Nobelists Carl and Gerty Cori were inducted posthumously into the St. Louis Walk of Fame on Sunday, May 15, at an outdoor ceremony. The recognition honored their scientific achievements in the catalytic metabolism of glycogen. Also honored were athlete Lou Brock, author A.E. Hotchner, designer Charles Eames, actress Agnes Moorehead, poet Sara Teasdale and soprano Helen Traubel, St. Louisans all.

There are now 57 sets of stars and plaques on the walk located on Delmar in the University City loop. Gary K. Ackers, Ph.D., Wittcoff Professor and head of the Department of Biochemistry and Molecular Biophysics (left), accepted the award on behalf of the Cori family. Presenting was Joe Edwards, founder of the Walk of Fame.
An illustration by New York artist Irving Geis — "the portrait artist of hemoglobin" — shows the protein's genetic coding regions and the characteristic way in which it folds. For more about hemoglobin and efforts to understand and redesign it by Gary Ackers, Ph.D., consult the story beginning on page 20.
Marshall's Contributions Recognized

Garland R. Marshall, Ph.D., professor of molecular biology and pharmacology and of biochemistry and molecular biophysics, has received the Vincent duVigneaud Award for his contributions to the chemistry and biology of peptides.

The Vincent duVigneaud Award

Marshall, who directs the Center for Molecular Design of the Institute for Biomedical Computing, received the award at the Gordon Research Conference held earlier this year. The award honors Vincent duVigneaud, Nobel laureate, who first synthesized the peptide hormones oxytocin and vasopressin.

Goldberg Joins HHMI Team

Daniel E. Goldberg, M.D., Ph.D., assistant professor of medicine and molecular microbiology, is the medical school's newest member of the prestigious Howard Hughes Medical Institute.

The Institute recently selected 44 researchers from a pool of 285 nominees gathered in a national competition. More than 200 institutions were invited to nominate scientists, and a panel of distinguished experts then helped make the final selection.

Goldberg joins a Washington University/Howard Hughes Medical Institute team composed of Andrew Chan, M.D., Ph.D.; David D. Chaplin, M.D., Ph.D.; Stanley J. Korsmeyer, M.D.; Dennis Y. Loh, M.D.; J. Evan Sadler, M.D., Ph.D., and Matthew L. Thomas, Ph.D.

The Howard Hughes Medical Institute, with assets of approximately $7.8 billion, is the largest private philanthropy in the United States. In 1993, it spent $268 million on biomedical research in five broad areas: cell biology and regulation, genetics, immunology, neuroscience and structural biology.

Jakschik Award Winner

Ilka Ruth Warshawsky, a student in the Medical Scientist Training Program (MSTP), has received the 1994 Barbara A. Jakschik Award.

Ilka Ruth Warshawsky

The award is presented annually to an outstanding female graduate student in her final year of doctoral research whose thesis focuses on metabolic regulation. Warshawsky is doing her thesis work in the laboratory of Alan L. Schwartz, M.D., Ph.D., Alumni Professor of Pediatrics and professor of molecular biology and pharmacology.

The recipient receives a $150 cash award, a certificate, and her name is added to a plaque being designed for permanent display in the offices of the Division of Biology and Biomedical Sciences.

The award honors Jakschik, who retired from the Department of Molecular Biology and Pharmacology in 1992 following a career devoted to research on mediators of inflammation.

Merit Status Granted

In recognition of his scientific contributions, Gustav Schonfeld, M.D., William B. Kountz Professor of Medicine, has received MERIT status for his most recent grant.
The five-year grant from the National Heart, Lung and Blood Institute totals more than $1.1 million and enables Schonfeld to continue research on the structure-function relationship of apoB, the major protein of LDL, "the bad cholesterol," and to ascertain how genetic defects and apoB may produce low levels of cholesterol.

Schonfeld's study, ongoing since 1989, involves looking for variants of the apoB blood protein responsible for carrying cholesterol and triglycerides. His goal is to find the structure-function relationship of apoB and its role in atherosclerosis.

Schonfeld has been conducting lipid research for more than 23 years and is head of the atherosclerosis, nutrition and lipid research division at the School of Medicine.

Royal Appointment

Henry D. Royal, M.D., professor of radiology and an internationally acclaimed expert on the effects of radiation exposure, has been appointed by President Bill Clinton to serve on the Advisory Committee on Human Radiation Experiments.

Royal joins a panel of 14 renowned ethicists, scientists and physicians to investigate the scientific and ethical history of government-sponsored ionizing radiation experiments conducted between 1940 and the mid-1970s. After reviewing the experiments, the committee will set ethical and scientific criteria for evaluating the experiments and will determine if the testing was in compliance with those standards. The committee also will recommend policies to ensure that present and future human experiments are conducted according to the prescribed standards.

The investigation was recommended by Department of Energy Secretary Hazel O'Leary after allegations were made in 1993 that patients were not informed about the risks of radiation exposure during government-sponsored experiments some 50 years ago.

Chaplin, Colten and Klahr Tapped As AAAS Fellows

David D. Chaplin, M.D., Ph.D.; Harvey R. Colten, M.D., and Saulo Klahr, M.D., recently have been named fellows of the American Association for the Advancement of Science for their distinguished scientific work and leadership.

Chaplin, chief of allergy and immunology in the Department of Internal Medicine, is associate professor of medicine, genetics and molecular microbiology and an associate investigator of the Howard Hughes Medical Institute. He is being recognized for his research into the genes of the HLA system and the relationship of inheritance of these genes to susceptibility to a variety of human diseases.

Colten is the Harriet B. Speohrer Professor and head of the Department of Pediatrics at Washington University School of Medicine and a professor of molecular microbiology and pediatrician-in-chief at Barnes and St. Louis Children's Hospitals. He is being honored for his ground-breaking research into the molecular genetics of complement deficiencies and of inherited lung disease.

Klahr is cochair of the Department of Internal Medicine and chief of medicine at Jewish Hospital. He is honored for his investigations into the causes of kidney disease and for extraordinary administrative service and leadership in the field of nephrology.
Alpers Celebrates 25 Years

A dinner banquet and daylong symposium in April highlighted the 25th anniversary celebration of David H. Alpers, M.D., as chief of the division of gastroenterology.

Faculty, alumni, fellows and friends joined in the celebration, "Twenty-five Years of Growth," honoring Alpers, who was named to the gastroenterology division's top post in 1969 by Carl V. Moore, M.D., former chair of the Department of Medicine.

Under Alpers' leadership, the division has expanded substantially and achieved excellence in patient care, teaching and investigation. Present research encompasses a range of disciplines from clinical investigation to molecular biology.

Among Alpers' accomplishments is refueling the fellowship training program with grant monies and increasing the number of trainees. Since 1969, 80 fellows have completed their training here. He also recruited and expanded the division faculty. Today, 13 of the 17 full-time faculty were fellows here, as were nine of the 12 part-time faculty.

Alpers' research, supported by the National Institutes of Health for more than two decades, centers on the physiology of enterocyte proteins. Alpers, along with colleagues Ray Clouse, M.D., and William Stenson, M.D., wrote the Manual of Nutritional Therapeutics, which has been an important resource for nutritional management of patients. He also helped establish a nutrition course for medical students at Washington University.

Outside the university, Alpers has been involved in many activities, serving as president of the American Gastroenterological Association and actively contributing to the research process, serving as associate editor of the Journal of Clinical Investigation and editor of the American Journal of Physiology - Gastrointestinal and Liver Physiology.

The events, held at the medical school and at the Adam's Mark Hotel, were sponsored by the division of gastroenterology.

Registry Established

The medical school is one of four medical centers in the United States designated by the National Cancer Institute (NCI) to develop a regional breast cancer tissue registry. The NCI is funding the St. Louis project with a $500,000 grant.

Information gathered from the regional registries will be pooled to create a national, computerized breast cancer tissue database which will help provide breast cancer tissue to researchers studying the disease. Progress in identifying a particular gene or genes that may predispose women to breast cancer has been hampered by the lack of available tumor tissue from patients with known outcomes.

"The database should dramatically improve access to breast cancer tissue," says Helen Donis-Keller, Ph.D., professor of surgery and the grant's principal investigator in St.

On Race And Medicine

Vanessa Northington Gamble, M.D., Ph.D., spoke to faculty and guests on the history of racism in American medicine at a luncheon in the Kenton King Conference Center in March. Gamble, professor of preventive medicine and family practice at the University of Wisconsin School of Medicine, is a nationally recognized expert on the history of African Americans in healthcare. The event was sponsored by Robert Lee, Ph.D., assistant dean for minority student affairs, with whom Gamble is pictured.
Louis. "In the long term, large quantities of tissue also will enable researchers to better predict which types of breast cancer are most treatable and which therapies are most effective."

A team of investigators at the medical school, led by Donis-Keller, will enter information into the database for an estimated 8,000 tissue samples from seven St. Louis-area hospitals. Beginning in 1995, scientists studying breast cancer will have access to the database, which will include patient information regarding tumor types, diagnoses, treatments and outcomes. At that time, an estimated 20,000 breast cancer tissue samples will be available for study, and researchers will be able to request tissue samples through the NCI.

12-Year-Olds And DNA

When geneticist Eric Green, M.D., Ph.D., received an invitation to speak to sixth graders at the Wydown Middle School, he proposed instead that the students of math and science teacher Nanette Albert-Thomas visit his laboratory at the medical school to learn firsthand how geneticists study DNA.

Forty-six sixth graders arrived in two groups on Friday, May 20, and were introduced to the concepts of basic genetics at five stations set up on the eighth floor of the McDonnell Sciences Building. Green addressed the students first with a display of the relative size of the genomes of organisms ranging from bacteria through yeast to human beings. The students went on to witness and participate in precipitating DNA samples, cloning DNA, analyzing DNA by gel electrophoresis, digitizing the gel results with a computer and determining DNA sequence. Each student left with several souvenirs, including a precipitated DNA sample and a photograph of a gel.

Green, assistant professor of genetics, says it was more instructive for the students to come to him and get their hands on the tools and the subjects of genetic investigations than for him to go to the students and lecture to them with the limited equipment he could transport. "I'm interested in getting kids turned on to science. Genetics and the genome project are exciting places to start," he says.

Ultimate Picnic

Donald W. Nielsen, Ph.D., (right) new director of Central Institute for the Deaf (CID), explores cochlear sound analysis with Julius L. Goldstein, Ph.D., senior research scientist at CID and research professor of electrical engineering in the Department of Speech and Hearing. Goldstein's work was part of a research display at CID's "Ultimate Picnic" in April which marked the institute's 80th anniversary and introduced Nielsen to the St. Louis community. Nielsen previously served as executive vice president at House Ear Institute in Los Angeles.
PET Tracks Learning Disabilities

The School of Medicine will use its advanced neuroimaging techniques to map areas in the human brain that may be critical for language development as part of the new $2.3 million Dana Consortium on Language-Based Learning Disabilities. Scientists will attempt to pinpoint the brain pathways that are believed to be involved in language-based learning disorders (L/LD), which affect at least 7 million U.S. children.

Marcus Raichle, M.D., principal investigator and professor of neurology, neurobiology and radiology, will direct a series of experiments using Positron Emission Tomography (PET), an imaging process that enables scientists to view brain processes during the performance of a specified task or in response to stimuli. The studies are designed to further define the neural processes underlying language and its impairments and to track brain reactions to such variables as the rate at which stimuli are presented to the brain.

The studies build on research conducted by the Dana Consortium's scientific director, Paula Tallal, Ph.D., of Rutgers University-Newark. Her work has demonstrated a pervasive deficit in the rate at which language-impaired individuals can process sensory information presented in rapid succession — such as certain speech sounds that individuals with language-based learning disorders have difficulty differentiating.

One goal of the Washington University studies is to better understand the basic science of speech processing in the brain. Another goal is to track differences in brain function as a result of any remediation strategies developed and performed by Dana Consortium partners at Rutgers University-Newark and the University of California at San Francisco.

Intensive Diabetes Therapy Safe For Children

Children newly diagnosed with diabetes can safely and feasibly follow intensive therapy for the disease.

The recent finding, says principal investigator Neil H. White, M.D., lays the foundation for determining whether strictly controlling blood sugar levels in newly diagnosed diabetic children can preserve pancreatic function and thus the ability to produce some insulin. Children who begin treat-

Longest Continuous DNA Sequence Completed

Genome researchers studying the worm, C. elegans, have "spelled out" the longest continuous DNA sequence from any organism to date. In the process, they sequenced DNA faster than was previously possible and uncovered nearly three times as many genes as they had anticipated.

The C. elegans genome has proven to be a treasure trove of genes. Nearly one of every three of these genes is similar to genes in humans and other organisms, says lead author Richard K. Wilson, Ph.D., research assistant professor of genetics.

Researchers at Washington University and the Sanger Center in Cambridge, England, contributed equally to the sequencing effort — each sequenced about 1 million nucleotides. The French group from CNRS-CNRM et Physique-Mathematique in Montpellier, France, helped with software design.

The team is collaborating on an ambitious project to sequence the entire genome of the roundworm. This project is considered by many to be crucial in further developing the tools and know-how to find and sequence the full complement of human genes buried within 3 billion nucleotides, chemical bases that compose the genetic code. The C. elegans genome consists of roughly 100 million nucleotides; about two percent of the genome has been sequenced.

With 98 million nucleotides to go, speed and cost are two crucial factors facing genome researchers. According to Wilson, this project proves that large scale sequencing is technologically feasible, fast and relatively inexpensive. He predicts a further increase in sequencing rates by next year. The group plans to finish sequencing the C. elegans genome by the end of 1998.
ment immediately after diagnosis still may have 10 to 15 percent of their pancreatic function.

Patients on intensive therapy take two to four insulin injections a day, as opposed to one or two doses in conventional therapy. They also exercise and adjust insulin doses according to food intake and blood sugars. In addition, they perform blood sugar tests four or more times a day.

In a large, nine-year diabetes study called the Diabetes Control and Complications Trial (DCCT), researchers found that strictly controlling blood sugar levels reduces damage to eyes, kidneys and nerves. The DCCT did not look at whether strictly controlling blood sugar levels had any long-term impact on pancreatic function, because the patients in the study no longer were producing any insulin when they began.

White, an associate professor of pediatrics, and his colleagues followed 34 children with newly diagnosed insulin-dependent diabetes mellitus (IDDM) for 18 months. Patients, who were 6 to 18 years old, were assigned randomly to a control group or an intensive group. Children in the control group used conventional therapy to manage their diabetes, and children in the other group followed intensive therapy.

Patients in both groups were able to lower blood sugar levels, and parents and children did not report any difference in quality of life and health status between the groups. However, patients in the intensive group had lower blood sugars and were at increased risk of suffering hypoglycemia.

White says his study is a stepping stone for determining if some of the pancreatic function of children with newly diagnosed diabetes can be saved. "We now know that intensive therapy is feasible in children. In 1995, we should know if children's pancreases will be preserved."

SPEAK For Better Hearing

A new cochlear implant system tested here dramatically improves the hearing ability of hearing-impaired patients who receive little or no benefit from even the most powerful hearing aids.

The Food and Drug Administration recently approved the new speech processing system, and it is now available for all patients implanted with the Nucleus cochlear implant system. Skinner and her colleagues have been studying the system since September 1993. Both the coding strategy and processor were developed by Cochlear Proprietary for an international clinical field trial that Skinner helped design. The trial included patients in the United States, Australia, Canada and England. The School of Medicine was one of three test sites in the United States.

With a multichannel cochlear implant, an external microphone placed above the ear picks up sound and relays it to the speech processor worn on a belt or attached to clothing. The processor sends the signal through the skin to a surgically implanted receiver. The sound is then sent to an array of electrodes in the cochlea and picked up by the nerves, allowing the patient to hear.

Dennis Diehl takes advantage of the latest in cochlear implant technology as he waits on a customer in the family business outside of Columbia IL.

The system includes SPEAK, a coding strategy now available in a new speech processor called Spectra 22. "More than 80 percent of the patients tested reported improvement in everyday listening situations, and in some cases that improvement is dramatic," says Margaret Skinner, Ph.D., associate professor of otolaryngology and a collaborating investigator in the clinical trial of the system.

Researchers tested 63 implanted patients to see how well they could understand speech in quiet and noise. Skinner said patients experienced approximately 10 percent hearing improvement in quiet and 25 percent improvement in noise.
In this image of a reconstructed synapse, red neurotransmitters are visible on the surface of a blue muscle cell. The green dots are boutons, regions of the presynaptic nerve terminal dense in neurotransmitter-containing vesicles.
After a 19-hour stint in the laboratory, Robert Wilkinson, Ph.D., was anxious to gather the final data of his 20-hour experiment and go home. He had only to stimulate a snake nerve with an electrode and measure the response from the muscle that it innervated.

"I had gotten 19 hours through it — almost to the end — when I accidentally bumped the nerve terminal with my electrode and it started to fall off of the muscle fiber. That meant my whole experiment was shot," Wilkinson says. "So I panicked and used the electrode to push the nerve terminal back onto the muscle. And the thing started working; I was able to get my data."

Synaptic Junctions Can Be Broken, Then Re-established

by Juli Leistner
At that moment, the significance of the event escaped Wilkinson; but it was the first time anyone had removed a nerve from a cell and reattached it to form a working connection. Not until a year later did he realize the accident held the key to learning more about nerve communication at its most basic level.

All movements, thoughts and even moods are controlled by complex, high-speed signals between nerves and millions of other cells all over the body. The critical communication occurs at tiny junctures—synapses—less than a thousandth of an inch in size. Over the past several decades, researchers have pieced together many of the basic principles of how synapses work. But other aspects of their function remain a mystery, because scientists have been forced to study them intact—as a “black box”—says Wilkinson, associate professor of cell biology and physiology.

“It’s been difficult to figure out the role of individual parts in the synapse because when you take it apart, it doesn’t work anymore,” he explains.

Wilkinson’s uneasy moment in the lab provided a key to unlock the black box. By accident, he demonstrated that these seemingly fragile communication centers could be taken apart, then reconnected, and continue to function. The feat, he later realized, might be repeated in the laboratory under controlled conditions to give researchers more options in exploring synaptic function. Among the possibilities: switching around synaptic parts or selectively altering their function, then observing the effects in the new, reconstructed synapse.

He and undergraduate student Scott Lunin have developed a synapse reconstruction technique in an abdominal muscle of garter snakes and use it to explore synaptic strength, a property that many researchers believe is involved in memory, learning, muscle function and in human diseases. “The key to our technique is that we literally pull the synapse apart, in effect duplicating the conditions of the accidental observations,” says Wilkinson. “It sounds easy, and it is, but it took two years of hard work before we learned to duplicate those conditions at will.” Lunin received Washington University’s Marian Smith Spector Prize for his research.

The technique requires a high-powered microscope, patience and steady hands. The investigators view a snake synapse on a video monitor and apply an enzyme to weaken the surrounding connective tissue. Then, using a glass probe—with a diameter of one-thousandth of an inch—they gently free the nerve from the muscle. The nerve terminal then can be manipulated back onto its original spot on the same muscle fiber or onto a different muscle cell to produce a working synapse once again.

Research on synapses reveals them to be marvels of nature’s engineering. As an electrical signal travels down a nerve and reaches its tip, neurotransmitters spill from the nerve’s endings. These messengers cross a tiny gap to the target—a muscle cell, gland cell or another nerve cell—and bind to special receptor molecules on its surface. Pores in the target cell then open, and charged particles are transported inside to cause the desired effect: A muscle cell contracts; a gland cell releases its hormone, or another nerve cell passes the message along.

Researchers would like to know more about how this complex chemical communication occurs. Wilkinson’s reconstruction technique should allow them to explore many facets of the process. He and his colleagues are using their technique to study synaptic strength, a measure of how strongly the target cell responds to the nerve signal. This property is thought to be involved in acquiring knowledge and improving physical skills such as muscle strength and coordination, Wilkinson says.

Academic learning may occur when the strength of certain synapses in the brain increases. Muscle coordination may be controlled by the same process; as a piano student progresses from playing chopsticks to mastering Mozart, brain synapses involved in coordinating that movement become stronger and stronger, according to the theory.

“This idea comes from the relatively recent observation that synapses change their strength in response to stimuli, such as growth of the target cell. When you use a synapse, its strength changes in some appropriate way,” Wilkinson explains.

“But the details of that are not known at all. We don’t know which part of the synapse is responsible for controlling synaptic strength,” he says. At least two possibilities exist; either the nerve starts sending out more neurotransmitter, or the target cell becomes more adept at responding to those transmitters. Current thinking leans toward the first explanation, he says.

In a study published recently in the Journal of Neuroscience, Wilkinson and his colleagues applied their reconstruction technique to learn...
The basic synapse in diagram, showing the presynaptic terminal in blue, its neurotransmitter vesicles in green and its energy-producing mitochondria in red. The purple release sites lie opposite black postsynaptic transmitter receptors. The folds in the postsynaptic sites are characteristic, but their purpose is not yet understood.

more about what controls one aspect of synaptic strength called quantal size. Quantal size is the response triggered by one vesicle, or bundle, of neurotransmitter. They took apart weak synapses and strong synapses, then switched the nerve terminals to create new synapses with various strength combinations. Then they measured the muscle cells' response to neurotransmitter release.

Muscle cells that originally had strong synapses still displayed strong responses, whether they were paired with a nerve terminal from a strong synapse or a weak one. Muscle cells that had weak synapses showed weak responses, no matter with which type of nerve they were paired.

"The conclusion is that something in the postsynaptic cell controls strength," Wilkinson says. In other words, no matter which nerve sends out the signal, the response it evokes is determined chiefly by characteristics of the target cell. Those characteristics might include possessing a greater number of receptors or receptors that are better at responding to neurotransmitters, Wilkinson says.

He points to the study as a first step in using his technique to explore synaptic communication. "So far, we’ve only applied it to tell whether a phenomenon is pre- or postsynaptic," he says. But the implications go beyond that. He sees the technique as providing researchers with more flexibility in pinpointing where synaptic signals come from and where they are aimed.

One example: exploring how synapses form during early development and during the reinnervation process that sometimes follows peripheral nerve injury. This process is thought to be controlled via a feedback mechanism in which chemicals from a target cell communicate with growing nerve cells. A natural approach to studying this phenomenon is to selectively block receptors in the synapse and observe the effect, Wilkinson says. But that has been difficult to do with intact synapses.

"Anything you did to one part of the synapse, you had to do to both ends. By separating them, you can alter one part, then put the synapse back together and watch for an effect."

The reconstruction technique eventually may help explain the cause of human diseases that result when synaptic communication breaks down, Wilkinson says. "In many diseases it seems that the problem is either too little synaptic strength or too much. The treatment for those diseases would benefit if someone could understand what the mechanism is that is making these changes in synaptic strength occur."

Some forms of depression, for example, may develop when synapses in the brain that respond to serotonin, a neurotransmitter, are too weak. The disease is frequently treated by giving patients the drug Prozac, which helps to prolong the life of naturally occurring serotonin in the brain. The neurological disorder Parkinson's disease results when brain synapses don't receive enough dopamine, another neurotransmitter. Currently, Parkinson's symptoms of slow movement, tremors and unsteady balance are treated by administering synthetic forms of dopamine in an effort to force-feed it to receptors in the brain.

And some muscle diseases and heart conditions can occur when nerve-muscle synapses are too strong.

"It is not always known in neurological diseases whether the problem is presynaptic or postsynaptic. If we can understand how and where the strength of the synapse is being regulated, then we might come up with ways of intervening that might address the problem more directly," Wilkinson says.

Like many discoveries, the reconstruction technique raises new questions even as it provides new answers. One question involves the extremely precise alignment that exists between a nerve and its target cell. In a synapse's normal state, it is densely packed with intricate structures that seem to be arranged systematically. For example, neurotransmitter receptors on the muscle cell surface sit bunched in groups exactly opposite the nerve's active zones, the spots where neurotransmitter is released. The very fact that reconstructed synapses work raises questions about the need for such precise alignment, Wilkinson says.

"It's virtually impossible that we managed to realign all those structures. So that either means that they naturally realign themselves, or that the purpose of that alignment is not rudimentary to basic synaptic function but has some other, more subtle role." Time and further investigations will tell, but with Wilkinson's evolving technique at the disposal of researchers, the mysteries of the synapse should begin to unfold more rapidly.
A year ago, Nedra Meiller struggled for nearly every breath. Simple tasks like taking a shower and making the bed had become arduous chores, requiring frequent rests.

Meiller's world was her home, except for doctor's visits; she could no longer go grocery shopping or walk to the mailbox. And she relied on a wheelchair to get to and from the car, which her husband drove. "I felt like I was suffocating," Meiller says. "The only time I could breathe was when I was sitting down, doing nothing."
Emphysema, with which Meiller had lived for 25 years, had taken hold of her lungs. At 58, suicide had become more than a fleeting thought, Meiller recalls. "I became so depressed because I couldn't do anything," she says. "I no longer felt like a wife or a mother. I wondered why I should go on. I wasn't living; I was existing."

But eight months after undergoing a new surgical procedure developed by lung transplant surgeon Joel D. Cooper, M.D., Meiller says there is virtually nothing she can't do.

During the operation, Cooper, professor of surgery, removed damaged portions of Meiller's enlarged lungs. Decreasing the overall size of emphysema patients' lungs literally gives the lungs more "breathing room," Cooper says.

"I can't believe the difference," says Meiller. "I'm a new person. I have more energy now than I've had in years."

Meiller now manages her St. Louis home with ease. She no longer stops to catch her breath while gardening, cooking or vacuuming. Her daily routine includes riding an exercise bike or walking on a treadmill for 30 minutes. For the first time in several years, Meiller has planted a garden.

She is one of the first 20 emphysema patients to undergo the procedure that dramatically improves lung function and helps patients breathe more easily.

For the first time in years, Nedra Meiller has been able to plant a garden. Innovative surgery lifted the burden of her emphysema.

"So far, we've seen an average improvement of 82 percent in patients' breathing capacity," says Cooper, who performed the first procedure in January 1993 at Barnes Hospital. "For these severely disabled patients, this translates into a marked improvement in the quality of their lives."

During the surgery, Cooper removes 20 to 30 percent of each lung — the most severely damaged areas. Within six months of their surgery, patients were able to resume many of the activities they had avoided for years. In the future, the surgery may be the treatment of choice for some patients with severe, debilitating emphysema who have failed to respond to medication, respiratory care and other medical therapy.

The Disease

Emphysema, most often caused by cigarette smoking, afflicts an estimated 1.6 million Americans. The previously irreversible disease causes the lung's tiny air sacs to over-inflate, damaging their ability to expand and relax as a person breathes. Therefore, less oxygen gets into the blood stream, and, to compensate, the lungs gradually enlarge until they fill the chest cavity and flatten the diaphragm, a muscle critical to breathing.
Ultimately, each breath becomes a chore.

As the disease advances, emphysema patients grow weaker. At first, they experience only slight shortness of breath, but gradually they may become incapable of minor physical activity. Some patients eventually become dependent upon supplemental oxygen even while resting.

"Emphysema is like breathing in as far as you can and having to live with your chest in that position for the rest of your life," Cooper says. "That's what progressively happens to these patients — their lungs are fully expanded and they can barely breathe."

"Until now, lung transplants offered the only substantial relief for patients with end-stage emphysema. But transplants — which subject patients to a lifetime regimen of anti-rejection drugs — are risky and used only as a last resort. Moreover, the supply of donor lungs is far short of the demand. As a result, not all suitable lung transplant candidates can get onto a transplant waiting list; some patients on the list die during the long wait for a suitable donor.

The concept of reducing the size of emphysema patients' lungs to help them breathe more easily is not new. It was first proposed some 40 years ago by the late Otto Brantigan, M.D., a surgeon at the University of Maryland in Baltimore. Cooper learned of Brantigan's work six years ago from a colleague in Quebec.

In the 1950s, Brantigan operated on 30 emphysema patients to remove damaged lung tissue. About one in six of the patients died following surgery, Cooper says, but 75 percent of the survivors claimed they felt better. Leading surgeons, however, dismissed the procedure, because Brantigan lacked any objective data to demonstrate that patients could breathe more easily following surgery.

Cooper's pioneering experience with lung transplants — he is credited with performing the world's first successful single- and double-lung transplants — led him to think that Brantigan may have had a good idea.

Immediately following a lung transplant, an emphysema patient's over-extended rib cage and flattened diaphragm return to a more normal configuration, Cooper observed.

While examining emphysema patients' lungs removed during transplantation, Cooper also noted that the severity of the disease varied throughout the lung. Removing the most damaged portions of emphysema patients' lungs could improve overall lung function, he reasoned.

"That gave credence to the notion proposed by Brantigan — that if you can improve the ventilation of patients with severe emphysema, you can improve lung function and relieve their shortness of breath," Cooper says.

Initially, Cooper offered the procedure only to emphysema patients who were too old or otherwise not suited for a lung transplant. After the procedure's early success, he expanded the criteria to include some emphysema patients who would otherwise qualify for a lung transplant. Only those who had given up smoking entirely were considered for the surgery. Patients who underwent the surgery ranged in age from 37 to 76 years (mean age of 56); 11 patients were male and nine were female.

All patients underwent a six-week lung rehabilitation program before surgery to improve their physical health and stamina, which helps to reduce complications afterward. The program includes walking on a treadmill or riding an exercise bike three to five times a week.

The Treatment

In surgery that takes two to three hours, Cooper and his team begin by ventilating both lungs. Then, working on one lung at a time, ventilation of one of the lungs is stopped. Without oxygen, the more normal portions of the lung collapse, while the severely damaged areas remain inflated. Cooper then removes the inflated areas. The procedure then is carried out on the other lung.

Initially, the procedure was complicated by multiple small air leaks in the lungs following surgery. The staples used to seal off the lungs leave small holes in the fragile lung tissue. Cooper solved the problem by using thin strips of tissue to buttress the staple line. The tissue is obtained from the strong, leathery pericardium of cows. The bovine
The enlarged and distended lungs of an emphysema patient before surgery, left, push against the chest wall and flatten the diaphragm, making it difficult to breathe. After surgery, the smaller lungs allow the patient more room to breathe; the chest returns to a more normal size, and the diaphragm resumes its curved shape.

tissue has helped to reduce the average hospital stay from 20 days to 13 days.

Cooper cautions that the surgery does not cure emphysema. “These individuals may continue to experience deterioration from emphysema, but if we can reset the clock by two, three, four or five years, maybe more, then we think it will be very worthwhile,” he says.

So far, results have been dramatic. James Henry, 77, of Clarendon AR, the first patient to undergo the procedure, now plays golf at least three times a week and rides an exercise bicycle every day.

Before the surgery, Henry recalls, “Everything I did was an effort. I could not walk 25 yards to carry the trash to the curb without stopping to sit down. But now, my quality of life is 100 percent.”

Bonnie Gillmore, 49, of Plainville MA, was diagnosed with emphysema 15 years ago. She says the surgery has given her a new life.

“Before the surgery, I had to keep my hair short because lifting my hands overhead to wash my hair was exhausting,” says Gillmore, whose emphysema was so severe she had to quit her job as a computer software engineer. “Walking down the block to pick up a newspaper was a major event. Now, I’m doing things I haven’t done in 15 years,” she says. “This operation has definitely given me back my life.”

Of the first 20 patients to undergo the procedure, 14 required supplemental oxygen during exercise or strenuous activities, including five who also required oxygen at rest. Three months following surgery, only two patients need supplemental oxygen during vigorous exercise; one patient requires oxygen at rest.

“Frankly, I hadn’t anticipated that so many of these patients would be able to discontinue oxygen,” Cooper says. “It was a pleasant surprise.”

While it is too early to determine the long-term effects of the operation, for most patients whose follow-up period has reached six months, lung function has continued to improve. Cooper has measured patient improvement objectively with breathing and exercise tests and subjectively using standard evaluations of quality of life. Consistently, patients report a significant improvement in their energy level and physical mobility and a reduction in health problems related to their job, housework, social life and hobbies following surgery.

Cooper attributes the success of the surgery to the skilled surgeons, anesthesiologists, respiratory therapists and nurses who all have extensive experience working with lung transplant patients. He predicts that thousands of emphysema patients will undergo the procedure as hospitals assemble skilled surgical and support teams.

Word of the new procedure has spread since Cooper presented his preliminary results in April at the American Association for Thoracic Surgery’s annual meeting. His office has fielded nearly 1,000 phone calls from patients around the country wanting to learn more.

If the early success of the surgery translates into a long-term benefit for emphysema patients, the procedure may become an alternative to a lung transplant for some patients and a means to postpone transplantation for others.
Guiding Technology

In medical school laboratories and offices, only the telephone is as ubiquitous. Not even the microscope is as universally essential to research. Whether it's considered a godsend, an instrument of the devil or a little of both, the computer is indispensable, "an essential part of the work environment," according to David States, M.D., Ph.D., associate professor of biomedical computing. "Nearly 100 percent of the faculty use computers," States says.

Overseeing the Institute for Biomedical Computing (IBC), one of the dominant entities in the complex world of Washington University computing, States is charged with building a research and training program in computational and quantitative biology. He says his group is "a catalyst and an incubator for new technologies, asking the question 'What are the possibilities?'" from the perspective of the computer as research tool.
The IBC is an autonomous unit within the University, with few counterparts at other schools. It differs from a traditional department in its approach: Instead of a group of scientists with much the same interest working together, the institute integrates large, interdisciplinary teams of engineers, computer scientists, programmers, optical specialists and biomedical investigators.

A joint program of the schools of medicine and engineering, the 10-year-old institute — which had its beginnings 30 years ago — recently gained degree-granting powers and will be training a new generation of students interested in the conjunction of computing, medical science and engineering. Master's and D.Sc. degrees will be awarded in biomedical engineering.

Demand for graduates should be strong, because the volume of data with which scientific research is concerned and the complexity of the questions being asked require the creative application of more powerful computers. No longer is it possible for the mind alone to encompass the investigational landscape.

David States, M.D., Ph.D.

— one arm of the IBC — is an example. Collaborating with geneticists to decipher and map the human genome and the genomes of other organisms, States manages data. “There is a common ground in these genome projects’ needs for computing,” he says.

Surprisingly, in a computer scientist’s terms, the actual volume of data is not large. “The entire human genome is the equivalent of about three minutes of digital television,” he says. The need for advanced computing lies not in the size of the data set, but in the ways in which access to it must be provided.

“In genome sequencing, one experiment gets you a short run of perhaps 400 base pairs,” States says. “And the data are fairly noisy — about two percent will be wrong. The chromosome you want to look at is tens of megabases long. The computer is essential in getting to the view that you need.” The computer also adds accuracy, because “humans would make too many errors copying just 10 pages of the four letters G, C, T and A.”

Further, the computer makes understanding the recipe conceivable. “Once you get the sequence, it’s still
just a long string of letters. The computer is the only way to answer the question of whether there is another gene that looks like one you know. The computer examines a DNA sequence, searching it against all known proteins. Using similarities, not identities, you can find genes," he explains, "you can get to usefulness."

Arriving at a useful view of the data is a theme that typifies the endeavors of all of the principals of the IBC. Lewis Thomas, M.D., originally an anesthesiologist with appointments in several departments but working primarily as professor of biomedical computing, directs the Biomedical Computer Laboratory (BCL), another of the institute's components.

Initially involved in the development of computer hardware, software and the training of biomedical scientists in computer literacy, BCL now focuses more directly on helping biological investigators apply computing to their research. "You can no longer do science on the back of an envelope," Thomas says. In fact, he believes that in many instances "the technology leads the research." By that he means that the availability of computing power makes it possible to ask scientific questions that previously were inconceivable.

Recently, Thomas noticed the similarities in computing needs between PET data interpretation (for which BCL already had developed sophisticated algorithms) and research using electron microscopic autoradiography. By applying computational methods developed for PET image analysis to the autoradiography project, statistically significant results were achieved where none had been possible before.

"We ask three questions: 'What ought to be computed?' 'Is it practical to compute?' and 'Can we reformulate an algorithm or apply advanced computing technologies to make it practical?"' Thomas says. The goal is to find ways to derive the desired quantitative information from the acquired data.

Much of that work is image-related, the "extraction and quantitative analysis of biomedical images." For example, Thomas explains, the image shown by a conventional microscope is contaminated by light from the specimen both above and below the plane of interest, by aberrations in the optical system and even by the image-collating camera. But if you know the "blur factor," you can remove corruption of the image data computationally and go on to compute an accurate estimate of the light from all of the planes in the specimen. The result: a reconstructed three-dimensional image.

Such images bring important analytical powers to investigators. But producing them requires sophisticated computing that it would not make sense for biomedical researchers to spend the time to master. It also requires great computing power; adding the third dimension to a single image might increase the size of a data-set a thousand-fold.

Pushing those boundaries is Thomas' goal. "The theoretical limits the practical," he says. "At the BCL, we deal with the practical issues of computing and how to remove the current bounds, with the availability of solutions and with the matching of capabilities to problems."

In the Center for Molecular Design, Garland Marshall, Ph.D., also forces back the boundaries. "Always work on a problem you don't know how to solve," he advises. "By the time you figure out how to do the problem, the (computing) power to do it will be there."

Marshall's work involves the computer-

Under the direction of Lewis Thomas, the computer provides usable information (left) from raw data that appeared as nothing more than a blur when collected (right).
aided design of molecules "that do what we want them to." His group employs computers to calculate the properties of molecules — their shapes, their ability to cross membranes, their affinity for their targets — for specific tasks. The computer also is provided with the parameters of the chemistry that the scientist is willing to do, so that no impossibly complicated molecules are suggested. The next step, says Marshall, professor of biomedical computing and of molecular biology and pharmacology, is to add the power to select which of the possible molecules will be most effective at performing the designated task. Already, the computer allows the simulation of a molecule's response to the forces of nature. By controlling time, the computer can model changes that may be too fleeting to observe experimentally.

Of the potential for the process, Marshall says the investigations may lead to the design of compounds that block the action of particular enzymes. If a molecule can be made to fit perfectly into receptors on the surface of a target enzyme, the enzyme will be rendered ineffective. Such an enzyme is HIV protease, essential to the life cycle of Human Immunodeficiency Virus. Creation of a molecule to render HIV protease neutral could produce immeasurable benefits. Such molecules are currently being tested in the clinic.

"The old way of finding such compounds was akin to the story of the monkeys at the typewriters," Marshall says. "Once you isolated the target, you tried all sorts of compounds against it. When something worked, you tested it against the virus. We make that process more rational by beginning with the molecular structure of the target."

Marshall's efforts aim clearly at clinical application, and part of the IBC's charge is clinical relevance. Most immediately applicable may be the work of Michael Kahn, M.D., Ph.D., and the Medical Informatics Group, specialists in the decision-making aspects of data.

Kahn recently accepted an appointment in the BJC Health System as director of advanced clinical information systems. His task is to build a computer network across the entire health system, including outlying hospitals and the medical school.

Corporate partners are assisting with fiber optics, high-speed telephone lines and networking. But Kahn, assistant professor of biomedical computing and of medicine, hopes that the huge scope of the project will attract biomedical engineering students to the program and fill the mandate for the IBC to be clinically active.

As the medical school and its investigations move into a world of ever more data, the IBC facilitates the kind of deep rethinking that the computer sometimes demands. David States offers this example: "When we first evaluated computer monitors and compared them to X-ray film, we worried that very expensive, high-resolution monitors would be required to meet radiologists' needs. But X-ray film is not color, and it's not three-dimensional. Those two elements — which the computer can supply — provide more information and more natural information, even in low resolution. The task is always to see the new technology next to the old and to aid in the transition."
A SYSTEMATIC APPROACH

Designing A Hemoglobin For Artificial Blood

by Jim Keeley

AIDS and other blood-borne viruses, the daily drain on blood supplies and mass casualty and disaster situations create a dire need for a usable synthetic blood substitute. In the hope of filling that need, pharmaceutical companies expend huge research efforts, aiming to tap a market estimated conservatively at $3 billion a year from hospitals, blood banks and the military. But so far, results have been less than spectacular. No suitable blood substitute is available now.
From the computer screen, a hemoglobin molecule shows its 574 amino acids in four subunits. Sites of naturally occurring mutations that have a large effect on regulating the oxygen-binding capabilities of the molecule are represented in yellow.
Those blood substitutes that have progressed to human tests have failed to duplicate all of the things natural blood does for the human body. Part of the problem, says Gary K. Ackers, Ph.D., Wittcoff Professor and head of the Department of Biochemistry and Molecular Biophysics, is that industry's approaches to this problem have been "hit or miss." They may begin with a reasonable idea, he says, but soon they suffer because not enough basic knowledge exists about two of blood's key components: red blood cells and hemoglobin, the oxygen-carrying protein inside red blood cells.

Researchers have been studying hemoglobin for more than 30 years, and significant discoveries have been made. Hemoglobin has been a prototype for structural and functional studies of proteins, and models of hemoglobin function are found in most biochemistry textbooks. There has been a sense in the biochemistry community that hemoglobin is a puzzle that has been solved, says Ackers' colleague Jo Holt, Ph.D., research assistant professor of biochemistry and molecular biophysics. "Many textbooks have conveyed the impression that hemoglobin is fundamentally understood."

Ackers and his research team at the School of Medicine believe that "the molecule is still laughing at us," he says. And if hemoglobin didn't have any secrets to yield, there might be a blood substitute available right now, he adds.

Ackers uses the image of the oxygen carrier as a finely-tuned Ferrari, cruising as easily through main arteries as it does through narrow, peripheral thoroughfares. "The best way to think of hemoglobin is as a tiny machine inside your body," he says. "It carries out processes that make it change its shape, breaking chemical bonds, and moves things from one place to another. It is able to do all these things in a highly specific and focused way. It's a very smart molecule."

Perhaps too smart. Until now, what's been missing from the effort to design a usable blood substitute is a rational, systematic approach to understanding the nature of hemoglobin's innate "intelligence." Ackers' research program recently received an infusion of $7.5 million from the National Heart, Lung and Blood Institute (NHLBI) as a program within red blood cells. "We are trying to define how hemoglobin works at the level required for a rational redesign of hemoglobin," Ackers says.

A Naval Research Advisory Committee (NRAC) formed to evaluate the progress of artificial blood development recently issued its report. One conclusion: Progress "appears to be stalled because of a lack of pertinent fundamental knowledge." The NRAC report concluded that for an effective blood substitute to arise, there must be a rational, systematic understanding of the science behind the materials.

The NHLBI must have been listening, because Ackers' charge is to provide that missing knowledge by networking a group of outstanding scientists who have complementary areas of expertise. The science is lacking in two areas, Ackers says: "One is in the understanding of the hemoglobin molecule itself. The other is knowing what hemoglobin 'sees' when it gets into the circulation."

While the temptation to steer the program project toward more "practical" purposes may exist, Ackers believes that is what has sabotaged previous efforts. Wary of being sidetracked, he says that the group's interest is not commercial. "I think it would be great if we produced something useful in the clinical sense, but we are here to do basic research...to develop a long-term knowledge base. We are really trying to force the molecule to reveal its secrets," he says. "It's basically a contest between us and the molecule. The molecule would like to keep its secrets, and we would like to force it to give up its secrets."

The success of the plan hinges on an array of sophisticated tools ranging from site-directed mutagenesis and X-ray crystallography to spectroscopy and enzyme kinetics. Each center involved in the program project grant specializes in using at least one of the tools. The...
Hemoglobin is an ancient protein. It is the principal oxygen-carrying molecule in nearly all mammals, as well as fish, birds and invertebrates. In humans, the molecule is constructed of 574 amino acid building blocks linked in four linear chains. Fortunately for us, but unfortunately for Ackers and his fellow scientists, nature has twisted those four chains into a tightly packed ball that allows for easy packaging inside red blood cells. Each red cell contains 280 million hemoglobin molecules. It's a tight fit, but with room enough for each protein to seat four oxygen atoms as it passes through the lungs on the road to oxygenating peripheral organs and tissues.

The four chains, or subunits, consist of two types, designated α and β. The tetramer, which is the functional form of the molecule, can be split into two dimers, each composed of one alpha and one beta subunit. Each subunit plays a vital role in determining hemoglobin's function as an oxygen carrier, as well as how it interacts with carbon dioxide, nitric oxide, organic phosphates and other chemicals it might encounter during its 120-day tour of duty in the body.

Ackers' team recently made a major contribution to understanding how hemoglobin works by decoding the rule that dictates how the subunits communicate with each other. This rule controls hemoglobin's ability to bind and transport oxygen.

It has been known that hemoglobin cycles between two structural forms, one that binds oxygen avidly and another that is less inclined to bind oxygen. The "symmetry rule," as it is called, states that when hemoglobin binds oxygen it changes its affinity for oxygen depending upon how many oxygen molecules are already bound by the protein. Hemoglobin changes its affinity for oxygen by changing its structure. "The symmetry rule is that if you bind oxygen on one dimer, it stays in the less avid orientation," Ackers says. "But if you bind any additional oxygen on the other dimer, the protein changes shape and becomes more interested in binding oxygen."

Ackers would like to see a structural understanding of the symmetry rule mechanism emerge from the program project grant. Researchers can't predict from computer modeling studies how a change in an amino acid will affect hemoglobin, says Holt. But the symmetry rule provides a good idea of the critical areas of focus in mutation studies. Ackers' article describing the symmetry rule was recently cited by the Journal of NIH Research as one of the most important papers representing advances in biophysics of the last 15 years.

Many insights have been gained by studying mutant human hemoglobins. Some of the most serious hemoglobin mutations cause sickle cell disease or thalassemia. But many others may go unstudied, because the mutation is not serious enough to cause the carrier to visit a research hospital where the mutation would be noted, characterized and distributed to investigators. Ackers has studied nearly 60 natural mutants, many of them the product of random genetic "noise," he says. All told, about 500 mutations are available for study.

With the revolution in molecular biology, scientists have been able to "speed up" evolution by creating recombinant mutant hemoglobins. The program project grant has allowed the creation of a recombinant core center that will produce a new mutant hemoglobin every two to three weeks.

These mutants also should prove more informative, because researchers can pinpoint which amino acid they want to change and make a substitution or a deletion. Once a new mutant is created, it will be distributed to the various centers that will put it through a battery of tests. One group will study its structure by bombarding it with X-rays to produce a molecular picture of the new hemoglobin. Ackers' team will perform the protein equivalent of a stress test, measuring how well the mutants bind oxygen and interact with a wide range of physiological chemicals.

The goal is to modify all of the amino acids in hemoglobin that have not been modified previously. The initial phase will be carried out on about 30 amino acid residues in the protein that are not well understood. "We are going to create new mutant hemoglobins in which every one of those sites is altered one at a time, and some of them two or three at a time."

If natural hemoglobin refuses to yield its secrets, then perhaps the mutants will have something to tell. Ackers believes it's worth a try. He says, "Although much has been learned, hemoglobin has been laughing at us for the last three decades. It's time things changed."
**Match Day 1994**

On March 16 — Match Day — results of the national residency matching program became known, and 66 of the 95 (fully 70 percent) members of the medical school Class of 1994 who took part received residency positions at their first choice of institution. Eighty-eight percent matched one of their top three choices. Both numbers are up dramatically from last year's figures of 56 percent and 82 percent, respectively.

Eighteen students found positions independent of the matching program or decided not to take residencies immediately. The primary care specialties of pediatrics, internal medicine and family practice captured the interest of 45 members of the class. Thirteen will go on in diagnostic radiology, and nine graduates will pursue Ob-Gyn.

Thirty-one of the new physicians will remain in St. Louis to do their residencies, with 29 of them at Washington University or affiliated institutions. Other popular destinations in 1994 were the State of California (8), Chicago (7) and Philadelphia (7).

### ARKANSAS

Little Rock
University of Arkansas
Radiology
Ramesh Avva

### CALIFORNIA

Bakersfield
Kern Medical Center
Surgery
Daniel R. Reichner

Irvine
Univ. of California - Irvine
Anesthesiology
Peter C. Jeng
Radiation Oncology
Steve J. DaMore

Los Angeles
Univ. of California - Los Angeles
Psychiatry
Leanne M. McBurney

### COLORADO

Denver
Univ. of Colorado School of Med.
Internal Medicine
Arlina Ahluwalia
Pediatrics
Carol R. Okada

### CONNECTICUT

New Haven
Yale - New Haven
Pediatrics
Ruth A. Choate

### DISTRICT OF COLUMBIA

Washington
Georgetown University
Internal Medicine
Ali R. Hamzei
Paul B. Keiser
Walter Reed
Surgery
Steven B. Cersovsky

### FLORIDA

Gainesville
Univ. of Florida - Shands Hospital
Internal Medicine
Nelida Sjak-Shie

### GEORGIA

Fort Gordon
D. Eisenhower Medical Center
Internal Medicine
Robert E. Burke

### ILLINOIS

Chicago
Loyola University Medical Center
Ob-Gyn
Martina F. Mutone
McGaw Medical Center
Internal Medicine
Ankit A. Shah
Thomas Devine
Ob-Gyn
Stephanie B. Cox
Orthopedic Surgery
Afshin Amimian
Brian J. Hartigan
University of Chicago
Internal Medicine
Michael D. Waldman

### INDIANA

Indianapolis
Indiana University Medical Center
Radiology
Te-Chung Hsu

### IOWA

Iowa City
University of Iowa Hospital
Urology
James C. Austin

### KENTUCKY

Louisville
University of Louisville
Surgery
Brett J. Guinn

### MARYLAND

Baltimore
Johns Hopkins
Internal Medicine
Lee M. Krug
Plastic Surgery
John A. Girotto
Psychiatry
Harmandeep Makkar
Radiology
Nicholas Franano
Fourth-year students Marc Boustany, Marc Bodenheimer and Kim Allman (L to R) share the excitement of Match Day as they discover where their medical training will continue.

MASSACHUSETTS
Belmont
McLean Hospital
Psychiatry
Stephen J. Steiner
Boston
Brigham & Womans Hospital
Internal Medicine
Thomas Niederman
Radiology
Lee Fox
Springfield
Baystate Medical Center
Radiology
Lorenz H. Schielke

Linda Lu
Ophthalmology
Kathy Lee
Scott M. Pinter

MINNESOTA
Duluth
Duluth Graduate Medical Program
Family Practice
Corina Jo Norrbom
Jennifer L. Paterson
Minneapolis
Hennepin County Medical Center
Transitional
Sebastian F. Cherian

Scott D. Groesch
Tricia V. Pavlopaoulos
Laboratory Medicine
Thomas Wilson
Ob-Gyn
Bernadette D. Bernardo
Gregory Joslin
Molly E. Klein
Timothy C. Philpott
Oncology
Mary Lynn Vest
Psychiatry
Darrin S. Friesen
Radiology
John B. Carico
John Neil
Myeong S. Yoon
Robert P. Guillerman
Surgery
Stephen M. Dodge
Surgery-Preliminary
Christopher E. Smith
John Jensen
Matthew G. Mutch

MICHIGAN
Ann Arbor
University of Michigan
Internal Medicine
Arvin S. Gill

MISSOURI
St. Louis
Barnes Hospital
Internal Medicine
Dana A. Hill
Mark A. Steiner

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St. John's Mercy
Family Practice
Charles M. Kodner
St. Louis Children's
Pediatrics
Amy M. Poole
Brad Schlagger
David Rudnick
Luke A. Bruns
Jackie Hoffman
Joseph H. Marceny
Rebecca Green
Victoria Fite Akins
St. Louis University
Surgery
Evon R. Kokoska
Washington University
Neurology
Tom Carmichael
Otolaryngology
Paul Sun

NEW MEXICO
Albuquerque
University of New Mexico
Orthopedic Surgery
Gregory E. Kenyherz
Radiology
Danica C. Holt

NEW YORK
Syracuse
SUNY Health Center
Surgery
Marc K. Boustany

NORTH CAROLINA
Chapel Hill
University of North Carolina
Pediatrics
Brian H. Cassidy
Durham
Duke University
Internal Medicine
Li Kuo Kong
Richard S. Bloomfeld
William Mariecheck

OHIO
Cincinnati
University of Cincinnati
Emergency Medicine
Marianne Ingels

OREGON
Portland
Oregon Health Science Center
Internal Medicine
Andrew P. Cott

Pennsylvania
Philadelphia
Hospital of Univ. of Pennsylvania
Internal Medicine
David Whellan
Internal Medicine-Preliminary
Darrell Kotton
Ob-Gyn
Catherine S. Bradley
Orthopedic Surgery
Steven Y. Wei
Pathology
Vivian Vanderlinc
Presbyterian Medical Center
Transitional
Mehryar M. Sadeghi
University of Pennsylvania
Otolaryngology
David M. Miller

RHODE ISLAND
Providence
Brown University
Neurological Surgery
Armond L. Levy

TENNESSEE
Chattanooga
University of Tennessee
Ophthalmology
Marc A. Bodenheimer
Memphis
Methodist Hospital
Radiology
Michael J. Raney
Vanderbilt University
Internal Medicine
Brian S. Wagoner

TEXAS
Dallas
Univ. of Texas SW Medical Center
Internal Medicine
Ray J. Lee

Surgery
Mathias J. Kill
Galveston
University of Texas-Galveston
Surgery-Preliminary
Arjav Shah

Houston
Baylor College of Medicine
Physical Med. & Rehabilitation
Susan V. Garstang
Radiology
Joseph Chan
University of Texas
Ophthalmology
Brenda Myers-Powell
San Antonio
Lackland Air Force Base
Internal Medicine
Stephen C. Wissink

WASHINGTON
Seattle
University of Washington
Internal Medicine
Nicholas C. Hunt
Otolaryngology
Donald G. Farwell
Urology
Elizabeth A. Miller

WISCONSIN
Madison
Medical College of Wisconsin
Ob-Gyn
Robert D. Southwick
University of Wisconsin
Radiology
Paul Ho

Dermatology Residencies
(Matched in the Fall)
Craig C. Miller
Maria Mariecheck
Alan Pitt

Research Fellowship
Gregory Krause
Eight Honored With Awards

Alumni Achievement Awards

Samuel P. Bessman, M.D. '44, is professor emeritus of pharmacology, nutrition and pediatrics at the University of Southern California School of Medicine. He introduced chelation therapy, the treatment of choice for lead poisoning, and he has made theoretical contributions resulting in improvements in clinical care.

A. Martin Lerner, M.D. '54, is clinical professor of internal medicine at Wayne State University School of Medicine in Detroit. He was chief of the division of infectious diseases there for 19 years and is known for the quality and quantity of his work in infectious diseases.

Raymond G. Schultze, M.D. '59, is director of the University of California at Los Angeles Medical Center and professor of medicine there. As director, he has responsibility for reconciling the requirements of patient care, education and research at one of the largest and most diverse academic medical centers in the nation.

Alumni/Faculty Awards

Benjamin Milder, M.D. '39, is professor of clinical ophthalmology. He is a nationally recognized authority on optics and refraction, with a private practice dating to 1944. Through the years, he has spent many hours training residents at the medical center.

Robert C. Drews, M.D. '55, is professor of clinical ophthalmology and has been in private practice since 1955. He is internationally recognized for his work in lens implantation and cataract surgery and is known for his surgical skill, his dedication to the education of residents and for pioneering computer technology in ophthalmology practice.

Stuart Weiss, M.D. '54, is professor of clinical neurology and maintains a private practice. He is an outstanding teacher of clinical neurology and a staunch supporter of the medical school and its activities. Highly respected by the residents he trains, he has been named "One of the Best Medical Specialists in the U.S."

Distinguished Service Awards

Paul E. Lacy, M.D., Ph.D., is Robert L. Kroc Professor of Pathology at the School of Medicine after serving for 24 years as chairman of the Department of Pathology. During his distinguished career, he has dedicated himself to research on diabetes mellitus, and his achievements have brought him international acclaim. In recent years, he has focused on the development of an insulin-producing islet cell transplant.

Oliver H. Lowry, Ph.D., M.D., is Distinguished Professor Emeritus of Molecular Biology and Pharmacology at the School of Medicine. He has been devoted to the school and has served it in a number of roles since 1947, including 29 years as head of the Department of Pharmacology. His research is applicable to almost any disease at the biochemical level, and medical scientists from many fields seek him out to learn his methodology.
John Sheridan, M.D. '69, reunion social chair, Class of '69, with Barry Siegel, M.D. '69, WUMCAA president and reunion class gift drive co-chair.

Prinny Proud and Robert Shank, M.D. '39, in conversation at their class dinner.

Jonathan Mann, M.D. '74, converses with classmate Wilfred Anderson, M.D. '74.

Virgil Loeb, Jr., M.D. '44, welcomes the Class of '94 into WUMCAA at the awards banquet. Loeb served as reunion social and gift chair, Class of '44.

At their class dinner, Joseph Kent, M.D. '84, Carolyn Cuvant and Howard Rowley, M.D. '84.
C. Garrison Fathman, M.D. ‘69, reunion class gift drive co-chair, challenges the Class of ‘70 to meet or exceed the amount given by this year’s 25th reunion class.

Paul E. Lacy, M.D., Ph.D., conducts a tour of the Barnes Hospital Islet Processing Laboratory for (L to R) C. Stuart Exon, M.D. ’44; Albert Bullock, M.D. ’44; Edward Elder, M.D. ’49; Lewis Wesselius, M.D. ’49 and Donna Wesselius.

Phillip Horwitz, Class of ‘95, with Catherine Sands Bradley, M.D. ’94.

Outgoing WUMCAA president Barry Siegel, M.D. ‘69, presents the gavel to David Ortbals, M.D. ‘70, incoming president.

Jean Rogier, M.D. ‘34, assists Verna Rogier with her name tag.
Laurens White, M.D. '49; Cooper Ray, M.D. '54 and Shirley Peterson, M.D. '49, greet a fellow reunion-goer.

Charles Kilo, M.D. '59, reunion gift co-chair for the Class of '59, talks with Charles Nordland, M.D. '59, reunion social chair for the Class of '59.

Darrell Kotton, M.D. '94, class president, responds to the welcome of his class into WUMCAA.

William A. Peck, M.D., executive vice chancellor and dean, presents the Alumni Achievement Award to Raymond Schultze, M.D. '59.

Wesley Fee, M.D. '44, and Ira Pollock, M.D. '44.

Allan McCown, M.D. '64, Sunny McCown, Paula Palmer and Robert Palmer, M.D. '64.
Milo Tedstrom, M.D. '24, is recognized on the 70th anniversary of his graduation from the School of Medicine. Responding enthusiastically are his daughter, Jeanne Dennis and Jean Rogier, M.D. '34.

Ruth Moenster receives an honorary membership in WUMCAA in recognition of 23 years as a member of the medical alumni office. Doing the honors is Barry Siegel, M.D. '69, WUMCAA president.

Sidney Smith, M.D. '49 and Herluf Lund, M.D. '49, serve themselves at the dean's luncheon.

Greg Farwell, M.D. '94 and Brian Cassidy, M.D. '94, representing this year's class.

Robert Kolodny, M.D. '69, reunion class gift drive co-chair, with Nancy Kolodny and Marilyn Siegel, M.D.

Milo Tedstrom, M.D. '24, is recognized on the 70th anniversary of his graduation from the School of Medicine. Responding enthusiastically are his daughter, Jeanne Dennis and Jean Rogier, M.D. '34.
Helen Aff-Drum, M.D. '34, relaxes with Ralph Berg, M.D. '34.

Margaret Kitchell, M.D. '74, Christine Osteen and Jon Blackman, M.D. '74.

Robert Leyse, M.D. '54, greets Gerald Behrens, M.D. '54, reunion social chair, Class of '54.

Edward Elder, M.D. '49; Paul Roesler, M.D. '49 and Robert Lyle, M.D. '49 renew acquaintances at the welcoming cocktail party.

Albert Rhoton, M.D. '59 and Joyce Rhoton with Paul DeBruine, M.D. '59 and Ruth DeBruine. The DeBruines sponsored a challenge for his class' gift effort.
Preparing to participate in commencement exercises, Amy M. Poole dons her mortarboard. In ceremonies held on the Hilltop Campus on May 20, the School of Medicine conferred 95 M.D. degrees, eight M.D./Ph.D. degrees and seven M.D./M.A. degrees.
Work continues on research facilities under construction at the medical school. Structural steel is going up for the new seven-story East McDonnell Sciences Facility (top, left). The 127,260-square-foot structure stands adjacent to the existing McDonnell Medical Sciences building to which it will be linked by an underground tunnel currently being excavated. The building should be completed by September 1995. Footings and foundations have been poured for the new 10-story North Tower Research Addition adjacent to the Clinical Sciences Research Building (top, right). The new 223,250-square-foot tower is scheduled for February 1996 completion. The 70,000-square-foot Imaging Center (bottom), being built to provide space for multidisciplinary studies using magnetic resonance and positron emission tomography, is an extension of the Mallinckrodt Institute of Radiology and the School of Medicine’s East Building at 4525 Scott Avenue. Completion is expected in October 1994.