Bob Morrison, animal handler of Busch Gardens Tampa Bay's 1995 Animal Tour, introduces “Shag,” a carpet python, to students at the Central Institute for the Deaf (CID). Carpet pythons, which are harmless, get their name from the distinct patterns on their backs that resemble oriental rugs. During the visit, CID students learned about animals with habitats in Africa, Brazil, Australia and the United States.
THE COVER

On Oct. 6, Mark S. Wrighton, Ph.D., was installed as Washington University's 14th chancellor. Nearly 3,000 people attended the ceremony in Brookings Quadrangle and watched as former Chancellor William H. Danforth placed the golden medalion, a symbol of the Office of the Chancellor, around Wrighton's neck.

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A Pioneering Immunologist

EMIL R. Unanue, M.D., Edward Mallinckrodt Professor and head of the Department of Pathology, has won the 1995 Albert Lasker Basic Medical Research Award for his pioneering work demonstrating how immune cells recognize invading organisms in the body.

The award — one of medical science’s highest honors — recognizes scientists who have made significant contributions to biomedical research. Unanue was one of five immunologists to receive the award.

Unanue discovered, in the late 1960s, that immune cells called macrophages roam the body to seek out and ingest foreign proteins. Once inside the macrophage, the proteins are broken down into peptides, small fragments of proteins, that are displayed as “markers” on the cell surface of macrophages. As such, the peptides are clearly recognized by the immune system’s trigger cells, called helper T cells.

His findings were initially greeted with skepticism by scientists who believed that macrophages were scavenger cells that destroyed foreign proteins and that immune responses were only directed against whole proteins. The results stood, however, when other investigators replicated Unanue’s work.

Unanue later determined that the protein fragments bind to the major histocompatibility complex (MHC) — a multi-gene complex that regulates an individual’s genetic variability to disease — inside the macrophage and together they are displayed on the macrophage’s surface. In a landmark paper published in 1985 in the journal Nature, Unanue and Paul Allen, Ph.D., Robert L. Kroc Professor of Pathology, conclusively demonstrated that it is the MHC-protein fragment complex that activates the immune system’s T cells to initiate an immune response.

Previous Lasker Award winners affiliated with Washington University are: Edwin G. Krebs, M.D., Rita Levi-Montalcini, M.D., Stanley Cohen, Ph.D., Paul Berg, Ph.D., and Earl Sutherland, M.D. All five later went on to receive Nobel Prizes for their work.

Welgus Directs Dermatology

HOWARD G. Welgus, M.D., professor of medicine, has been named director of the division of dermatology at the School of Medicine and at Jewish Hospital.

Welgus succeeds Arthur Z. Eisen, M.D., the Winfred A. and Emma R. Showman Professor of Dermatology.

Welgus’ research focuses on metalloproteinases, enzymes that degrade connective tissues in the body. His work has helped to explain that metalloproteinases promote skin healing by allowing certain skin cells to migrate over wounds and form new skin. He and his colleagues also have shown that when these enzymes are produced in excess, they can prevent healing and lead to chronic skin ulcers by degrading newly formed tissue. Welgus has studied their role in skin cancer as well, finding that tumor cells use metalloproteinases to degrade tissue so that they can invade the skin and establish tumors.

Welgus collaborated with several other Washington University researchers to uncover the key role metalloproteinases play in causing smokers’ emphysema. He also is studying the role of these enzymes in destabilizing atherosclerotic plaques, which may contribute to heart attacks.

Rumbough Awardee

ALAN Permutt, M.D., professor of medicine, has received the 1995 David Rumbough Award from the International Juvenile Diabetes Foundation.

“The award from the Juvenile Diabetes Foundation is special for me,” says Permutt. “I have juvenile diabetes myself. But in addition, this is an organization that has lent a great deal of support to my research over the years. It’s nice to be recognized by a group that I’ve been a part of for so long.”

Permutt studies the genetic causes of diabetes. He found the first genetic marker for non-insulin-dependent diabetes, also called Type II diabetes. His lab has since identified several other genetic mutations responsible for various subtypes of non-insulin-dependent diabetes, and Permutt continues to search the entire genome to map genes responsible for diabetes. He has published more than 100 scientific articles on his research.

Permutt serves on the board of directors of the St. Louis Chapter of the Juvenile Diabetes Foundation and also serves on the Medical Science Advisory Board of the national organization.

The award was established by actress Dina Merrill in honor of her late son, David.
Schaffer Receives Wieland Prize

Jean E. Schaffer, M.D., assistant professor of medicine, has received the Heinrich Wieland Prize, an international award for outstanding research related to the biology of fats and lipids.

In 1994, Schaffer discovered the gene for a protein called FATP, which facilitates cells' ability to take up fatty acids. Fatty acids are vital nutrients stored as a potential energy source in fat tissue and used by heart muscle cells as a primary source of energy. FATP is embedded in the cell membrane of heart cells and fat cells.

During her training as a cardiologist, Schaffer became interested in the controversial subject of how heart muscle takes up fatty acids from the circulation. She suspected that the heart must have a mechanism for efficient uptake of this essential energy source. Schaffer identified FATP using sophisticated gene cloning methods. The discovery provides the first explanation of how the heart acquires enough fatty acids to meet its tremendous energy demands and of how the heart might control uptake of these fatty acids. Schaffer made her discovery as a postdoctoral research fellow in the laboratory of Harvey Lodish, Ph.D., at the Whitehead Institute for Biomedical Research in Cambridge MA. Her work was published in the journal Cell in 1994.

Schaffer joined the Washington University faculty in July as an assistant professor of medicine and of molecular biology and pharmacology. Prior to this appointment, she was an instructor in medicine at Harvard Medical School and a postdoctoral fellow at the Whitehead Institute.

Senior Merit Scholar

Robert Bane, a fourth-year medical student, has received the Senior Merit Scholarship for academic performance in the first three years of medical school. The scholarship has been provided by an anonymous donor.

Bane, 25, has been commended by faculty members for outstanding work in anatomy, human physiology, neuroscience and molecular biology. Among the awards he has received are the Carl F. and Gerty T. Cori Prize in Biochemistry, the Edmund V. Cowdry Prize in Histology, the McGraw-Hill Book Prize, the James O'Leary Neuroscience Prize, the Howard A. McCordock Book Prize in Pathology and the Lange Medical Publications Book Prize for outstanding performance in his second year of medical school. He has also been elected to Alpha Omega Alpha.

"I consider it a great honor to have received such a prestigious award and am very pleased with my educational experiences at Washington University," says Bane.

Bane, who plans a career in orthopaedic surgery, graduated summa cum laude from the University of Illinois, Urbana/Champaign, with a major in biology and a minor in chemistry. He is married to Amy Elizabeth Bane, a third-year medical student.

Powderly Shares Directorship

William G. Powderly, M.D., has been named co-director of the division of infectious diseases and chief of the division's clinical section.

Powderly, an associate professor of medicine, is principal investigator of Washington University's federally funded AIDS Clinical Trials Unit. He will share the directorship with Eric Brown, M.D., who oversees the division's research section. In his new role, Powderly will direct the division's clinical activities, including inpatient and outpatient clinics and clinical research involving AIDS, tuberculosis, sexually transmitted diseases and hospital-acquired infections.

Powderly's research focuses on testing new drugs for the treatment of AIDS and its life-threatening complications, including pneumocystis pneumonia, Kaposi's sarcoma and fungal infections. His studies have helped to improve the way physicians treat AIDS patients.

In two recent studies, Powderly showed that drug therapy can prevent the onset of pneumocystis pneumonia and invasive fungal infections in AIDS patients.
A Face Lift For Forest Park Southeast

In partnership with the City of St. Louis and Forest Park Southeast residents, Washington University has received a $2.4 million, five-year grant from the U.S. Department of Housing and Urban Development to revitalize the Forest Park Southeast neighborhood.

Washington University Medical Center Redevelopment Corp. (WUMCRC) will implement the project. During the past 20 years, WUMCRC has revitalized the area north of the Medical Center by spurring about $430 million in residential, commercial and institutional reinvestment.

WUMCRC will funnel $1.6 million in matching funds into the Forest Park Southeast project. The funds are being provided by the Medical Center’s sponsoring institutions: Barnes, St. Louis Children’s and Jewish hospitals of BJC Health System, Washington University and the Central Institute for the Deaf.

The City of St. Louis will maintain its existing level of funding to the Forest Park Southeast neighborhood, subject to the availability of Community Development block grants from HUD and approval of the city’s Board of Aldermen. The city also will make HOME and HOPE III funds available for selected rehabilitation projects in Forest Park Southeast.

Revitalization plans include:
- Preserving the current residential mix while substantially increasing home ownership by buying and rehabilitating dilapidated buildings and converting two- and four-family flats into marketable rental units and affordable townhouses.
- Establishing a management assistance program to help landlords improve the quality of their rental units.
- Starting a pilot repair program for existing homeowners.
- Increasing security by expanding the Neighborhood Safety Network, a supplementary patrol of off-duty St. Louis police officers.
- Creating, with the help of Washington University’s George Warren Brown School of Social Work, a consortium of social service providers in order to pool and expand existing resources. In addition, the medical school’s Program in Occupational Therapy will increase its activity with the neighborhood shelter, Shalom House, by working to provide a comprehensive continuum of care for women who are homeless and mentally impaired.
- Beautifying the neighborhood by improving streets and lighting and landscaping public spaces, with advisory support from the University’s School of Architecture and School of Engineering.

HUD requested proposals from institutions of higher learning to undertake large-scale, long-term community revitalization programs in partnership with local governments and community residents. Only five out of more than 100 universities that applied received the Joint Community Development Program awards, which are administered by HUD’s Office of University Partnerships.

Hats Off To STATS

The Students Teaching AIDS to Students (STATS) program was a semi-finalist in the Association of American Medical Colleges Secretary’s Award for Innovations in Health Promotion and Disease Prevention.

Third-year medical students Scott Sagel, Debbie Lindes and David Serlin received the recognition for a manuscript they wrote that described the STATS program. The 10,000-word manuscript detailed the STATS curriculum and results from pre- and post-tests of middle school students who have taken part in the HIV and AIDS education program.

The STATS program involves medical students visiting middle school classrooms to discuss HIV and AIDS prevention.
Lasala Lends A Hand

John M. Lasala, M.D., Ph.D., assistant professor of medicine and co-director of interventional cardiology at the School of Medicine, was among a team of U.S. physicians who voluntarily traveled to Russia this fall to provide medical expertise to physicians working in an impoverished healthcare system.

Lasala and five physicians from Yale University—a cardiothoracic surgeon, anesthesiologist, pediatric cardiologist, electrophysiologist and a non-invasive cardiologist—made the journey to St. Petersburg in early October. While there, they worked at St. George's Hospital, a regional facility that provides care to patients in outlying areas. St. Petersburg is the second largest city in Russia.

Americares, a nonprofit organization, sponsored the physicians whose purpose was to upgrade the facilities and technical expertise in adult and pediatric cardiology and cardiovascular surgery.

Although Lasala has volunteered in medically underserved areas before, he says he was not prepared for the situation that exists in a “first world” country such as Russia. Russian physicians, most of whom are women, are poorly paid and have little or no budget to purchase necessary supplies and/or maintain hospital equipment. When equipment breakdowns occur, it can take at least two to three months for repairs. As a result, hospitals often go without supplies and are forced to limit services, he says.

Even though the situation is discouraging at the moment, Lasala says the physicians he met were proud of their work and highly dedicated to those they serve.

“It was a rewarding experience and gratifying to share with them techniques and procedures they would like to adapt into their own healthcare system,” he says.

Medicine At The Millennium

The William H. Danforth Scientific Symposium has been established at the School of Medicine to honor the former chancellor’s longtime association with the medical school and to highlight current investigative activities.

“The Danforth Symposium will be held every other year to honor our former colleague,” says John P. Atkinson, M.D., head of the Department of Medicine who helped establish the event. “Speakers will be outstanding Medical Center scientists.”

Danforth, who began a medical residency at Barnes Hospital in 1954, served as vice chancellor for medical affairs and president of Washington University Medical Center from 1965-71. He was named chancellor of Washington University in 1971, a position he retired from this year after serving for 24 years.

This year’s symposium, titled Medicine at the Millennium: A School of Medicine Tribute to a Distinguished Colleague, was held in December. Speakers included William A. Peck, M.D., executive vice chancellor and dean of the medical school; Marcus E. Raichle, M.D.; Robert H. Waterston, M.D., Ph.D.; Jeffrey I. Gordon, M.D.; Stanley J. Kormayer, M.D., and David M. Kipnis, M.D.

Eric P. Newman Education Center

The Eric P. Newman Education Center opened in style on Dec. 1 with a black-tie event for some 1,200 invited guests. The three-story continuing medical education facility features a 450-seat auditorium with state-of-the-art audio-visual equipment, a main level great room which is adjacent to the glass-enclosed atrium/lobby, seminar and conference rooms on the second and third levels, a business center and two pedestrian bridges that connect the building to the rest of the Medical Center. The 44,000-square-foot facility was made possible, in part, by a $2.2 million gift from the Harry Edison Foundation and Andrew E. Newman. It is named in honor of Andrew’s father, Eric P. Newman.
URGEONS at the School of Medicine performed St. Louis' first double liver transplant by dividing a single donor liver between two recipients. The patients received their new livers during separate operations at Barnes and St. Louis Children's hospitals.

The recipients — a 47-year-old Lemay woman and a 5-month-old Florissant girl — are in good condition following the August 21 transplant operations, says Jeffrey Lowell, M.D., one of several surgeons who performed the procedures. "Both livers are functioning very well," he says. "The patients are in very good condition."

Lowell, Todd Howard, M.D., and Surendra Shenoy, M.D., performed the transplants after completing a delicate three-hour procedure to divide the donor liver. "Both livers are functioning very well," he says. "The patients are in very good condition."

Vitale suffered from cirrhosis and had been waiting for a liver transplant since June. She was born with a cyst that blocks the bile duct, preventing bile from draining out of the liver. Stasiak also suffered from cirrhosis. Her condition was ultimately caused by an earlier surgery. She was listed for a transplant in August.

The first successful double liver transplant in the world was performed in 1988 in Europe, but soon afterward surgeons all but abandoned the procedure because of poor results. Updated surgical techniques and a severe shortage of donor livers have renewed surgeons' interest in performing double liver or split liver transplants.

Double liver transplants could help reduce the severe shortage of donor livers. Nationwide, 5,000 patients now are waiting for a liver transplant. In 1994, U.S. surgeons transplanted 3,650 livers.

A MUTANT cancer gene can be passed from parent to child, causing pancreatic cancer, malignant melanoma and other tumors to develop within a family, researchers here have discovered.

The previously unrecognized family cancer syndrome also includes oral cancer and may involve other inherited tumors. "This is just the tip of the iceberg in terms of defining all the tumors associated with a defect in this gene," says Paul Goodfellow, Ph.D., an associate professor of surgery and lead author of the report, which appeared in the New England Journal of Medicine.

Researchers identified the syndrome in a family referred to the School of Medicine for evaluation. The mutation was passed through the mother's side of the family. The researchers analyzed blood samples from family members and found that family members with cancer had the mutation, while healthy family members did not have the mutation.

The genetic defect occurs in the p16 gene, a tumor suppressor gene that normally keeps cell growth in check. The gene already has been shown to be important in sporadic cases of pancreatic cancer and inherited malignant melanoma. But this is the first report showing that the p16 gene appears to play a key role in an inherited syndrome that involves pancreatic cancer.

In family cancer syndromes, each child born to an affected parent has a 50-50 chance of inheriting a defective cancer gene as well as an increased risk of developing cancer. The findings should offer insight into the development of sporadic cancers, which occur when the gene is inherited in its normal form but later is damaged by environmental factors or other causes.
Closing The Transplant Gap

A study by surgeons at the School of Medicine shows that the severe nationwide shortage of kidneys could be alleviated if more medical centers would transplant kidneys from living, but biologically unrelated, donors such as spouses or friends.

Today, most transplanted kidneys come from cadavers, which undergo extensive tissue typing and are allocated to recipients with the closest genetic match. But genetic tissue matching may not be necessary for a successful kidney transplant, the surgeons say. Kidneys donated by spouses or friends—although they don’t match genetically—function better and last longer than kidneys donated by cadavers, they report.

In the study, Jeffrey Lowell, M.D., a transplant surgeon and the study's lead investigator, working with Todd Howard, M.D., director of the School of Medicine's kidney and liver transplant programs, and transplant nephrologist Daniel Brennan, M.D., evaluated the success of 852 kidney transplants that occurred between 1983 and 1994 at Barnes Hospital. The surgeons transplanted 543 kidneys from cadavers; 279 kidneys from living-related donors, including parents, children or siblings, and 30 kidneys from living, unrelated donors including spouses and friends.

They found that graft survival—the length of time the kidney functioned—varied significantly among the groups. Five years after transplant, only 71 percent of cadaver transplants still were functioning, compared with 83 percent of the living, related transplants and 86 percent of the living, unrelated transplants. Chronic organ rejection was the main reason patients lost kidney function.

Alcoholics Face An Early Grave

Alcoholics with a history of heavy drinking are at risk for a host of health problems, and now medical school researchers say they are more likely to die prematurely.

The researchers followed 259 male and female alcoholics who were hospitalized for treatment in the late 1960s. Overall, they found that nearly half of the alcoholic women and almost 60 percent of the male alcoholics died within a 20-year follow-up period. Most patients were in their 30s or 40s at the time they were hospitalized for treatment.

"These men and women were dying as much as 20 years prematurely," says lead investigator Elizabeth M. Smith, Ph.D., associate professor of social work in psychiatry. "We're talking about people who should be living into their 70s, but instead they're dying in their 50s."

The average age of death for both male and female alcoholics in the study was 56. The time from hospital admission to death averaged nine years for men and 10.5 years for women.

Most of the men had been problem drinkers since before the age of 25. Most women in the study had been problem drinkers for seven to 10 years.

Eat Your Greens

Beta-carotene, the pigment in carrots and many other orange or dark green fruits and vegetables, may prevent heart disease, says researchers here.

"Epidemiological studies have shown that people who eat foods rich in beta-carotene and vitamin E have a decreased risk for heart disease, suggesting that vitamins with antioxidant properties might prevent atherosclerosis," says Jay W. Heinecke, M.D., assistant professor of medicine. "We looked for more direct evidence by feeding antioxidants to rabbits that had high levels of 'bad cholesterol.'"

The rabbits were candidates for heart disease because they lived on high-cholesterol diets. Some received antioxidant supplements, and others did not. The latter developed fatty plaques in their arteries. But those whose high-cholesterol diets were supplemented with beta-carotene developed only half as much arterial plaque.

Bad cholesterol — low density lipoprotein or LDL — must be oxidized before it can damage arteries. Scientists think that antioxidants may prevent atherosclerosis by protecting LDL from oxidation. But Heinecke and his colleagues found that LDL from the rabbits that received beta-carotene was just as susceptible to oxidation as LDL from the rabbits that received no supplement.

"Beta-carotene appears to inhibit atherosclerosis by some mechanism other than prevention of LDL oxidation," he says.

The study suggests that beta-carotene itself might be therapeutic in humans. A large-scale human trial is underway.
Soon after actor Christopher Reeve suffered his riding accident, he received injections to protect his spinal cord from further damage. The drug, methylprednisolone, was the first spinal cord protectant on the market. It will limit damage to the spinal cord by shielding healthy nerve tissue from damage by toxic molecules called free radicals. A compound to curtail brain damage in Parkinson's disease is also available for clinical use.

by Linda Sage

Much of the damage from stroke, trauma or cardiac arrest occurs in the hours or days after the event. After neurons are injured, the damage spreads like rot in a melon, destroying parts of the brain.

Working to deter such damage, the Center for the Study of Nervous System Injury (CSNSI) is determining how neurons die after neighboring cells are damaged and how to prevent this untimely cell death.

CSNSI Director, Dennis W. Choi, M.D., Ph.D., Jones Professor and head of neurology, likens the center to a development pipeline that is initiated by research on molecules and cultured cells. The findings then are tested in animal models of disease. It is hoped that out of the pipe will come drugs to help the millions of Americans who suffer acute brain or spinal cord injury or the ravaging effects of neurodegenerative disease.

The center was established in 1992 under an $8 million, five-year collaborative agreement with Hoffmann-LaRoche Inc., a pharmaceutical company in Nutley NJ. The company committed another $3 million in 1995. The center also received a $5 million grant from the National Institute of Neurological Diseases and Stroke this year.
CSNSI research ranges from nervous system development to the genetics of neurofibromatosis. But many investigators are studying the way neurons die after neighboring cells are damaged by stroke and other clinical conditions. Injured neurons can kill neighboring cells in the brain, increasing the risk of death or serious disability.

"Rather than set up a stroke center or a Parkinson’s disease research center, we decided to go after core principles," Choi explains. "One can gain powerful insights by studying the common features of seemingly different diseases."

How Neurons Die

Much of the center’s work focuses on cell death from glutamate exposure — death by too much of a good thing. Glutamate is widely used in the brain for cell-to-cell communication. Secreted from neurons in minuscule amounts, it activates proteins called glutamate receptors on neighboring neurons. But like all communication systems, this one can go awry. When neurons are deprived of oxygen and nutrients, they release their glutamate all at once, overstimulating the receptors of nearby neurons.

Top row: Slices of rat brain prepared at intervals after the right hemisphere of living rats was briefly deprived of blood. The slices show the development of an area of dead tissue. Such dead areas appear in the brains of stroke victims. Bottom row: Slices from rats that received the experimental drug dextromethorphan before blood deprivation show much less tissue damage. Below, CSNSI Director Dennis Choi, M.D., Ph.D.
One can gain powerful insights by studying the common features of seemingly different diseases.

Choi and collaborators at the University of California, Irvine, are exploring the relationship between calcium and AMPA receptors, which once were thought to admit only sodium ions. They found that an unusual brand of AMPA receptor that admits calcium makes neurons especially vulnerable to glutamate damage. This receptor lacks a protein subunit called GluR-B, the researchers determined. And it occurs mostly on neurons that dampen cell-to-cell communication by releasing an inhibitory neurotransmitter. "Brain inhibition appears to be especially vulnerable to this type of toxicity," Choi says. "So even though this type of AMPA receptor-mediated damage might not involve many neurons, it could be important with regard to subsequent risk for developing seizures."

Mark P. Goldberg, M.D., assistant professor of neurology, has found that activation of AMPA receptors also can damage housekeeping cells called glia, which allow neurons to survive and function. "We need to find ways to protect both glial cells and neurons from glutamate," he says. "Otherwise neurons that survive a stroke will later die without support from glia."

Goldberg also is studying the intracellular consequences of receptor overstimulation. When he examined glutamate-treated neurons with the center's confocal microscope, he was surprised to see varicose bulges along their dendrites, which reach out to other neurons.

Suspecting that something was amiss with the cell's internal skeleton, he stained neurons for tubulin, a skeletal protein. Tubulin molecules normally form a net around the cell body and line up along the dendrites. But after glutamate treatment, the skeleton collapsed within minutes, leaving a disorganized array of tubulin molecules.

Mark Goldberg, M.D.

A normal neuron from mouse brain, left, communicates with other neurons using its star-shaped extensions or dendrites. When neurons are exposed to glutamate, the normally smooth dendrites rapidly develop a beaded appearance, right.

Choi's research at Stanford University pointed to a type of glutamate receptor, called the NMDA receptor, as the chief culprit in glutamate damage and to calcium as the main destructive agent. When the NMDA receptor encounters glutamate, it opens a channel that admits calcium and sodium to the cell. Overexcited, it lets in lethal amounts of calcium.

The damage induced by NMDA receptors may be reduced when the brain becomes mildly acid, as happens when the entire brain is deprived of oxygen or during the first stage of a localized stroke. In 1989, Choi showed that mildly acid conditions make neurons more resistant to glutamate and calcium damage by this mechanism.

Another glutamate receptor called the AMPA receptor may become a major player under these conditions. Choi and neurology resident John W. McDonald, M.D., Ph.D., recently discovered that AMPA receptors preferentially injure neurons under acid conditions, perhaps by rendering normal levels of calcium harmful.

This finding suggests new strategies for helping stroke victims. "During the acute phase of focal ischemia, treatment with AMPA receptor blockers may be more effective," McDonald says. "NMDA receptor blockers might become more important after blood flow resumes in the blocked vessel and shifts the pH back up to normal."
Using calcium-sensitive fluorescent dyes, Goldberg is trying to determine whether calcium destabilizes the cellular skeleton. "The ultimate hope is to find ways to hold the cytoskeleton together after glutamate levels rise, so there would be less damage," he says.

Geriatrician Laura L. Dugan, M.D., assistant professor of neurology, is studying another consequence of glutamate receptor overactivation, the production of damaging free radicals, which have a fleeting existence. "Mostly, they just leave their footprints behind," she says, "like evidence at a crime scene."

Using oxidation-sensitive dyes to reveal these footprints, Dugan has found that mitochondria — the cell's powerhouse — produce bursts of free radicals when the NMDA receptor is activated. "Knowing the major source of radicals in glutamate-damaged cells may allow us to develop drugs to block the process," she says.

Preventing Neuronal Death

Several CSNSI investigators are identifying promising targets for drug development. Kelvin A. Yamada, M.D., assistant professor of neurology, has found a novel site on the AMPA receptor.

In 1990, Yamada was in Steven M. Rothman's lab, studying communication between neurons. He electrically stimulated one neuron to make it release its glutamate onto its neighbor's AMPA receptors. Then he recorded the resulting synaptic current in the second neuron. In some experiments, he added diazoxide, a drug prescribed for hypertension. He and Rothman thought the drug would inhibit the second neuron's response, perhaps protecting it from glutamate damage. Instead, the responses were larger and longer, and diazoxide enhanced glutamate toxicity.

It was known that the AMPA receptor-channel snaps shut within a split second after glutamate opens it, cutting off the flow of current. This property is called desensitization because the receptor behaves as if glutamate no longer is present. Yamada and Rothman determined that diazoxide increased the synaptic current by inhibiting the desensitization of the AMPA receptor. They also found that desensitization may protect neurons from excessive glutamate exposure.

By evaluating drugs similar to diazoxide, Yamada discovered that a diuretic called cyclothiazide was 100 times more potent at blocking AMPA receptor desensitization. The researchers thought these drugs might act via a regulatory site on the receptor that differed from the glutamate-hindering site.

Yamada and Douglas F. Covey, Ph.D., professor of molecular biology and pharmacology, now are synthesizing cyclothiazide derivatives to determine how these compounds interact with the AMPA receptor. This work has given them important leads to drugs that may reduce rather than enhance receptor activity. "Such drugs are potential neuroprotectants, because they would not block the AMPA receptor directly and would be less likely to hamper normal neurotransmission," Yamada says.

Animal Models

While studies of cultured cells point to promising new drugs, animal studies show whether such compounds can protect the intact brain, where many different types of cells interact. "Most human drug studies are initiated because of animal data," says Chung Y. Hsu, M.D., Ph.D., professor of neurology, who coordinates the center's animal studies. "It's a common approach in stroke, head and spinal cord injury to use animal models to obtain better treatments for human disease."

The center is using two rat models of stroke in which one or more arteries are occluded to cause regional loss of blood in the brain. It also has developed a global ischemia model in which the entire brain is deprived of oxygen. The animal models are vital for testing compounds that protect against glutamate damage. Choi's group found that dextrophan, an NMDA receptor blocker that protected cultured neurons in cell cultures, halved the area of brain damage in the stroke model.

The center has just added a model of spinal cord injury to the stroke models, and models of neurodegenerative diseases, such as amyotrophic lateral sclerosis (Lou Gehrig's disease), are being imported from other institutions. "If an idea looks good, we will find out if it can help an animal," Choi says. "The next stage is human trials."

Because the CSNSI was established only four years ago, it has not yet brought a novel drug to human trials. But Choi is optimistic that more rationally designed drugs soon will be ready for testing. "Once one has a good idea that fits basic principles and evidence that it works in animals, one is in a good position to move to human trials. The CSNSI's mission is to promote every stage of this development, all the way from the bench to the bedside."
SETTING THE TONE

Chancellor Mark S. Wrighton On Change And The Future

BY STEVE KOHLER
Speaking candidly about the University and its future, Mark S. Wrighton — recently inaugurated as the 14th chancellor of Washington University — returns regularly to themes he already has clearly established for the University: oneness, excellence and integrity.

Foremost among those principles is oneness, the "big picture" commitment that all elements of the University must come together to form an integrated whole. "If we are to achieve the next level of the great educational institutions, we must draw together to articulate the academic priorities that we stand by," he says. "We are not eight separate endeavors.

"Every person must adopt a commitment to excellence and to continuous improvement. All of us have responsible roles to play," he says. By combining energy, he believes that no problem is too difficult to tackle, as he said in his inaugural address, "Learning and Discovery: Gateways to the 21st Century."

If the members of the University community collaborate effectively, in Wrighton's view not even the No. 1 position in American higher education is beyond Washington University's reach. "Harvard will continue to be the flagship, but things around Harvard are changing. It's not necessary that Harvard will be number one in all areas of intellectual activity. There's much substance to be derived from our interdisciplinary, collaborative efforts," he says.
One of his jobs as chancellor, Wrighton says, is to assist the heads of the schools “in understanding how the oneness principle will be effective for them. This University’s organizational style, what’s called the ‘Reserve System’ (a phrase that impresses him as “a bit of jargon”) is near the extreme of decentralized management. Essentially, there are eight provosts here. The heads of the schools are the CEOs of their areas. I’m the CEO of the CEOs.”

The management approach — called the University Council — put in place by the new chancellor involves all of the leadership. “Everyone must understand what the others are doing and why,” he says. “From the trivial to the substantive, it makes a difference what each element does.”

Combined resources are an asset to all parts, Wrighton believes. “The best medical faculty will be more proud to be associated with a university that also has excellence in all of its academic programs,” he says. “A stand-alone School of Medicine will not be great. There can be no truly great medical school with out a great university. So we must establish incentives to assure that the intellectual agenda drives the decision-making process. In the future, we will be more interdependent, not less.”

To gain a better understanding of the way the University operates today, Wrighton says he has repositioned himself in the system “to get an idea of the intellectual agenda. I am more hands-on because I’m just learning the job. I want to know how decisions are made and why.”

In search of a grass roots insight into the University, Wrighton has visited its halls and offices. He says he has “prowled” the medical school, finding it “exciting” and “stimulating to see all the possibilities of moving from basic science to premature babies and the elderly who can be helped by that basic science.” Intrigued by technology in general, Wrighton says he also was “excited to see so much state-of-the-art technology applied.”

Meetings with the School of Medicine’s department heads have shown most to be aware of a need for change and generally “fretful about the future but confident of ultimate success,” Wrighton says. “They are incredibly supportive of Dean Peck, with much to be optimistic about. There’s a sense of self-confidence at the medical school that some others see as arrogance. But I have that same sense that our leadership is strong, resilient and able. The faculty is creative, talented and very hard-working.”

Wrighton’s involvement with medicine at this level is new for him, although in his former position as provost at MIT he collaborated on projects with representatives of Harvard Medical School. His understanding is that medicine runs a wider range of intellectual activity than engineering or science, where his experience is deepest. But he notes with a smile that engineers, like physicians and researchers, are self-confident, “particularly when speaking to scientists.”

He senses at the School of Medicine “an awareness that no matter how well we do individually or institutionally, external forces that we may influence but cannot control are at work.” Acknowledging that continuing changes in the healthcare system may require quick adjustments, he says, “We are fortunate that we don’t have to respond in a crisis mode. We’re strong. There should be no need for rapid, draconian changes, so we must take care that our excellence is sustainable, not just as one of the pack but always growing in impact.”

Clearly, the new chancellor sees increased prominence ahead for the School of Medicine. “We may need new alliances. We may have to take the lead in healthcare delivery,” he says. “And more interaction is required; the combination of people interested in science, engineering, social work and medicine is powerful.”

Despite the challenges, he anticipates an environment favorable to the school’s progress. “I am convinced that the federal government sees medical research as an investment; it’s not a contentious issue,” he says. “And the public understands, too.
When someone is sick, he or she wants state-of-the-art care; a patient seeks those who know the most. So research-driven institutions are in the best circumstances. And our record is exemplary.

"The concern is how to continue our support in an era of overall constraint. The tendency is to spread out the support and leave everyone with too little, to put some money everywhere and not enough anywhere. I am not a fan of sub-critical support.

"We must do our part to educate the public that it is an investment in the future to support the coupling of research and education that goes on at our universities. I am struck that in five years, 10,000 people will have left here. Our success is in our students, the people who do the risk-taking and innovation," he says.

Himself a noted innovator, Wrighton has called for the "internationalization" of the University. It is one area in which he believes the medical school can lead the University. "As the best-known component of the University outside of the country, the School of Medicine can lead the way in building relationships around the world. Then, as the University becomes more internationally known, that will benefit the medical school by making its partners aware of its role as part of a great university," he explains.

Wrighton points to the medical campus’ new Eric P. Newman Education Center as the embodiment of a "great opportunity to bring people here from around the world, to engage them in education, research and clinical programs."

As for his own arrival in St. Louis, Wrighton has found the city to be generous and warm in welcoming him. St. Louis' sense of pride and involvement in Washington University is not lost on him, and, in his characteristic way of moving on to a higher level, he says he hopes to expand the feeling to a larger constituency.

Assuming the office of chancellor from William H. Danforth, who served the University in that position for 24 years, has not been as daunting to him as others may have thought it, Wrighton says, because "Bill Danforth laid the groundwork for change; the community was prepared. Almost everything is in good shape, and people are ready for new things. What is daunting is to live up to all of the things that have been said about me."

But when he characterizes himself, the first point that Wrighton makes is that he has "always been attracted to learning new things. I enjoy dealing with large sets of information."

With the University and its future stretching out before him, Wrighton has the challenge that he enjoys. He believes that "it may take longer to achieve results now than it did in my discovery-oriented research, but by looking at Bill Danforth, you can see how much can be done to help so many people. I have the opportunity to assist tens of thousands of people to fulfill their potentials." That pleases him and sets the tone for the University, its schools and its people.
Five-year-old Cate Wirth says the bone marrow transplant she received in October at St. Louis Children’s Hospital will “make me stronger.” Her parents, Mary Biechler and Dan Wirth, hope it will save their daughter’s life.

Cate was born with an extremely rare immunodeficiency that has virtually depleted her arsenal of T cells. Without this critical line of defense against foreign pathogens, Cate’s immune system eventually would become unable to fight off even ordinary infections, such as a cold or the flu.

Her T cell count, a gauge of immune system function, had plunged to 35 by early October. (Typically, a child’s count hovers near 1,000.) A bone marrow transplant, which has replaced Cate’s damaged immune system with a healthy one, is her only hope for a cure, say her doctors at the School of Medicine. Even then, she faces a 50-50 chance that her body will reject the donor’s bone marrow.

Cate has overcome the odds so far. By mid-November, her T cell count had jumped to 500. Her rapid recovery surprised her family and her doctors, who allowed Cate to return to her home in Eureka MO just days before Thanksgiving.
Talal Chatila, M.D., an associate professor of pediatrics, suspects Cate lacks an immune system protein called Jak-3 kinase. This signaling protein appears to be indispensable for early T cell development, he says. To confirm his suspicions, Chatila and his coworkers are searching for a mutation in Cate's Jak-3 gene.

If a mutation is found, Cate will be one of only a handful of children worldwide known to have a Jak-3 defect. In recent issues of the journals Nature and Science, U.S. and Italian researchers described the first two patients known to have a Jak-3 mutation. Like Cate, both patients were severely immunodeficient and lacked sufficient numbers of T cells to fight infection.

**From Devastation To Discovery**

Discerning the role of specific proteins within the immune system may eventually enable scientists to develop innovative therapies for severe immune deficiencies. Ironically, children like Cate, whose immune systems are devastated by inherited genetic defects, are giving scientists at the School of Medicine a close-up look at just how the immune system works.

By studying patients who lack a particular immune system protein, researchers can better understand its specific function and why the immune system goes awry if the protein is missing.

In fact, today's vision of the specialized nature of the immune system is due, in part, to the discovery of a number of extremely rare inherited immune deficiencies during the past 50 years.

"Immune deficiencies are not only a confirmation or elaboration of a concept we know," Chatila says. "These experiments of nature introduce us to new ideas about the way the immune system works."

That notion is underscored by the discovery in 1992 of ZAP-70, an immune system protein critical for normal T cell development and function. Andrew Chan, M.D., Ph.D., an assistant professor of medicine and pathology and a Howard Hughes Medical Institute assistant investigator, identified and cloned the protein while working as a postdoctoral fellow at the University of California at San Francisco. At the time, there were few clues to suggest that ZAP-70 was so critical to a healthy immune system.

Only in 1994, after Chan and others first identified patients who were missing ZAP-70, did scientists realize that the protein is essential for T cell function. The patients all had a form of severe combined immune deficiency disease in which their T cells were either non-existent or non-functional.

Several hundred people worldwide may have an inherited genetic immunodeficiency in which ZAP-70 is missing. But far greater numbers stand to benefit from ZAP-70's key role in T cell activation, which is being studied here by Chan and Andrey Shaw, M.D., an assistant professor of pathology.

ZAP-70 enables T cells to respond to invaders such as viruses and bacteria by becoming "active" and producing chemical signals to marshal immune defenses into action. In that role, ZAP-70 offers a promising target for developing better therapies for autoimmune diseases such as lupus and rheumatoid arthritis and for transplant rejection. All involve the abnormal activation of T cells.

"If pharmaceutical companies could develop a specific inhibitor of ZAP-70, it could revolutionize the way we treat autoimmune diseases and transplant rejection," Chan says. Such inhibitors may hold a definite advantage over current immunosuppressive drugs. For example, Prednisone, a steroid often prescribed to treat arthritis and lupus, suppresses the entire immune system, leaving patients prone to infection. Potent anti-rejection drugs like cyclosporine and FK-506 act more selectively to inhibit T cells but also target cells in the kidney and liver. Not surprisingly, a major side effect of both drugs is kidney and liver toxicity.

Researchers are hoping that an inhibitor of ZAP-70, which is found only in T cells and other immune cells called natural killer cells, will be an even more selective target of immune suppression without toxic side effects. Chan cautions, however, that ZAP-70 inhibitors will not be a panacea.

"These drugs, if they can be developed, would still suppress the immune system," he says.

**A Chance Finding**

Chan first discovered ZAP-70 while studying how T cells are activated to respond to infection. His work focused on molecules that bind to the T cell receptor; one of those molecules was ZAP-70. Initially, however, there was no evidence to show that the molecule was important. "At the time, it was another molecule that associated with the T cell receptor," Chan says. "The important issue was to find out the functional importance of this association."

Chan became intrigued, however, when he found that ZAP-70 only
bound to activated T cell receptors and not to resting or defective receptors. Moreover, when Chan cloned ZAP-70, he discovered that it belonged to a family of protein tyrosine kinases, which are known to be key signaling molecules in the body. A protein tyrosine kinase is like a light switch within cell membranes that, when turned on, can send signals to other molecules. In the immune system, once the T cell receptor is activated, ZAP-70 is recruited to the receptor, where its signal is turned on and eventually leads to T cell proliferation.

But the first functional evidence of ZAP-70’s role did not come until Chan analyzed the blood of three severely immunodeficient patients who doctors believed were born with a T cell signaling defect. Their T cells were either non-existent or non-functional. When Chan looked for ZAP-70 in the patients’ blood, he found none. “There was no ZAP-70 in any of these patients, and levels of all the other kinases we examined were normal,” Chan says.

Chan and other researchers at the School of Medicine recently established the critical role of ZAP-70 in T cell development in a paper published in the Aug. 3, 1995, issue of Nature. Chan, working with Dennis Loh, M.D., a former professor of medicine and Howard Hughes investigator, demonstrated that ZAP-70 is essential for the development of immature T cells.

In humans and mice, there are two main types of T cells circulating in the bloodstream. Helper T cells (CD4+) recognize foreign invaders and signal other cells, such as B cells to make antibodies. In contrast, killer T cells (CD8+) can directly destroy the invaders.

In the study, Loh bred mice lacking ZAP-70 by “knocking out” both copies of the ZAP-70 gene. The mice were born with no functional T cells. However, when the researchers examined the mice, they found immature T cells in a state of arrested development.

“This tells us that ZAP-70 is critical for the development of both CD4+ and CD8+ T cells,” Chan explains. “Without ZAP-70, these mice have no T cell function whatsoever and are immunodeficient.”

Chan and his co-workers then introduced human ZAP-70 back into the immunodeficient mice and showed it can effectively reconstitute their immune systems. The mice went on to develop normal immune systems with both CD4+ and CD8+ cells.

Chan and others believe that ZAP-70 also may be critical during development to enable the immune system to delete T cells that attack, the body’s own cells. In the same study, they found that normal mice could delete self-reactive T cells, while mice without ZAP-70 could not.

In related work, Andrey Shaw and co-workers in his laboratory have been working to understand ZAP-70’s interaction with the T cell receptor. His work focuses on a segment of the T cell receptor called the ITAM, a so-called immune receptor tyrosine-based activation motif, which he has demonstrated to be a specific binding site for ZAP-70.

Shaw’s studies have established a lock-and-key fit between the ITAM and ZAP-70. The ZAP-70 protein, he notes, has two sites that can bind the amino acid tyrosine; one of the ITAM’s most prominent features is its two tyrosines.

“All of the features required for ITAM-mediated signaling are also features that are required for ZAP-70 binding,” Shaw explains.

He suspects that the ITAM’s only function is to bind ZAP-70, which would emphasize ZAP-70’s key role in the immune system.

Despite the fast-paced advances in ZAP-70 research, Shaw and Chan are still working to define how ZAP-70 signals the attention of other immune cells, which ultimately leads to T cell proliferation. “Clearly, major signaling pathways get activated downstream from ZAP-70, but we’ve not yet been able to demonstrate what those pathways are,” Shaw says.

Chan also hopes to identify the molecules that regulate ZAP-70, including those that turn off its activation. Pinpointing these molecules may give researchers another way to control the aberrant activation of T cells in autoimmune diseases and transplantation rejection. “We’ve solved only a very, very small percentage of the way ZAP-70 works,” Chan says. “But we think we’re headed in the right direction.”

Just days before a bone marrow transplant at St. Louis Children’s Hospital, 5-year-old Cate Wirth is all smiles with her parents Mary Biechler and Dan Wirth. Since the transplant, Cate’s immune system has rebounded and her T cell count continues to climb.
Rooftop of Children’s Hospital

CHANGE THE POINT OF VIEW AND SCRAMBLE THE COLOR; THE RESULT IS AN INFORMATIVE PERSPECTIVE ON THE MEDICAL CENTER. OUT OF THE ORDINARY IMAGES BY BOB BOSTON.
View from Children's Hospital's old helicopter landing pad
From the rooftop of the former Nurses' Building

Children's Hospital cafeteria
Master Teachers

Each year, Washington University welcomes 120 new medical students eager to begin their four-year apprenticeships in which they receive the tools they will need to continue their educations through residency, fellowship and as attending physicians. The training of physicians - which includes two years of basic science curriculum, followed by two years in clinical settings - is no easy task, so students are grateful and have long-lasting respect for those teachers who are enthusiastic and skilled at sharing their expertise.

Since 1986, the School of Medicine has honored exemplary professors with annual teaching awards. The first- and second-year classes each select a Professor of the Year and a Lecturer of the Year and designate a number of Distinguished Teaching Awards to recognize and thank their most memorable instructors. The classes of 1997 and 1998 honored their 'master teachers' from the 1994-95 academic year on Dec. 8 with an awards ceremony in the Eric P. Newman Education Center that was attended by medical students, faculty and administration.

Robert Wilkinson, Ph.D., course master of first-year physiology, has been named Professor of the Year by the class of 1998. His interest in teaching dates back to his undergraduate years at Rice University and his graduate training at the University of Texas. As a teaching assistant and instructor of physics, Wilkinson turned difficult concepts into simple analogies and demonstrations. He brought clinical relevance to the pre-medical laboratory he designed by using EKG's to demonstrate electric dipoles and muscular movement to teach the physics of vectors. He arrived at Washington University in 1975 and began teaching neuroscience courses. Soon after, he was lecturing in physiology and working with one of his mentors, Stanley Lang, Ph.D. Lang was course master of systems physiology for many years, and Wilkinson remembers his lessons well: "He was a true physiologist who cared about students and was extremely dedicated to teaching," he says.

Wilkinson says his teaching strategy is based on demonstrations to "rigorously prove to students why things happen so they can later return to the basics and prove it to themselves again." This is the second year in a row that Wilkinson has been named Professor of the Year. He attributes the success of his course to the subject matter and the enthusiastic participation of other lecturers, some of whom are recipients of Distinguished Teaching Awards.

When asked how he became interested in teaching, Scot Hickman, M.D., says, "As a medical student I was impressed by good teachers who were role models, and so I try to teach as they did." Named Professor of the Year by the Class of 1997, Hickman is course master of hematology-pathophysiology. As a Washington University medical student, Hickman was taught and greatly influenced by Carl Moore, M.D., an internationally recognized hematologist and head of the Department of Medicine from 1955 to 1972. "Dr. Moore was very much a professor and a student advocate; he spent a lot of time with medical students," Hickman recalls. So impressed was he with Moore that he completed a medicine residency and hematology-oncology fellowship here. When asked to define good teaching, Hickman says that fun, fairness and providing students with a challenge...
is key. He says his most memorable instructors made him want to learn, not because he feared them but because he wanted to please them.

Now standing at the podium himself, Hickman says he tries to "present the knowledge that is classical pathophysiology, while keeping in mind that clerkships are just around the corner." He includes clinically relevant material such as case discussions and a venipuncture exercise every year. The challenge in lecturing, he says, is to "provide enough basic material while still introducing the new, important information to reach those students who might be interested in hematology as a specialty."

Hickman also credits the success of his course to the enormous support he receives from other faculty, noting that junior faculty and fellows will often ask to participate as lecturers.

Named Lecturer of the Year for a second consecutive year, Dana Abendschein, Ph.D., teaches in the cardiovascular and respiratory sections of first-year physiology. He attributes his interest in medical education to master teachers at both Purdue University and the University of California-San Francisco, where he completed his graduate and postdoctoral training, respectively. His mentor's philosophy, 'If you can't teach physiology, it's not worth learning,' is one Abendschein has put into practice throughout his training and career. His clear, conceptual teaching style was developed when he taught an entire systems physiology course at the University of Indiana. Abendschein tries to bring clinical relevance to his lectures to help students realize how the basic sciences will be useful to them later. He is perhaps best known among first-year students for his innovative demonstrations. He encourages students to think about, not memorize, facts, and he pays close attention to which approaches are most effective. He restructures his lectures every year, a process that "keeps teaching exciting and keeps [him] looking for new ways to get the message across." In defining his role as a professor, Abendschein says, "I strive to build a conceptual framework for students that they can use later in their careers."

"Teaching was a blast!" is how Steven Carroll, M.D., Ph.D., describes his first experience lecturing in second-year pathology. "The students were willing to be engaged in discussion about the material. It kept it interesting for me and hopefully for them as well," he says. Carroll is the newest addition to the team of faculty that teaches neuropathology in the second year and has been named Lecturer of the Year by the Class of 1997.

Though new to the lecture hall, he is no stranger to Washington University. After receiving his medical and graduate degrees at Baylor University, he completed his pathology residency and fellowship here. His teaching style is derived from how he learned the material as a student. "Pathology gets very complicated very quickly, but it doesn't need to. There are a few principles that guide everything. Once you figure them out, you've learned most of it," he says.

He credits his success in teaching laboratories to faculty members he came to know during his residency, including Robert Schmidt, M.D., Ph.D.; Mark Wick, M.D., and Kevin Roth, M.D., Ph.D.

"I pass specimens around and ask students questions to make sure that they really understand what's going on," he says. "Once you think about why things look the way they do, it always sticks with you." This year, neuropathology and pathophysiology of the nervous system will be taught as one course instead of two distinct courses. Carroll is looking forward to taking part and says that "it will provide a new perspective to students and attendings (physicians) as well."

In addition, Distinguished Teaching Awards were distributed to 23 other faculty as commendation for their outstanding lectures:

Class of 1997
Elliot A. Abbey, M.D.
Edmond C. Crouch, M.D., Ph.D.
Rosa Maria Davila, M.D.
William C. Dunagan, M.D.
James Ferrendelli, M.D.
Eugene M. Johnson, Jr., Ph.D.
Leslie E. Kahl, M.D.
James B. Letkowitz, M.D.
Alan L. Pearlman, M.D.
Calixto Romero, M.D.
Kevin A. Roth, M.D., Ph.D.
Jeffrey E. Saffitz, M.D., Ph.D.
Clay Semenkovich, M.D.
Sherry Shuman, M.D.
Lawrence Tykhasen, M.D.

Class of 1998
Glenn C. Conroy, Ph.D.
Elaine Davis, Ph.D.
S. Bruce Downton, M.D. (Syd.)
Jeffery Lichtman, M.D., Ph.D.
Robert P. Mecham, Ph.D.
David N. Menton, Ph.D.
Robert W. Mercer, Ph.D.
Stanley Misler, M.D. Ph.D.
Jane Philips-Conroy, Ph.D.

Students are grateful and have long-lasting respect for teachers who are enthusiastic and skilled.

Outlook. Winter 1995
For The Greater Good — Carolyn Robinowitz, M.D.

by Kleila Carlson

MORE than 35 years ago, Carolyn B. Robinowitz postponed graduate studies in music at Wellesley College to explore the possibility of a career in medicine. With little scientific background, she enrolled in pre-medical courses at Boston University while supporting herself as a church organist and choir director. She told herself that if she did well with her coursework, she would apply for medical school. She did — Washington University was one of seven medical schools to which she applied and was accepted.

"I loved music, but I wasn't sure what its benefits were to the world, and I wasn't sure I wanted to spend the rest of my life in music," says Robinowitz, M.D. '64, about her leap from pianist to practitioner. "I knew with medicine that I never would be bored, that there always would be some new adventure, some new road or some new patient to care for. I was right. Medicine has kept me enthusiastic, stimulated and challenged."

Robinowitz has never regretted her decision, and, like the young woman of 1959, she continues exploring possibilities for the greater good. For most of her career, she has worked on behalf of the field of psychiatry and psychiatric patient care.

She spent 18 years with the American Psychiatric Association (APA), an organization that provides continuing medical education for its 38,000 members, sets educational standards for medical school psychiatry and residency programs around the country and works with the federal government to establish health policy. For 10 years, she served as the APA's deputy medical director and director of the office of education; the last eight years, she was the organization's senior deputy medical director and chief operating officer, responsible for the day-to-day management of the association and its 200 staff members.

In addition, Robinowitz maintained a small private practice and was clinical professor of psychiatry and behavioral sciences and child health and development at George Washington University, and a professorial lecturer at Georgetown University and at the Uniformed Services University of the Health Sciences.

"I have always seen myself as an educator," she says. "My first job after my residency involved teaching pediatricians about child development and childhood mental health. At the APA, I was interested in the content of the education and how to educate colleagues, as well as public education and how to work with non-medical or mental health professionals to teach them about mental illness."

Her natural leadership qualities led her to be the first female psychiatrist elected a director of the American Board of Psychiatry and Neurology. Robinowitz worked her way up through its ranks from secretary to vice president to president. She also was the first woman to be elected president of the Council of Medical Specialty Societies, an organization that represents some 250,000 medical specialists nationwide.
At the APA, she worked with some of the foremost leaders in the field of psychiatry and was called upon to assist in shaping public policy for the appropriation of funds for psychiatric research, improved patient care and development of new drugs.

"As a medical student, I never dreamed that I would one day be concerned about the financial well-being of a national organization (APA), but when I saw it as a means to improve patients' lives and care, it meshed with a remaining idealism of mine," she says.

That lingering idealism also steered Robinowitz to the School of Medicine at Georgetown University, where she has been associate dean for students and a professor of psychiatry for almost a year. "What an opportunity to have a direct impact on young people — the doctors of tomorrow — who will be setting the course for the future of medicine," she says. "The changes going on in medical education today are very exciting. It is a different pattern of teaching and learning that reflects how physicians are going to practice in the future."

Unlike the traditional teaching methods used when she was a student, Robinowitz says more attention now is paid to data collection, reasoning and problem-solving. Students learn how to approach difficult problems, how to use computer-based resources and how to work in teams.

"Thirty years ago, the professor presented the material and the student read the text and took an exam," she says. "Students did not have the same stake in their education that they do today. We no longer simply ask students 'What is the biochemical formula for this?' we talk about problems that depend upon their knowing the information."

Robinowitz views this as a positive change, much like others she has seen taking place in the medical profession, such as its increasing number of women. This year, women make up 42 percent of Georgetown's first-year class. "We are making more of an effort to recruit and retain women, and this is a high for us," she says of the first-year class. "But medical schools and the medical profession were designed by men, and they are becoming more female-friendly. I have been pleased to see it moving from a predominantly white male profession to a more broad-based profession that involves women and people of diverse backgrounds."

Medicine as a field also is becoming more broad-based, she says, as more and a greater variety of factors are considered when providing healthcare, from cultural issues to the mind-body connection. "We have a greater molecular understanding of physiology and pathophysiology than ever before, and, at the same time, people are working to understand mind-body interactions," she explains. "Stress reduction, meditation, yoga — relaxation techniques that were scoffed at a few years ago — point out our understanding of the interface of mind, brain and body."

Robinowitz, who had an interest in psychology and human development before she entered medical school, thought initially that she would study pediatrics or pediatric hematology — specialties extremely well taught at the School of Medicine and that were appropriate for women at the time, she says. Once involved in the specialty, she found that a significant component of pediatrics concerned behavioral aspects of children that she did not know about or understand. Her shift into psychiatry followed, with the idea that she would learn about child behavior and development and eventually return to pediatrics.

Robinowitz recalls her first year of medical school and says she felt "adrift. Were it not for a caring and concerned faculty, she says she might have dropped out to resume studying music. "I had a difficult first year; I was not as well-prepared for medical school as some," she says. "But the faculty was very responsive. There were some who went out of their way to be helpful and supportive and to make every day a day you looked forward to. My experience at Washington University was positive; I left with a very good feeling for the school."

There were eight women in Robinowitz's graduating class, and she says that they all have had fulfilling and successful careers. Robinowitz says her involvement in a national organization and her belief that women 'can and should' contribute have enabled her to help others. "One thing I have tried to do is to identify bright women who I think can make a significant contribution. I see myself as an agent for change but also someone who is in a position to promote and enhance the careers of others. Helping others achieve their goals and do well is very satisfying to me."
Second Century Award Winners Honored

THE School of Medicine’s Second Century Awards for 1995 were presented at a gala dinner held at St. Louis’ Ritz-Carlton Hotel on Oct. 6.

“The Second Century Award honors those whose dedication, intellect and illuminating spirit empower the important work being done at the School of Medicine,” says William A. Peck, M.D., executive vice chancellor for medical affairs and dean of the School of Medicine.

The School of Medicine also was privileged to welcome Mark S. Wrighton, Ph.D., just hours after his formal inauguration as the 14th chancellor of the University.

The honorees for the year were Bernard Becker, M.D., Paul O. Hagemann, M.D., and Raymond H. and Roma Broida Wittcoff.

Becker is professor and emeritus head of the Department of Ophthalmology and Visual Sciences at the School of Medicine. During his 35 years as chairman, he led the department to an international reputation for exemplary teaching, research and patient care and earned worldwide recognition for his own research on glaucoma. Many of his former students now hold prominent positions in academic ophthalmology throughout the country.

Becker has been an untiring and unselfish advocate for the School of Medicine, helping to advance both programs and facilities. He is especially appreciated for chairing the committee that oversaw design and construction of the library, completed in 1989 and named The Bernard Becker Medical Library in his honor earlier this year. The Becker Collection of rare books on ophthalmology and the visual sciences is a major component of the library’s rare book collection.

Paul O. Hagemann, M.D., is professor emeritus of clinical medicine at the School of Medicine. Whether as clinician, teacher, administrator or volunteer, he has been compassionate, dedicated and generous. His eloquent example and advocacy have been a major influence in engendering support for the school.

Hagemann has served the school in many volunteer posts, chairing class reunions and the Annual Fund and participating in other fundraising efforts. During 1955 and 1956, he was president of the Medical Center Alumni Association. He is a member of the school’s Eliot Society Membership Committee and until recently devoted many hours as chairman of Planned Giving.

Raymond H. and Roma Broida Wittcoff have been community leaders and major benefactors in St. Louis and to Washington University and the School of Medicine for many years.

Mr. Wittcoff chaired the mayor’s committee responsible for the founding of KETC, as well as the National Citizen’s Committee for Educational Television, which promoted non-commercial television throughout the country. Mrs. Wittcoff has served on many boards, among them the Opera Theatre of St. Louis, the St. Louis Symphony Society and the American Jewish Committee, as well as both local and national boards of the American Society for Technology. Mrs. Wittcoff is also an emeritus trustee of the Missouri Botanical Garden.

Following her first husband’s death, Mrs. Wittcoff established in his memory the Dan Broida Professorship in Operations and Manufacturing Management in the School of Business in 1984. Mr. Wittcoff established the Wittcoff Professorship in the School of Medicine’s Department of Biochemistry and Molecular Biophysics in 1989.

Both Wittcoffs are members of the School of Medicine’s National Council.
Medical Reunion Plans Underway

Registration materials with a detailed schedule will be mailed in January.

Calling All 1972 Internal Medicine House Staff

New Address For Alumni Office

Please note the new mailing address for Medical Alumni and Development Programs staff, who moved into new quarters Nov. 1. The new address: 4444 Forest Park Blvd., Box 8509, St. Louis MO 63108. The new phone number is (314) 286-0086; fax number is (314) 286-0066.
Robert S. Merrill, MD ’46, has retired after 38 years of federal service. He is now living in Appleton WI.

Kenneth R. Dirks, MD ’47, retired from the faculty of Texas A&M University College of Medicine August 31, 1995. He is now professor emeritus of pathology and laboratory medicine.

Grace (Mrs. T. Everett) Peters, HAP ’50, writes from St. Louis that she and her husband travel frequently. “We started when the children were out of diapers and took them to 49 states. We have been to 70 countries, many of them two or three times.”

Jack Wilson, PT ’53, has been elected chairman of the Children’s Services Operating Board of Alliant Health System in Louisville KY.

Philip S. Crossen, MD ’54, is retired but applying for a limited license in Florida so he can volunteer at Planned Parenthood in Naples.

Richard C. Braun, MD ’55, reports that he retired in September 1993. From September 1994 to March 1995 he was a volunteer physician at Tansen Hospital in Nepal and is presently a part-time public health physician in Tennessee.

Hubert C. Huebl, MD ’56, continues to practice general surgery at Oakwood Hospital in Dearborn MI.

Frank A. Riddick Jr., MD, HS ’57-’61, continues his role as CEO of Alton Ochsner Medical Foundation in New Orleans, but stepped down as head of Ochsner Clinic in 1993. He was elected to the AMA’s Council on Judicial & Ethical Affairs this year.

James C. Gaither, MD ’61, writes that he is still in Newton NC, with Rachel. He reports that they have four grandchildren and invites classmates to stop and visit.

Marilyn Foster, OT ’62, won first place in acrylic painting and third place in drawing at the Currahee Arts Festival in Toccoa GA.

John D. Rich, MD ’62, has been elected president of the Aurora-Adams County (Georgia) Medical Society for 1995-1996.

Pat Gregory Ceresoli, OT ’63, lives with husband, Ray, and daughter, Cristina, in Peoria IL. She teaches at Illinois Central College Occupational Therapy Assistants Program in East Peoria, consults in mental health occupational therapy and is working on a master’s degree in art therapy at Illinois State University in Normal.

Donald K. Chung, HS ’63-’67, a cardiologist in Long Beach, was among the dignitaries at the dedication of the Korean War Veterans Memorial in Washington D.C. in July. He donated the largest gift to the project — all money raised from the sale of his book, “The Three-Day Promise.” When he fled North Korea in 1950, Chung promised his mother that he would return in three days, but he was not able to do so until 1983, after she had died. He then vowed to write a book and dedicate it to her, designating the proceeds for the veterans monument. Sales of the book skyrocketed as a result of publicity in the syndicated “Dear Abby” column. Chung has since published a sequel, “Remembrances of the Forgotten War,” with profits designated for the Korea/Vietnam Memorial National Education Center in Pennsylvania.

Morton Glickman, MD ’63, is professor of diagnostic radiology at Yale Medical School and was recently appointed associate dean. He served as acting department...
chairman until Bruce McCellan, MD, a former Washington University School of Medicine professor, was appointed.

Charles A. Johnson, MD, HS '64-'69, writes from Sarasota FL, that he is recovering from a 1993 CVA.

Brian H. Gross, MD '65, is currently director of anesthesia at Vencor Hospital in Boston, the Fertility Center of New England in Reading MA (an I.V.F.-dedicated surgercenter facility), R.E.P.R.O. Woman's Care in Brookline MA, and Gynecare Woman's Care in Boston.

Gail Levine, OT '65, married Roger E. Moore on July 4, 1995. The couple resides in Glendale WI.

James E. Marks, MD '65, has been named as a fellow of the American College of Radiology in recognition of his outstanding contributions to the field.

M. Alan Permutt, MD '65, recently was awarded the International Diabetes Foundation's prestigious David Rumbough Scientific Award for his achievement in and commitment to diabetes research. Permutt is professor of medicine at Washington University.

Charles D. Setliffe, HA '65, retired as president/CEO of Wilson Memorial Hospital, Inc. in Wilson NC in 1991. He is now a consultant to Coastal Physicians Services, Durham NC and University Surgical Associates, Inc. in Chattanooga TN.

David G. Kemp, MD '67, recently joined the Easton (PA) Hospital staff in the Department of Medicine as the new director of the internal residency program. He formerly held the prestigious post of commanding officer of the Naval Health Sciences Education and Training Command, overseeing graduate medical education for the U.S. Navy. In addition, he served as the commanding officer of the Naval Hospital at Bethesda MD and most recently served as internal medicine consultant to the Surgeon General of the Navy.

Joel M. Karlin, MD '68, recently became president of the Colorado Medical Society. A member of the Colorado AMA delegation, Karlin was appointed to the AMA Council on Legislation.

'70s

Chauncey C. Maher III, MD '72, has returned home to Springfield IL, to practice there for after 70 years in Washington DC. He writes, "Emily went off to college this fall; Chauncey is a high school junior, and my twin sons are almost 2!"

Lary A. Robinson, MD '72, has been appointed director of the division of cardiovascular and thoracic surgery at the University of South Florida at Tampa. He and his wife, Susannah, as well as their two sons, Schuyler, age 4, and Joshua, 1, moved to Florida a year ago.

Raymond F. Cerand, HAP '73, of Seattle recently was elected governor of district seven of the American College of Healthcare Executives.

Harvey S. Glazer, MD '76, has been named as one of the 130 new fellows of the American College of Radiology.

G. Terry Hammons, MD '76, has a new position as vice president for performance improvement at The Johns Hopkins Hospital.

Richard Allen, HAP '78, recently was named chair-elect for the American Hospital Association's section for rehabilitation programs. He resides in Overland Park KS.

Thomas Dumler, MD '79, is assistant professor in the Department of Radiology at Baylor Medical College, chief and medical director of the Department of Radiology and chief of staff at Polly Ryan Memorial Hospital.

'80s

Thomas A. Rupp, HAP '80, has been promoted to colonel and assigned as commander of the 66th Medical Group at Hanscom Air Force Base in the Boston suburbs.

John D. Roberts, MD, GM '81, has completed 10 years on the research staff of the National Institute of Environmental Health Sciences in Research Triangle Park, NC. Lee Ann Roberts, MD '80, has spent this time in private Ob/Gyn practice in Raleigh. They have two sons, David, 15, and Brian, 10.

Brian C. Organ, MD '83, represented Crawford Long Hospital as the Young Surgeon of the Year for the State of Georgia at the American College of Surgeons annual meeting. Organ practices general surgery in Atlanta.

Howard J. Eisen, MD, HS '84-'87, is medical director of the heart transplant program at Temple University School of Medicine, the largest transplant program in the United States, and associate professor of medicine and physiology. His wife, Judith E. Wolf, MD, HS, is director of the residency program in the Department of Medicine at Graduate Hospital.

Paula Katharine Berman, OT '85, is a senior occupational therapist at Laurelwood Care Center, a 225 bed long-term care facility. She writes that she "enjoys Seattle, loves the rain, the flannel shirts and the mountains."

Gary R. Collin, MD '85, is presently associate director of trauma, Roanoke Memorial Hospitals, and a certified instructor of Fundamental Critical Care Support (FCCS), the only instructor in the State of Virginia.

Jill S. Huppert, MD '85, is now on the faculty at the University of Cincinnati in the Department of Obstetrics and Gynecology. She is also residency coordinator. Her husband, Brian E. Volck, MD '85, works at a community health clinic and "struggles daily with health care reform." Sons Will, 6, and Peter, 2, are thriving in Cincinnati's "green and wet climate."
Carla Cay Niemeyer, OT '85, married David P. Williams in July 1993. She is the owner/operator of Kidpower Therapy Associates, a pediatric therapy private practice that provides occupational therapy, physical therapy and speech/language therapy for children in Albuquerque NM.

Lyn McDuffit Duncan, MD '86, is director of Harvard Medical School's dermatopathology training program, living in Cambridge with husband Tim, daughter Micki, 6, and son Elias, nine months.

Susan Mendelson Markman, HAP '86, and Scott Markman, BFA '81, became parents of a son, Leland, on April 8, 1995.

Lisa Ann Ferguson, PT '88, is practicing in Largo FL. Her husband, Peter, whom she married in November 1991, is a computer sales representative for Tech Data Corporation.

Yin Yin Lim, MD '88, writes that she and her husband, Ajith Kumar, MD '86, have two "wonderful" children, Priyanka, 3 1/2 years old, and Alex, 2 years, 2 months. They moved to Philadelphia in July where Kumar will finish a cardiology fellowship at the University of Pennsylvania.

Glenn Shopper, MD '88, is having a good time with Lisa, raising kids (Daniel, 3 1/2, and Molly, 7 months) grilling dinners and growing fescue.

Kamil Dostalik, PT '89, has a daughter, Sandra, born on May 8, 1993.

John Christopher Lang, HAP '89, moved in November to Sheboygan WI to become director of ambulatory services at St. Nicholas Hospital. The Langs have a new addition to the family, Hannah Marie Lang, born on August 22, 1995.

**'90s**

David Lee Knocke, HAP '90, has returned to St. Louis as regional administrator of SSM occupational medicine. He is married and has one child, Elizabeth, now 2 years old.

Lawrence L. Yee, MD '90, writes that he currently is in private practice in San Jose CA, following four years in the military at Walter Reed Army Medical Center.

Jane Burton, PT '91, is working at Children's Hospital in Birmingham. She started a cystic fibrosis PT program and is organizing a PT program in the neonatal intensive care unit.

Katherine A. Conrad, HAP '91, is a senior consultant with KPMG's National Healthcare Strategy Practice in Kansas City MO.

Neil Worrall, MD '91, reports that Dawn, Neil, and big sister Emily welcomed Peter Nelson Worrall on September 13, 1995. They live in Chesterfield MO.

Capt. Julie Hall, HAP '92, USAF in Almagordo NM, has been promoted to major. She will do an internship at Johns Hopkins in Baltimore in August 1996.

Angie Wright, OT '92, married Tim Knapp on August 13, 1995. They reside at 7502 County Road 53, Lewistown OH 43333.

David Councilman, MD '93 and Robin Councilman, MD '93, are in their third year of residency in the family practice program of Hennepin County Medical Center in Minneapolis.

Amy Bolden, PT '94, works in rehabilitation at St. Francis Medical Center in Pittsburgh.

**IN MEMORY**

Elizabeth Thompson Koppenaal, MD '24, died August 19, 1995, at the age of 99 in her home in Lombard IL. She was one of four women in her medical class, choosing medicine as a career because she believed in community service. She was a founding fellow of the American College of Obstetricians and Gynecologists.

Melvin A. Roblee, MD '25, died on September 28, 1995, in Richmond VA. He was in private practice in St. Louis for almost 50 years and was professor emeritus of obstetrics and gynecology at the School of Medicine. Among the survivors are his wife, Elizabeth Barker Roblee, a daughter, Elizabeth Roblee Smylie of Richmond, and a son, the Rev. Melvin Barker Roblee of Perry IA.

Robert C. Treiman, MD '29, died September 29, 1995. He was chief of the outpatient clinic at Missouri Pacific Hospital until his retirement in 1975. He is survived by his wife, two daughters, four grandchildren and five great-grandchildren.

Edna Heman, NU '31, died of cancer on July 29, 1995, at the age of 85. She had worked at St. Louis Children's Hospital for more than 40 years prior to her retirement in 1974, and had spent most of that time as supervisor of night nurses.

Ellen Leffel, MD '35, one of the first female obstetric-gynecologists in the St. Louis area, died August 15, 1995. She was in private practice in the city for almost 40 years and was an advocate for girls and young women. A past president of the Women's Physicians Association of St. Louis, she retired in 1977. Among the survivors are her husband, a daughter and three grandchildren.

Ralph B. Woolf, MD, former professor of obstetrics and gynecology, died February 2, 1994, after suffering from cancer. He was 79. Woolf joined the faculty as an instructor in 1941 and was appointed a full professor in the 60s. He left the medical school in 1972 to pursue a master's degree in public health at the University of Michigan. From 1976 until 1982, he was a professor at Case Western Medical School in Cleveland. He retired in 1982. Among his survivors are his wife, Esther, two daughters and three grandchildren.
Gustav Schonfeld, M.D., William B. Kountz Professor of Medicine, right, spoke on behalf of the School of Medicine in welcoming Mark S. Wrighton, Ph.D., as the University’s 14th chancellor during his inauguration on Oct. 6.
The pedestrian bridge that crosses Children's Place provides an opportune vantage point from which to capture the Medical Center. For more interesting perspectives, turn to page 20.