the rich diversity of the biosphere. Sustaining Life reminds us that we can no longer see ourselves as separate from—and unaffected by—the natural world. Chicago alumnus Bernstein is a research associate at the Center for Health and the Global Environment, as well as a clinical fellow in pediatrics at Harvard Medical School and Boston University School of Medicine.

Biopsychologist Maestripieri offers us the fruits of more than 20 years of studying the macaque community with their “Macachiavellian” intelligence that sometimes seems to caricature human social interaction. Maestripieri’s work helps us understand how Rhesus monkeys—and humans—have survived in a complex and sometimes hostile world. His portrayal of human social interaction. Maestripieri’s work helps us understand how Rhesus monkeys—and humans—have survived in a complex and sometimes hostile world. His portrayal of how the production of food on land and in oceans, the emergence and spread of infectious disease, human medicines and biomedical research are dependent on biodiversity. More than 100 scientists contributed to 10 chapters that cover everything from how human activity threatens biodiversity to how we can help conserve the rich diversity of the biosphere. Sustaining Life reminds us that we can no longer see ourselves as separate from—and unaffected by—the natural world. Chicago alumnus Bernstein is a research associate at the Center for Health and the Global Environment, as well as a clinical fellow in pediatrics at Harvard Medical School and Boston University School of Medicine.

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