

The discovery of DNA's double helix structure is 50 years old.

Rowley, the Blum-Riese Distinguished Service Professor of Hematology and Oncology, and Nancy Cox, PhD, associate professor of human genetics and of medicine, joined Watson, Crick and others as they spoke about their genetics research in a celebration of DNA's 50th anniversary.

Rowley reviewed her 1972 discovery of the translocation of chromosomes 9 and 22 in chronic myeloid leukemia (CML). Her major scientific finding led to the development of Gleevac — a drug that is bringing hope to those who suffer from CML. Rowley received the 1998 Lasker Award, the 1999 National Medal of Science and the 2003 Benjamin Franklin Medal for her work.

Even in the 1970s, a generation after Watson and Crick published their findings, new chromosome staining methods continued to emerge that were independent of any understanding of the structural basis of the double helix and heredity, according to Rowley.

"I would say that by the late 1980s we began to use our understanding of DNA and the pattern of the specific nucleotides within DNA to develop probes that could identify specific genes in cells," she said. "If we'd known the sequence of the gene, we could have prepared appropriate probes to synthesize them or have a company synthesize them."

"So knowing those sequences of genes was extremely important," she continued, "because we knew that if we prepared a copy of that sequence we would then have a probe that was specific for the gene we were wanting to study."

Cox, who uses statistical methods to analyze genetic data, spoke on what she believes are the short- and long-term challenges to gain a more complete understanding of the genetic component to diabetes. She also reviewed what those findings could mean for patient care and the prevention of diabetes and its complications.

After the double helix

The year was 1961 and geneticist Janet Rowley was setting up her chromosome research lab in what was then called the Argonne Cancer Research Hospital, having just moved to the University of Chicago.

Eight years earlier James Watson and Francis Crick had rocked the foundations of genetics with their discovery of DNA's double helix structure, the architectural secret of life.

But the ripples of their radical double helix discovery would come relatively late for Rowley and many other geneticists around the world. Even a decade after the double helix revelation, Rowley's investigations into the genetic nature of cancer proceeded independently of the double helix structure.

"It took a while for the Watson-Crick discovery to actually percolate down into laboratory studies," said Rowley, PhD '45, SB '46, MD '49.

"I was using radioactively labeled material — precursors of DNA — to study the pattern in which chromosomes make copies of themselves, but that was a technique in use a while before we knew the structure of DNA," Rowley told a Washington, D.C., audience at the April "Scientific Symposium: From Double Helix to Human Sequence — and Beyond."



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Barrington Brown/Photo Researchers

"It was a bombshell. ...It just seemed too pretty not to be true. And it was true!"
— James D. Watson, on his 1953 discovery with Francis Crick of the double helix structure of genes.

Inset: Watson (left) and Crick in 1953.

Both women said they felt honored to be included in the celebration.

"It was meaningful to participate in this celebration," Cox said. "We have a lot to celebrate, not the least of which are the new challenges that we can tackle given the information infrastructure that has been generated."

Rowley said she sees the genetic revolution gaining speed with the discovery of the human genome and the research that branches from that discovery. "The challenge," she said, "is to use all of the information that comes from sequencing the human genome to move much more quickly to identify the functional effects of the translocations and to find effective therapy."

Biodefense center proposed

The Roman Empire and Justinian's plague. The Aztec empire and smallpox. The Allied troops of WWI and trench fever. History repeatedly shows that even the most powerful nations can succumb to the spread of infectious diseases.

Lest anyone forget, the University of Chicago's Olaf Schneewind, MD, PhD, pointed out this fact of life in proposals worth \$80 million that he recently submitted to the National Institutes of Health. The professor of molecular genetics and cell biology wants to establish a regional center for biodefense and emerging diseases and a related biocontainment laboratory. More than 100 scientists from six states contributed intellectually to the proposals and would be affiliated with the new facilities.

"We bring a lot of expertise to the table," said Schneewind, who spent a year developing the proposals. "Still, this would be a daunting project."

The proposals came in the wake of the fall 2001 anthrax attacks in the United States that killed five people and frightened thousands. The federal

government responded with the largest funding increase in biomedical research history. NIH is expected to fund up to four regional centers and four to six regional laboratories, all focused on biodefense issues.



Photo courtesy of ANL

biologically important molecules. Stringent precautions would protect lab employees and people who live or work nearby. And in a bioterrorism emergency, laboratory and

Argonne National Laboratory, the site for a proposed biodefense center, is about 25 miles southwest of Chicago.

Chicago's regional center will comprise researchers who study the detection, prevention and treatment of biological hazards such as anthrax, botulism, smallpox and the plague. A regional biocontainment laboratory, to be located at Argonne National Laboratory in Chicago's southwest suburbs, would support the center by safely conducting research on microbes that cause potentially lethal diseases.

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Plus there's the proximity to Argonne's advanced facilities in computation and proteomics, not to mention its Advanced Photon Source, the world's most powerful source of X-rays and a leader in X-ray crystallography — a powerful tool for understanding proteins and other

center personnel would assist national, state and local public health experts.

At the height of the 2001 bioterrorist attacks, Chicago police and public health officials logged more than 8,000 telephone calls daily requesting information about potentially infectious material. Schneewind's proposal stated that the deluge of queries quickly swamped these agencies.

In addition to conducting research, the center will train personnel to help respond to similar occurrences in the future.

"That's absolutely what you need," Schneewind said, "the people who know how to handle this."

Postdocs find collective voice

University of Chicago postdoctoral students are joining their colleagues nationwide by stepping out of their laboratories and into the public arena to seek better working conditions, stipends and benefits.

In November 1999, postdocs from the Biological Sciences Division formed the BSD Post Doctoral Association (BSD-PDA), which now represents one of more than 70 campuses affiliated with the recently organized National Postdoctoral Association.

The NPA received a \$450,000 grant from the Alfred P. Sloan Foundation and grants from other major scientific funding organizations to support the planning and development of the organization.

The BSD-PDA started its work by conducting a survey to find out what was on the minds of fellow BSD postdocs. More than 60 responded, indicating they wanted more voice in their institution's administration and they needed more career guidance. Their "urgent issues" included a concern that postdoc salaries fall below national standards of fair compensation and the lack of "rational, equitable and university-wide benefits coverage."

Orfeu Buxton, PhD, a fellow in the department of medicine, is a member of both the university and national organizations. He said that postdocs need a stronger sense of community and a network of support, which the BSD-PDA now is providing. "When you come to an institution as a postdoc, you're a new person who is not part of a program or class of people who have arrived at the same time," Buxton said. "We arrive at any time during the academic year, and we come to work not necessarily for the institution but for a mentor."

Postdocs often find themselves isolated in their laboratories — cut off from a community and institutional resources

or benefits. To make matters worse, this period of living on the fringe, according to Buxton, has grown over time. What used to be a transitory year or so of post-doctoral training has expanded to four years or more of serious and productive laboratory work.

Today, the university association communicates regularly with the 271 bioscience postdocs and research associates on campus and offers a roster of social and professional activities. BSD-PDA members now have opportunities to meet and discuss common issues, share their research and work together directly with administrators on improving those conditions.

One such administrator is Nancy Schwartz, PhD, professor of pediatrics and of biochemistry and molecular biology, and dean for graduate affairs. She is the association's adviser and advocate within the BSD, as well as on the national level, where she is an NPA advisory board member and a postdoc affairs committee chairwoman for the Association of American Medical Colleges.

"Postdoctoral education and training play prominent roles in the national research enterprise and in the biomedical sciences at Chicago," Schwartz said. "The importance of postdocs to the productivity of the scientific enterprise is profound, so their own efforts to improve the training environment can be expected to have a broad impact on biomedical science overall."

"Given the high level of education and professional skills of postdoctoral fellows and most research associates, these conditions could lead to a crisis in higher education if institutions don't respond to them in an organized and cooperative manner," she said.

The BSD-PDA works closely with BSD Dean James Madara, MD, to improve conditions for postdocs. Madara appointed Schwartz to co-chair the postdoc advisory committee along with a postdoctoral researcher. The committee, composed of both faculty and postdocs, works to create policies and guidelines for improving the training environment for postdocs within the division.



Arieh Shalhav, MD, (front right) performs kidney surgery using the Da Vinci Surgical System.

Robodoc debuts

Just four days after surgeon Arieh Shalhav, MD, removed Christine Fulara's defective kidney, the 70-year-old was back on her feet. Instead of a long scar from traditional kidney surgery, Fulara went home with just four small incision marks on her belly.

This past December Shalhav, associate professor of surgery and a pioneer in minimally invasive urology, performed the first robot-assisted operation at the University of Chicago Hospitals using the Da Vinci Surgical System.

The \$1.2 million Da Vinci system consists of a robot with three arms that are positioned above a patient's abdomen; two are operating arms and one holds a camera. The robot is linked to a nearby console where the surgeon sits, pressing buttons with his feet and moving two joysticks with his hands to control the camera and robotic arms.

"The surgeon can do everything from the console," Shalhav said. "He can focus the camera for a sharper view of the surgical area, zooming in and zooming out as desired. And he can operate surgical tools inside the patient's abdomen by manipulating the joysticks."

The system has to be set up very precisely for surgery. But since the surgeon does not make direct contact with the patient, he can sit at the console in T-shirt and sneakers. "It's a very comfortable position in which to do surgery," Shalhav said. "You can stay in the position for hours without getting tired."

Still relatively new, robotic surgery can take twice as long as conventional surgery to perform and costs \$2,000 more per operation, but it requires shorter time in post-op.

Unlike ordinary laparoscopic techniques, the Da Vinci system provides the surgeon with a three-dimensional image of the surgical area, the result of two telescopes in the robot's camera. The robotic system is easy to operate, enabling beginning surgeons to use it.

"The only handicap is that the system does not provide the surgeon with any tactile feedback," Shalhav said. "For example, while suturing up an incision, you could break the string because you might be pulling it too hard without realizing it."

Shalhav and his UCH colleagues are using the robot for a range of abdominal surgeries: to remove prostate glands in prostate cancer, to perform a radical nephrectomy by removing defective kidneys or to widen the urinary tract. They also are using the system for cardiac surgery.

"Using the system, it is possible to perform cardiac procedures without making a large skin incision and without splitting the chest bone [sternum] in half," said Emile Bacha, MD, assistant professor of surgery and pediatrics. "This translates into less pain, shorter recovery times and better cosmetic results."

New path to an old bug

Until recently scientists were puzzled by how the bacterium *Staphylococcus aureus* manages to acquire iron from its host's red blood cells. Capturing iron is a critical step in how this disease-causing bacterium causes life-threatening infections and how the microbe has grown ominously resistant to antibiotics.

A team of University of Chicago researchers led by Olaf Schneewind, MD, PhD, recently discovered and described the entire pathway of how *S. aureus* nabs iron from its host.

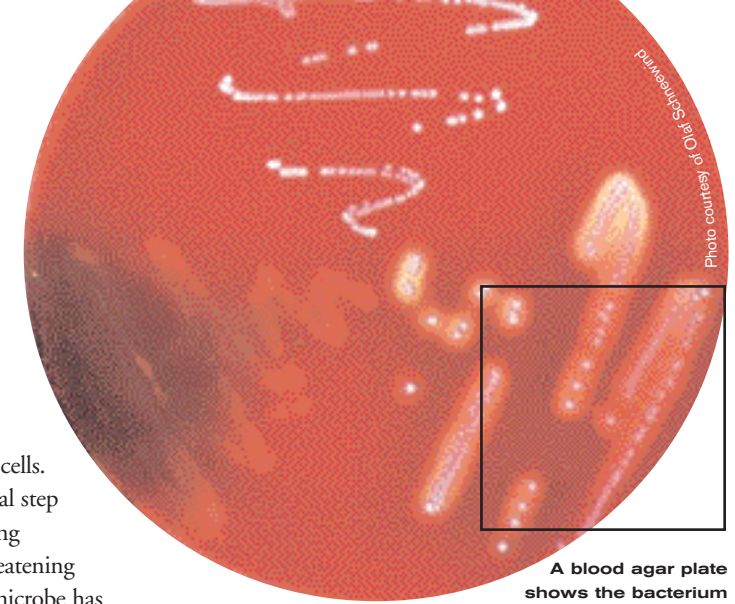
It's a beautiful system, a complete and very elegant pathway.

— Olaf Schneewind, MD, PhD, professor of molecular genetics and cell biology

The bacterium bursts open the host's red blood cells, captures the hemoglobin inside and removes the iron-containing heme groups. Then it transports the kidnapped heme groups across the bacterial membrane and extracts the iron.

The university finding, published in *Science* this past February, suggests new ways to combat this common pathogen. The researchers also found that anthrax and listeria use this same method. "It's a beautiful system, a complete and very elegant pathway," said Schneewind, professor of molecular genetics and cell biology. "It involves six different proteins, each with a specific function."

"Our findings could be used to develop drugs that would disrupt the staphylococcal iron uptake systems, which could, in turn, prevent infection," said co-author Eric Skaar, PhD, research associate in molecular genetics and cell biology. "Having the entire pathway provides us with multiple new drug targets."



A blood agar plate shows the bacterium *Staphylococcus aureus* acquiring iron from red blood cells.

With one known exception (*Borrelia burgdorferi*, the bacterium that causes Lyme disease), pathogens must scavenge iron from their host in order to survive, grow and cause disease. Body fluids

from humans and other mammals contain very little free iron, one of their most important defenses against infections. So bacteria have evolved specialized ways to obtain iron from a host's body. In humans, hemoglobin is the most abundant iron source.

Schneewind and colleagues found that the *S. aureus* genome contains a family of iron-regulated surface determinant (*isd*) genes, which encode factors that bind hemoglobin and transport the iron it contains across the cell wall and into the cell's interior.

These genes are activated when the bacteria arrive in an iron-poor environment, such as a surgical wound, the gastrointestinal tract or virtually any other site in the human body.

The next step, the researchers said, is to find ways to inhibit this iron-gathering process. Since humans do not have an iron-gathering pathway, drugs that could disrupt the process might provide a safe and effective therapy.

IN BRIEF

HIPAA compliant

This past April brought more than its usual tax deadline for the University of Chicago Hospitals. New rules under the Health Insurance Portability and Accountability Act of 1996 were put in place April 14.

HIPAA establishes federal standards to protect patients' health information, and it creates patient rights for how such information is used and disclosed. The act is intended to provide people with health care protections similar to those that govern consumer financial information. Health care providers, health insurance companies, pharmacies and related entities affected by HIPAA privacy rules were required to begin testing their electronic transaction systems by April 14, 2003. HIPAA standards for electronic transactions become enforceable Oct. 16, 2003.

The new rules apply to all health care providers and health plans. Entities like the University of Chicago Hospitals are allowed to band together with certain other organizations and call their group an Organized Health Care Arrangement. University of Chicago's OHCA is composed of the Hospitals, its regional doctors' offices, the Friend Family Health Center, the Biological Sciences Division and all other units of the university that create, receive, use or disclose an individual's health information.

Good Samaritan donates kidney

Since last June, Willie Morris, 53, of Chicago, has been kept alive by a kidney donated "to whoever needed it" by Bill Van Pelt, 41, of Frankfort, Ill.

The exchange commenced two years earlier when Van Pelt decided to donate one of his kidneys. But when he called a Chicago-area hospital, they "did not take me seriously" he said. On his third call, this time to the University of Chicago, he found doctors willing to listen.

"They took the time to understand and realized I really meant it," said Van Pelt who was inspired to act after reading a newspaper account of a teacher in North Carolina who donated a kidney to one of her students. Also, in his job at Federal Express, Van Pelt made regular stops at a dialysis center where he saw dozens of people who depend on this technology to stay alive. "It was sobering to see," he recalled. "It did not seem like a fun kind of life."

Transplant surgeon J. Richard Thistlethwaite, MD, PhD, worked with ethicist Lainie Ross, MD, PhD, to set up guidelines for how a "good-Samaritan" donation should be handled. The physicians agreed that if both donor and recipient were willing, the two patients could meet at least one month after the operation when the initial period of surgery and recovery were completed.

At the time of Van Pelt's phone call, Morris, whose kidneys had failed six years earlier, was at the top of the recipient list. His wife, two daughters and four sons had volunteered to donate but were ineligible.

After the procedure, Van Pelt recovered quickly and was back at work within six weeks. Morris also recovered well, and said he feels "fabulous, better every week."

Finally, the two men met. Morris said he has been waiting a long time to thank Van Pelt.

"This was a marvelous thing he did," Morris said. "He's like a Superman to me."

Kidney recipient Willie Morris (left) recently met his good Samaritan donor, Bill Van Pelt.



Chicago Tribune file photo



Researchers shined a synchrotron X-ray beam through the head and thorax of this ground beetle to view the compression and expansion of tracheal tubes.

X-rays show how insects breathe

Scientists at the University of Chicago and Argonne National Laboratory have discovered a surprising new insect breathing mechanism that is analogous to lung ventilation in humans.

"The discovery of this fundamental aspect of respiratory biology for insects could revolutionize the field of insect physiology," said Mark Westneat, PhD, a lecturer in the Committee on Evolutionary Biology at the university and the lead author of the study published in the Jan. 24, 2003, issue of *Science*.

Until now, it has not been possible to see movement inside living insects, but Westneat, Argonne physicist Wah-Keat Lee, PhD, and their collaborators found that a synchrotron, which generates one of the strongest X-ray beams in the world, could provide X-ray videos of living, breathing insects.

"This is the first time anyone has applied this technology to study living insects," Lee said.

Insects — the Earth's most numerous and diverse group of animals — do not have lungs. Instead, they breathe through a system of internal tubes called tracheae that exchange oxygen through slow, passive mechanisms, including diffusion.

As a result of the synchrotron, we now know that beetles, crickets, ants, butterflies, cockroaches and dragonflies, to name a few, breathe using rapid cycles of tracheal compression and expansion in the head and thorax.

"Hospitalists" improve care

Physicians who specialize in the relatively new field of hospital care produce better results for patients than the general internists who traditionally manage patient hospital stays. That's the conclusion of a study by University of Chicago researchers published this past December in the *Annals of Internal Medicine*. The study found that "hospitalists" can reduce short-term mortality, decrease hospital stays and cut costs. The benefits, though modest at first, increased as the hospitalists — a relatively new specialty — gained experience.

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The differences between the two groups slowly emerged over the course of the two-year study. In the second year, for example, short-term mortality fell by 37 percent among patients cared for by hospitalists. At 30 days, 6 percent of the internists' patients had died compared with 4.2 percent of those cared for by hospitalists. At 60 days, the difference persisted, with internists losing 8.8 percent of patients and hospitalists losing 6.8 percent. Hospitalists also had slightly lower rates for in-hospital mortality (1.9 percent compared with 2.2 percent for internists), 30-day emergency department visits (7.6 percent compared with 8.2 percent) and 30-day readmission rates (10.8 percent compared with 12.2 percent).

"Study after study has demonstrated a close relationship between volume and outcome for surgical procedures," said the study's lead author David Meltzer, MD, PhD. "Our findings, for the first time, extend this phenomenon to hospitalized patients with common medical conditions, those usually cared for by general internists." Meltzer is an associate professor in the departments of medicine and economics and in the Harris School of Public Policy.

In the first year of the study, patients cared for by hospitalists stayed in the hospital about one-third of a day less than those cared for by internists. By the second year, the difference increased to half a day — an average of 4.59 days for internist care and 4.1 days for hospitalist care. Hospitalists also reduced costs. While average adjusted costs per patient increased by \$100 (from \$8,701 to \$8,801) for the generalists from year one to year two, they fell by \$629 for the hospitalists (from \$8,648 to \$8,019), for a total difference in year two of \$782 per patient. Even in this small trial, savings amounted to more than \$600,000.

The researchers attribute most of these gains, which continued to mount during the second year of the study, to the increased experience of the hospitalists in handling the hospital care of patients with specific diseases.

The study involved 6,511 patients admitted to the general medical service at the University of Chicago Hospitals between July 1, 1997, and June 30, 1999. Every fourth day, new patients were assigned to the care of one of two hospitalists. A pool of 58 general internists cared for patients admitted on the other three days. Patients in both groups were similar.

The two hospitalists, part of a new service begun at the Hospitals in 1997, devoted six months a year to the care of hospitalized patients. Each of the 58 general internists, on the other hand, continued to see other patients in the outpatient setting and spent two months or less each year caring for hospital patients.

Celiac disease common

Celiac disease is much more common in the United States than previously believed. A massive, multi-center study published in the *Archives of Internal Medicine* this past February found that one of every 133 Americans has celiac disease. Since only one of 4,700 or so Americans has been diagnosed, 97 percent of cases in this country go undetected.

Celiac disease is a digestive disorder triggered by the protein gluten, which is found in wheat, barley and rye. While symptoms vary among individuals, the most common are diarrhea, constipation and abdominal pain. Diagnosis can be difficult because symptoms also can include weight loss, anemia, osteoporosis, lassitude and depression. And sometimes, there are no symptoms.

In people who have genetic susceptibility to the disease, gluten can trigger an autoimmune reaction, preventing proper absorption of food and nutrients and leading to serious health consequences. By following a gluten-free diet, however, people with celiac disease can lead normal, healthy lives.

“When this disease is diagnosed and treated early we can prevent complications,” said Stefano Guandalini, MD, director of the University of Chicago Celiac Disease Program and one of the study’s researchers. “But there is so little awareness of celiac disease in this country, even among physicians, that we often see people only after they develop severe problems. For a disease that can usually be treated effectively with a modified diet, that’s a horrible waste.”

This new study demonstrates the disease is just as prevalent in the United States as in Europe, where it is considered common and affects an estimated one out of 130 to 300 people.

“Equal recognition of celiac disease has been frustratingly slow to reach the U.S.,” said Guandalini, who trained in Italy. “In Europe, it typically takes a few weeks to go from the first symptoms to a diagnosis. In the U.S., the average lag time between onset and diagnosis is 11 years.”

The disease’s prevalence among Americans is far higher for those considered at risk. The study found that people who have a first-degree relative with the disease have one chance in 22 of having the disease.

For second-degree relatives the chance decreases to one in 39. For those

with the disease’s symptoms but no diagnosed relative, the chances drop to one in 56 people.

“If physicians believe that [celiac disease] is rare,” the authors noted, “they are less likely to test for it.”

This study, the largest ever on the prevalence of celiac disease in the United States, took place over five years and tested blood samples from 13,145 adults and children from 32 states. Approximately 9,000 people who were considered at risk because their relatives had the disease, and another 4,000 who were not considered at risk because they had neither symptoms nor affected relatives.

Because celiac disease is an autoimmune disease, scientists now are beginning to suspect it may “set the stage” for other autoimmune disorders, such as type 1 diabetes or rheumatoid arthritis, Guandalini said. “People who are diagnosed late or who continue to eat gluten have a higher prevalence of autoimmune diseases.”

The study supports the benefits of screening for the disease, and a blood test costs about \$80. The study also found that insurance companies denied payment for an additional intestinal biopsy to confirm the diagnosis for 21 percent of the patients with positive

blood tests. Such delays can compound the disease’s health consequences.

“We are not ready to test the general population,” Guandalini said, “but it now makes sense to screen those at risk.”

AOA elects 15

The prestigious Alpha Omega Alpha Medical Honor Society welcomed 15 new members — all from the class of 2003 — at a campus reception in March. The inductees are: Benjamin Breyer, Scott Diede, Stephen Keefe, Leah Kelley, Anjali Krishnan, Nicholas Leeper, Tamara Levin, Jimmy Lu, Mecca Maxey, Melissa Munsell, Claire Najim, Andrew Pennock, Daniel Refai, Elizabeth Sailhamer and Eric Seeley.

Election to the society is based on U.S. Medical Licensing Board scores, third year clinical performance, and research and leadership accomplishments.

“It’s a very prestigious award,” said recent medical school graduate Daniel Refai, who started his neurosurgery residency at Washington University in St. Louis in July. “It’s an honor to be elected to AOA because you are joining a community of individuals who seek excellence in their academic careers, including their clinical work and research.”

Exercising their privilege to name and induct additional members from among non-AOA residents and house staff, the new members selected: Elizabeth Oh, MD, third-year resident in obstetrics/gynecology; Joshua Robinson, MD, second-year resident in pediatrics; Maura Quinlan, MD, assistant professor of obstetrics/gynecology; and Monica Vela, MD, clinical associate of medicine.

John Asplin, MD, clinical associate in the department of medicine’s nephrology section, received the Volunteer Faculty Award.

The University of Chicago AOA chapter was established in December 1902.

NOTEWORTHY

Thomas Rosenbaum, PhD, the James Franck Professor in Physics, was appointed vice president for research and for Argonne National Laboratory. Rosenbaum now oversees a combined research enterprise of more than \$700 million. In addition to his responsibilities for research across the university and for Argonne, Rosenbaum also chairs the new Science Council, which is charged with the coordination and promotion of scientific research at the university and Argonne.

Keith Moffat, PhD, the Louis Block Professor of Biochemistry and Molecular Biology, and in the Institute for Biophysical Dynamics, was appointed deputy provost for research. In addition to assisting the provost with academic personnel and administrative issues, Moffat serves on the newly created Science Council.

Arthur F. Haney, MD, a specialist in reproductive endocrinology, infertility and the prevention of adhesions following gynecologic surgery, was appointed professor and chairman of the department of obstetrics and gynecology. Haney comes to Chicago from Duke University where he was the Roy T. Parker Professor and director of the division of reproductive endocrinology and infertility in the department of obstetrics and gynecology.

Graeme Bell, PhD, the Louis Block Professor of Biochemistry and Molecular Biology, of Medicine and of Human Genetics, and an investigator with the Howard Hughes Medical Institute, was awarded the J. Allyn Taylor International Prize for Medicine. The \$10,000 award, which has been presented annually since 1985, honors scientists who make significant contributions to a field of basic or clinical research.

David Faxon, MD, chief and professor of cardiology in the department of medicine and the current president of the American Heart Association, received the association’s Distinguished National Leadership Award. Faxon and two association volunteers, Lawrence Sadwin and Gayliss Ward, received the award, which recognized their leadership during the 2001 fiscal year.

Stephen Kent, PhD, professor in the department of biochemistry and molecular biology, the Institute for Biophysical Dynamics, the department of chemistry, and the College, was appointed director of the IBD, which fosters collaboration among researchers in the biological and physical sciences.

Willard Manning, PhD, professor in the department of health studies and in the Harris School of Public Policy Studies, received the 10th annual Kenneth J. Arrow Award in Health Economics from the International Health Economics Association. The award recognizes Manning’s paper — co-authored with John Mullahy, PhD, of the University of Wisconsin — titled, “Estimating Log Models: To Transform or Not to Transform?” published in the *Journal of Health Economics* in 2001.

David Meltzer, MD, PhD, associate professor in medicine and economics, received the inaugural Eugene Garfield Economic Impact of Medical and Health Research Award, presented by the board of directors of Research!America, an alliance for discoveries in health. Meltzer was honored for his work across the disciplines of medicine and economics.

Paul Rathouz, PhD, assistant professor in health studies, received the James E. Grizzle Distinguished Alumnus Award for 2003 from the department of biostatistics at the University of North Carolina. The award recognizes a biostatistics alumnus for outstanding contributions to biostatistical methodology, consulting and/or teaching.

Janet Davidson Rowley, PhB '45, SB '46, MD '49, the Blum-Riese Distinguished Service Professor of Medicine, of Molecular Genetics and Cell Biology, and of Human Genetics, was awarded the 2003 Benjamin Franklin Medal for Distinguished Achievement from the American Philosophical Society and the 6th Women in Cancer Research Charlotte Friend Memorial Award from the American Association for Cancer Research. Rowley also won the Mendel Award from Villanova University. The awards recognize Rowley’s outstanding contributions both as a basic and translational scientist, and as a mentor for women scientists.

Gopal Thinakaran, PhD, associate professor in neurobiology, pharmacology and physiology, received the 2001 Ruth Salta Junior Investigator Achievement Award from the American Health Assistance Foundation and a 2002 Zenith Fellow Award from the National Alzheimer’s Association. Both awards recognize Thinakaran’s contributions to Alzheimer’s disease research.

Black Contractors United presented their annual President’s Award to the **University of Chicago Hospitals** for their “extraordinary effort on behalf of African-American contractors” in the construction of the new Comer Children’s Hospital. The award honors UCH’s commitment to “go beyond the call of duty” in their efforts to include minority and women contractors in the construction process.

Managing better health care

Tens of millions of patients with chronic diseases in this country are not receiving the type of care management that has been proven to be effective.

That's the latest finding from a nationwide survey of physician organizations published by researchers at the University of Chicago and the University of California-Berkeley in the January issue of the *Journal of the American Medical Association*.

The processes we studied are known to improve the quality of patient care.

— Lawrence Casalino, MD, PhD, assistant professor of health studies

“The results suggest that Americans are not receiving care that is as good as it could and should be,” said Stephen Shortell, PhD, the principal investigator of the study. “In many ways, physicians are still organized to practice medicine the way they did 100 years ago.” Shortell is professor and dean of UC-Berkeley's School of Public Health.

The researchers found that physician groups on average use only one-third of 16 recommended care management processes. One physician group in six uses none.

These processes include:

- using nurse case managers to maintain contact with patients,
- teaching patients how to understand and care for their illnesses at home,
- keeping a list of patients with each disease,
- developing timely reminder systems for patients and caregivers, and
- providing feedback to physicians on the quality of their care.

“The processes we studied are known to improve the quality of patient care,” said Lawrence Casalino, MD, PhD, assistant professor of health studies at the University of Chicago and lead author of the paper. “Our research indicates that physician organizations are beginning to create effective processes to increase quality, but most still have a long way to go.”

The researchers focused on care for asthma, congestive heart failure, depression and diabetes, which together account for 140,000 deaths and \$173

billion in costs each year in the United States. They surveyed 1,040 medical groups and independent practice associations with at least 20 physician members. The presidents, chief executive officers or medical directors of the groups took part in one-hour telephone surveys from September 2000 to September 2001.

Seven in 10 physician groups surveyed do not keep a list of patients who have serious chronic diseases such as diabetes. Half of the groups reported having no electronic data systems to track patients' illnesses, medications and laboratory results.

Physician groups are more likely to use organized processes to improve care when they have clinical information technology in place and when they are given external incentives to provide high quality care — such as financial rewards, public recognition or better contracts with health plans.

“We know incentives work, but for the most part they are not being used,” Casalino said. “The federal government and large employers have the most leverage to establish incentives. They have the opportunity and the responsibility to do so.”

Casalino pointed out that some Fortune 500 companies have set up successful programs to do just that, and that Medicare and Medicaid recently created demonstration projects that reward quality. In addition, six California health plans recently started a new pay-for-performance initiative designed to reward physician groups for achievements in documented performance measures.

But such programs remain the exception, and the use of organized processes to improve quality is still uncommon. Given that most physicians practice in smaller organizations with fewer resources to implement care management processes, Casalino said, the study probably underestimates the extent of the problem in this country.

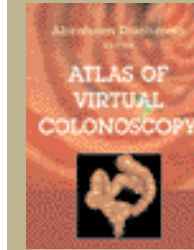
“There are now 125 million Americans suffering from chronic illness, and that number is only going to grow,” Shortell said. “We have an opportunity to provide much better care for ourselves than we do now.”



Match Day

Elizabeth Sailhamer (right) celebrated with Vanessa Gomez at this year's Match Day on March 20. The two medical school graduates will do their residencies at Massachusetts General Hospital. Sailhamer will specialize in surgery; Gomez, in pediatrics.

BOOKMARK



Biography

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*University of Chicago faculty

Healthy, wealthy and wise

Extreme poverty has long been associated with reduced life span.

Now more and more studies are showing that people in each socioeconomic category also have worse health than those in the group just above them. It's not simply income or access to medical care. New studies have shown that personal, social and financial resources often determine the length and quality of life. It turns out deprivation, of any sort, can impair well being.

The pioneers in this emerging field — known as the social determinants of health — argue that people who work in public health should expand their focus beyond germs and genes. They also should include such factors as financial resources and social status, cognitive skills and educational background, racial attitudes and ethnic practices, personal behavior and lifestyle, even a person's neighborhood and friends.

Many of these ideas can be traced to a handful of people, among them Alvin Tarlov, MD '56, who chaired the department of medicine at the University of Chicago from 1968 to 1985. His protegee, Mark Siegler, MD, a physician with a penchant for ethics, along with Richard Epstein, a lawyer with a taste for economics, pulled together a conference this past November to discuss the "Social Determinants of Health and Disease: Recognizing the Contributions of Dr. Alvin R. Tarlov."

The conference was divided into six sessions:

- inequality and health,
- social connections and health,
- social and medical factors related to obesity,
- how sex and gender affect health,

- the economics of medical innovation and
- the role of the legal system in public health and health care.

Speakers included distinguished faculty from business, economics, law, medicine, psychology, public health, public policy and sociology.

The idea is catching on. Three months after the Chicago conference, the president of the American Association for the Advancement of Science opened its annual meeting in Denver with a plea for more research of this type.

"The puzzles of better health promotion and disease prevention," said former editor-in-chief of *Science* Floyd Bloom, PhD, "may be approached more rapidly and effectively through intensified social science research."

Daily dose

Taking one aspirin a day can prevent the development of pre-cancerous polyps in people who have increased risk for colorectal cancer, according to a multi-center study published this past March in the *New England Journal of Medicine*. Aspirin's protective effect was so significant that the study was stopped early.

"Aspirin had a significant protective effect," said senior author Richard Schilsky, MD, a professor of medicine at the University of Chicago. "It clearly reduced the formation of polyps in this study of high-risk individuals, which is good news because it provides a new way to lower the risk of recurrence in patients who have had colon cancer."

Conceived and organized by Cancer and Leukemia Group B (CALGB), this study and a related one published in the same issue provide a significant boost to the mounting evidence that aspirin and related drugs can reduce the risk of colon cancer — the second-leading cancer killer in the United States.

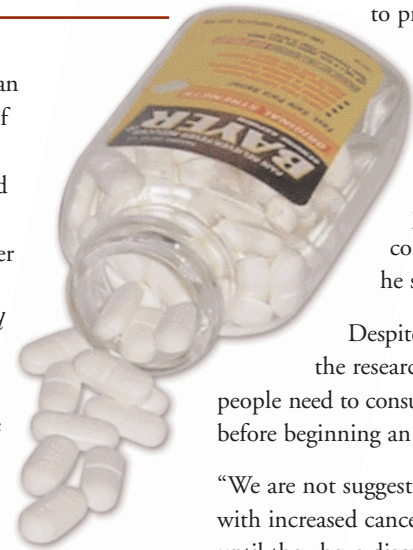
An aspirin a day, the researchers found, reduced the occurrence of adenomas, precancerous polyps in the colon, by about one-third in patients with a history of colorectal cancer. Patients on aspirin who did get polyps took longer to develop them, and they had fewer polyps than those not taking aspirin.

"This suggests that aspirin and similar anti-inflammatory drugs may help prevent this disease in average-risk individuals," said Schilsky, the CALGB chairman.

Although these drugs are not without risks, many people already take a daily aspirin to prevent cardiovascular disease. "Now we have one more reason to consider recommending aspirin for prevention in patients with no contraindications," he said.

Despite the good news, the researchers caution that people need to consult their own physicians before beginning an aspirin regimen.

"We are not suggesting that even those with increased cancer risk take aspirin until they have discussed it with their doctors," added Robert Sandler, MD, professor of medicine and epidemiology at the University of North Carolina, lead author of the CALGB paper and a co-author of the second study. "For those who have had polyps or previous colon cancer, regular colonoscopy and polyp removal remain the first step in prevention, possibly supplemented by aspirin."



Blocking the ills of painkillers

A drug designed to relieve the intractable constipation associated with opioid pain relievers, such as morphine, codeine and OxyContin, entered phase III clinical trials in December. Methylnaltrexone, or MNTX, was developed at the University of Chicago in 1979 and recently was acquired by Progenics Pharmaceuticals.

Cancer patients on heavy doses of opioid drugs can go a week without a bowel movement. The crippling state can make it difficult to eat, work or even walk. Laxatives are ineffective in such cases, and lacking other therapies, the only alternative is to cut off the painkillers.

Opioids relieve pain by interacting with receptors in the brain and spinal cord. However, they also affect other receptors in the body, including those in the digestive tract. MNTX blocks the digestive-tract receptors, and because the drug is unable to penetrate the brain, it doesn't interfere with pain relief.

Methylnaltrexone was invented by the late university pharmacologist Leon Goldberg who wanted to help a dying friend suffering from morphine-induced constipation. Goldberg started with naltrexone, an established drug that completely blocks the effects of morphine. He altered the drug slightly by attaching a methyl group, which changed the charge of the molecule so that it could no longer cross the protective barrier that surrounds the brain. Consequently, the molecule did not interfere with morphine's effect on pain, which is centered in the brain. But it did block morphine's effects on gut motility, which is mediated by receptors in the peripheral gastrointestinal tract.

It worked like a charm for his dying friend, who then shared the drug with several other friends who also were taking opioid drugs for cancer pain. The drug's initial success in this compassionate-use setting drew notice from Goldberg's colleagues. After Goldberg's death, they continued to develop the compound, testing it in animals, performing the initial human safety trials and completing a series of pre-clinical studies in volunteers.

The phase III trials — the final lap before Progenics can apply for FDA approval — involve 150 cancer patients who are taking plentiful amounts of narcotics. This phase evaluates whether a single injected dose of MNTX or a placebo will induce laxation within four hours. The double-blind trials mean neither patient nor physician knows whether a drug or a placebo has been dispensed.



Wielding shovels are (left to right) Richard Saller, provost; Don Michael Randel, president; Keith Moffat, deputy provost for research; Donald Reaves, vice president for administration and chief financial officer; Thomas Rosenbaum, vice president for research and for Argonne National Laboratory; David Oxtoby, dean of the Physical Sciences Division; and James Madara, vice president for medical affairs and dean of the Biological Sciences Division and the Pritzker School of Medicine.

Breaking ground for Collaboration

With shovels in hand, University of Chicago officials gathered on the corner of Drexel Avenue and 57th Street this past November to break ground for one of the largest interdisciplinary science buildings on any Midwestern university campus. The 430,000-square-foot Interdivisional Research Building, slated for completion in 2005, will have seven floors covering nearly 10 acres.

The \$200-million facility will enable biologists and physical scientists to work on projects that cross traditional boundaries of scientific inquiry, bringing together such diverse fields as condensed-matter physics and molecular biology.

The IRB will house faculty from the Institute for Biophysical Dynamics, the Howard Hughes Medical Institute, the Ben May Institute for Cancer Research, the James Franck Institute and the chemistry department.