Outlook
Washington University School of Medicine
Spring 1994

Anti-Adhesives  Bacterial Resistance  Transplant Tolerance
First Lady Hillary Rodham Clinton visited the School of Medicine on March 15, learning firsthand about the merits of exercise for older people when she met with members of the school's Exercise and Aging Program (above). In a small group session hosted by William A. Peck, M.D., she also heard from students, faculty and staff regarding the special attributes of academic health centers. Later in the day, Mrs. Clinton delivered a 30-minute address on healthcare reform to a crowd in the Field House.
THE COVER

To test the efficacy of antibiotics, microbiologists apply clinically approved drugs (on the small white disks) to bacterial cultures. Results like those on the green plate at the top show that antibiotics have killed or inhibited the resident bacteria. As bacterial resistance to antibiotics has emerged, results have begun to resemble those of the green and red plates on which none of the drugs applied had an effect. For more, see the story beginning on page 16.

Photograph by Tom Heine.

FEATURES

Sticky Business 8
Researchers pinpoint the receptor for an ulcer-causing bacteria. New therapies may follow.

Pieces Of The Immunological Puzzle 12
Looking for transplant tolerance; defeating chronic organ rejection.

Emerging Resistance 16
When bacteria respond to pressures in their environment, miracle drugs lose their punch.

A Cooler Heart 21
Lowering blood temperature protects surgery patients from spinal cord ischemic injury.

DEPARTMENTS

People 2
Events 4
Research 6
Silhouette 24
Student Stage 26
Alumni Report 28
Class Notes 31
Chancellor Danforth Announces His Impending Retirement

WILLIAM H. Danforth, M.D., chancellor of Washington University, has announced that he will retire June 30, 1995.

Danforth joined the Washington University faculty in 1957 as an instructor at the medical school after serving his internship in medicine at Barnes Hospital and his residencies in medicine and pediatrics at Barnes and St. Louis Children's hospitals between 1951 and 1957. He was named assistant professor in 1960, associate professor in 1965 and full professor — a position he still holds — in 1967.

In 1965, he was appointed vice chancellor for medical affairs. In 1971, he was appointed chancellor, succeeding the late Thomas H. Eliot. He is the 13th chancellor to lead the university since it was founded in 1853. His tenure, nearly 23 years, is one of the longest among active educational leaders.

“The last two decades have been remarkably good to Washington University,” says William M. Van Cleve, chairman of the Board of Trustees. “Bill and Iby have worked tirelessly for the university, for its faculty, its students and its alumni. St. Louis is fortunate to have here one of the world’s great teaching and research universities — one that has accelerated its growth and prosperity in stature and quality under his leadership. The hallmarks of the Danforth era are attracting and retaining outstanding people and managing our resources superbly.”

The Board of Trustees soon will appoint a search committee of trustees, faculty, students and alumni to seek input from all constituencies of the university in the nationwide search for Danforth’s successor.

Physicians’ Advocate

JAMES Crane, M.D., associate vice chancellor and associate dean for clinical affairs at the medical school, has been named to the newly created position of executive vice president for medical affairs for BJC Health System. The position is one of several changes in recent administrative restructuring.

Crane, whose responsibilities in medical school administration will remain the same, will serve as an advocate for the medical staff and provide physicians a strong voice within the BJC Health System. Crane, a quality committee chairman of the Greater St. Louis Health Alliance, also will oversee development of uniform clinical outcome measurement tools.

Creation of the new medical affairs position resulted in part from conversations between William A. Peck, M.D., executive vice chancellor and dean of the medical school, and Fred Brown, president and CEO of BJC, regarding the need for a comprehensive approach to involving physicians in the evolving BJC Health System.

“Jim has done a tremendous job coordinating the clinical affairs area within the school and in shepherding the development of the Washington University Physicians Network,” says Peck. “We're certain his skills, knowledge and talents will be especially valuable to the BJC Health System, which is tied to the school through Barnes and Jewish hospitals, our close partners in the

Olin Fellows Named

Fourteen medical students have been named 1993 Spencer T. and Ann W. Olin Medical Scientist Fellows. They are: (seated, left to right) Russell Johnson, Patrick Jay, Maria Mariencheck, Michael Kolodney, Gregory Mathews, Charles Roberts, (standing, left to right) Christopher Nelson, Iris Chan, Joseph Smith, Thomas Deckwerth and Ilka Warshawsky. Not pictured are Bruce Sachais, Deborah Veis and Jason Kimata. Recognized for achievement in biomedical research, Olin Fellows look forward to outstanding careers in medically relevant areas of basic science. The fellowships are funded by a $30 million commitment to the Division of Biology and Biomedical Sciences made in 1986 by the Spencer T. and Ann W. Olin Foundation.
Washington University Medical Center.

The system also selected a new name. The integrated healthcare delivery system created by Barnes and Jewish hospitals and Christian Health Services has been named BJC Health System.

The new name and logo have begun appearing in publications and advertising as well as on name badges and signs.

### DiPersio Directs New Division

**John F. DiPersio, M.D., Ph.D.**

DiPersio, who joined the faculty as an associate professor of medicine, came from the University of Rochester, where he was an assistant professor of medicine and director of the Strong Memorial Hospital bone marrow transplantation center since 1990. He also conducted research on pharmaceuticals to enhance transplant patients' immunity and growth factors to speed up recovery of patients' white blood cells after transplantation.

### Waterston Heads Genetics

**Robert H. Waterston, M.D., Ph.D.,** has been named James S. McDonnell Professor and head of the Department of Genetics at the School of Medicine.

The McDonnell Professorship in genetics was established in 1975 through gifts from the late James S. McDonnell and the McDonnell Foundation.

Waterston's research focuses on muscle development and finding and sequencing genes of the nematode, C. elegans. This work, part of the larger international effort to map the human genome, also is considered by many to be crucial in developing the tools and know-how to find and sequence the full complement of human genes. An associated goal of developing software and automation procedures to expedite DNA sequencing also is underway.

In addition to the C. elegans project, Waterston is helping to complete the genetic sequence of the yeast, S. cerevisiae.

### Cream Of The Crop

**John F. DiPersio, M.D., Ph.D.**

The book, which includes 95 medical school physicians, was compiled by asking doctors across the country to recommend a specialist to whom they would send a relative or friend if they needed care. After one year and more than 13,000 phone calls and 11,000 letters, 7,200 physicians were selected in more than 350 areas of medical expertise.


### New Division, New Director

**Daniel C. Ihde, M.D.,** former deputy director of the National Cancer Institute (NCI), now directs the new division of medical oncology within the Department of Medicine. Ihde, who joined the School of Medicine faculty as a professor of medicine, also will direct the Barnard Cancer Center.

**Daniel C. Ihde, M.D.**

Ihde had worked at the NCI for 20 years. He became a senior investigator at the NCI Veterans Administration Medical Center in 1975 and later was named deputy chief of the Naval Medical Oncology Branch at the National Naval Medical Center.

### Dacey To Preside

**Ralph G. Dacey, Jr., M.D.,** professor and head of neurological surgery, has been named president-elect of the Congress of Neurological Surgeons. Founded in 1951, the neurosurgical organization has more than 3,000 members. The Congress promotes and supports the continuing education of young neurosurgeons in the United States and overseas.

Dacey served as treasurer of the Congress from 1990 to 1993. His term as president begins in October.
The chair was established by Richard A. Sutter, M.D., and his wife, Elizabeth Henby Sutter, who donated $1 million toward its support. The Sutters are graduates of Washington University’s College of Arts and Sciences class of 1931. Sutter received his medical degree from the School of Medicine in 1935 and is a pioneer of occupational medicine.

Bradley Evanoff, M.D., who received his medical degree from Washington University, is a former instructor in the Occupational and Environmental Medicine Program at the University of Washington in Seattle. He is the first incumbent of the endowed chair which supports the study and treatment of work-related injuries and illnesses.

Richard A. Sutter, M.D., (second from left) and Elizabeth Henby Sutter are joined by William A. Pock, M.D., John Atkinson, M.D., and David M. Kipnis, M.D., at the announcement of the Sutter Chair.

“Individuals and families affected by psychiatric illnesses often ask what the genetic connections mean to them. We can determine their risks, and we can explain what this means,” Moldin says. “We can then offer people support to deal with the stress and challenge associated with having a family history of mental illness.”

Harvey A. and Dorismae Hacker Friedman have donated $1 million to the School of Medicine to establish an endowed chair within the Department of Internal Medicine. The chair will serve to foster initiatives in the field of human genetics and will support clinical, educational and research activities. At this time, the position has not been filled.
Louis Simchowitz, M.D., professor of medicine and vice chairman for research affairs in the Department of Internal Medicine, who is on the committee to establish the division, says the chair will be instrumental in furthering efforts to create a center for human genetics. The new center will involve numerous departments from within the School of Medicine. Currently, faculty from the departments of genetics, pediatrics, pathology and medicine are pooling resources to develop the division. But Simchowitz says that the project could ultimately involve other departments with interests in human genetics.

The division has not been formally named, but it will be housed in the former Dental School building, where Simchowitz says 8,500 square feet of space has been committed.

The Friedmans, members of the Eliot Society, have long been active in the St. Louis and Washington University communities.

On Domestic Violence

SECOND-year medical student Hilarie H. Cranmer has launched an organization for medical students and healthcare workers in St. Louis to increase the awareness of domestic violence.

Cranmer says the goals of the organization, called Domestic Violence Action or D-VA, are six-fold: to change the educational curriculum at the School of Medicine to include domestic violence in both clinical and psychiatric evaluations; to educate the healthcare community with a symposium on domestic violence that will provide continuing medical education credit; to provide opportunities for medical students to become involved through volunteer work at local shelters for battered women and various outpatient facilities at Barnes Hospital; to develop an up-to-date resource list of local shelters and hotline numbers for victims of violence, and to hold letter writing campaigns to local, state and federal politicians to increase awareness and provide incentive for the introduction of legislation to reduce domestic violence.

Cranmer’s interest in domestic violence was sparked after she heard experts discuss the subject at an American Medical Women’s Conference last year. She fueled that interest by serving as a research assistant for an emergency room physician at Boston City Hospital who is studying domestic violence.

Cranmer says faculty and students have been supportive of the group’s efforts. Already, several faculty members have agreed to discuss some aspects of domestic violence in their lectures to first- and second-year medical students.
A Neonatal Brain Disorders Center is being established at the Medical Center with a $1.5 million grant from the National Institute of Neurological Disorders and Stroke. The center will include investigators from the departments of psychiatry, radiology, biostatistics, pediatrics, obstetrics/gynecology, chemistry, occupational therapy, neurology and neurosurgery.

Researchers will examine several potential mechanisms of brain injury in newborns, including those that result from an insufficient supply of oxygen or nutrition to the brain. Also planned is an effort to develop techniques for evaluating newborns at risk so that babies who will benefit from new therapies can be identified early.

"Right now, it's very hard to determine whether experimental treatments that we might want to use will have a beneficial effect," says Steven M. Rothman, M.D., program director of the grant and the A. Ernest and Jane G. Stein Professor of Developmental Neurology in Neurology, Pediatrics and Anatomy and Neurobiology. Coprincipal investigators are T.S. Park, M.D., professor of neurological surgery, and F. Sessions Cole, M.D., professor of pediatrics.

Collaborators in the Neonatal Brain Disorder Center will include radiologist Benjamin Lee, M.D., (left) and pediatric neurologist Jeffrey Neil, M.D., Ph.D.

Researchers will examine several potential mechanisms of brain injury in newborns, including those that result from a supply of oxygen or nutrition to the brain. Also planned is an effort to develop techniques for evaluating newborns at risk so that babies who will benefit from new therapies can be identified early.

"Right now, it's very hard to determine whether experimental treatments that we might want to use will have a beneficial effect," says Steven M. Rothman, M.D., program director of the grant and the A. Ernest and Jane G. Stein Professor of Developmental Neurology in Neurology, Pediatrics and Anatomy and Neurobiology. Coprincipal investigators are T.S. Park, M.D., professor of neurological surgery, and F. Sessions Cole, M.D., professor of pediatrics.

Collaborators in the Neonatal Brain Disorder Center will include radiologist Benjamin Lee, M.D., (left) and pediatric neurologist Jeffrey Neil, M.D., Ph.D.

A large international trial has concluded that a drug frequently used to control high blood pressure may dramatically improve the fate of insulin-dependent diabetics with kidney disease.

Researchers from the medical school, Rush Presbyterian-St. Luke's Medical Center in Chicago and more than two dozen other centers in North America took part in the testing of the drug captopril, an angiotensin converting enzyme, or ACE inhibitor. Treatment with the drug reduced by 50 percent the risk of death or rapid progression to end-stage renal disease — characterized by the need for dialysis or kidney transplantation.

Coinvestigator Janet McGill, M.D., assistant professor of medicine, says the study provides solid evidence that progression of kidney disease can be slowed in insulin-dependent diabetics. "The benefits of the therapy speak for themselves," McGill says. "We now have therapy that can offer these patients hope for..."
both longer life and better quality of life."

The study was conducted at 30 centers in the United States and Canada. It involved 409 patients between the ages of 18 and 49 who had developed insulin-dependent diabetes prior to the age of 30. Those enrolled were diagnosed with early diabetes-induced kidney disease identified by the presence of protein in their urine. About 75 percent of the patient group also had high blood pressure.

Captopril therapy delayed the progression of diabetic kidney disease in all study patients, and the benefit was independent of its blood pressure lowering effect. While all patients with high blood pressure were treated with antihypertensive therapy, those who received captopril experienced improvement in survival and reduced development of end-stage renal disease.

**To Screen Or Not To Screen?**

THE Medical Center is one of 10 centers participating in a large-scale study to determine whether the widespread use of screening tests for cancers of the prostate, lung, colorectum and ovary can save lives.

The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) will enroll 16,000 men and women volunteers ages 60 to 74 in the St. Louis area. Screening tests will be administered at Barnes West County Hospital.

Nationwide, 148,000 men and women ages 60 to 74 will participate in the study. The $87.8 million study is being funded by the National Cancer Institute.

"Despite the use of screening tests for prostate, lung, colorectal and ovarian cancers, there is no scientific proof yet that screening for these particular cancers actually saves lives," says Gerald Andriole, M.D., associate professor of urologic surgery and the principal investigator in St. Louis. "This study is designed to find out whether screening leads to early cancer detection and whether early detection, followed by aggressive treatment, actually reduces cancer deaths."

Together, prostate, lung, colorectal and ovarian cancers account for 43 percent of the cancers diagnosed each year in the United States and 48 percent of the annual cancer deaths. This year, 500,000 Americans will be diagnosed with either prostate, lung, colorectal or ovarian cancer, and about 250,000 will die of these diseases.

**An Aspirin A Day: The Gender Gap**

ASPIRIN'S ability to help break up blood clots is less potent in women than in men, according to a report by researchers here.

The study provides the first evidence that may explain why daily aspirin is more protective for men than women in preventing heart attack and stroke.

"This study is important because it gives us a hint about why women seem to respond differently to aspirin than do men. It is likely to open up a new area of inquiry," says Allan Jaffe, M.D., professor of medicine and principal investigator of the study.

Jaffe and his colleagues gave six men and six premenopausal women one aspirin (325 mg) a day for a week. In lab tests, the investigators used a natural clot buster to break apart, or lyse, blood clots. They measured the rate of clot lysis for each person at the start of the study and again after one week of treatment with aspirin. In men, the rate of lysis increased in response to aspirin, but no such change occurred in women.

Jaffe says that when similar tests are performed by adding aspirin to blood after it is drawn, no gender differences are found. "There is something about how aspirin is processed by men and women after it is ingested that is key to these gender differences," he says.

As a result of clinical studies performed primarily in men, low-dose aspirin is commonly recommended for heart attack and stroke prevention in people at risk for cardiovascular disease. But several large clinical trials have found that women may not gain the same benefits as men, Jaffe says. To find an explanation, investigators have looked for gender differences in the cells that line blood vessel walls and in aspirin's effect on platelets. Until now, differences had not been reported, Jaffe says.

"We don't know of any previous biochemical evidence to suggest why there should be differences between men and women," Jaffe says. He and his colleagues plan to continue the research in a larger group of patients and with higher aspirin doses.
Doctors have been aware for decades that people with type O blood are more likely to develop stomach ulcers than those with blood types A or B. Missing has been an explanation for this phenomenon.

Last year, when researchers at the School of Medicine pinpointed a natural target receptor for Helicobacter pylori, a bacterial pathogen that is believed to cause gastritis and some ulcers and may cause stomach cancer, the answer to the conundrum finally became apparent.
The bacterium's portal of entry is a blood group determinant found in abundance in people with type O blood. That determinant — the Lewis b (Le\(^b\)) blood group antigen — is a carbohydrate structure that protrudes from cells lining the stomach's surface, says the study's lead author, Thomas Borén, L.D.S., Ph.D., a National Institutes of Health Fogarty Fellow in the Department of Molecular Microbiology.

*Helicobacter* forms an intimate bond with the Lewis\(^b\) antigen. Once the bacterium is in place in the stomach, it is substantially anchored and ready to weather years of assault from acids and digestive enzymes. The bacteria's capacity to survive and thrive in its hostile setting is a matter of importance for scientists and physicians, because peptic ulcers affect nearly 4 million Americans and many millions more worldwide.

Among those concerned is Staffan J. Normark, M.D., Ph.D., former head of the Department of Molecular Microbiology and now a research professor in the same department. Normark and Borén believe that, despite its reputation as a tough customer in some patients, *Helicobacter* might be vulnerable to a new generation of drugs that curtail its sticky nature. Anti-adhesives, as the new structures are called, interfere with the invading bacterium's ability to bind to its receptor. If *Helicobacter* can't bind to the Lewis\(^b\) antigen, Normark believes it won't be able to cause disease and distress.

Why did it take so long for scientists to find a cell receptor for *Helicobacter* and, with it, a plausible explanation for the link between type O blood and ulcers? Part of the reason is that for most of the 40 years, physicians were unaware that a bacterium could be the cause of ulcers. Common wisdom during those years said that most ulcers were caused by increased acid production, decreased duodenal bicarbonate production and a volatile mixture of genes, temperament and stress. Inherit or develop the wrong combination, and ulcers are a higher risk to form.

Then, in 1982, Barry Marshall, M.D., and his colleagues at the Royal Perth Hospital in Australia isolated a corkscrew-shaped microorganism, *Helicobacter pylori*, from human stomach tissue and proposed that gastritis and ulcers were kindled by infection with *Helicobacter* — a persistent, simmering infection that produces chronic superficial inflammation of the stomach, leaving it vulnerable to injury. One early skeptic of the proposal, Washington University gastroenterologist David H. Alpers, M.D., professor of medicine, says that he and many of his colleagues began to take the theory more seriously when compelling scientific data on the response of ulcers to antibiotic eradication therapy became available.

Many physicians, however, may have been reluctant to accept the new *Helicobacter* theory. The struggle for recognition and acceptance of the *Helicobacter* theory has been — and still is — a matter of debate in the popular media worldwide, in addition to medical journals.

In 1984, when opposition was strong, Marshall was so convinced he was correct that he tried out a proof on himself by ingesting a beaker of *Helicobacter*, Borén says. The experiment worked — Marshall developed a bad case of gastritis almost immediately — but some questioned his quaffing a potentially dangerous brew. More troubling, in Alpers' opinion, was the way the media covered the debate, making it seem that the medical establishment was snubbing or ignoring this emerging theory and its proponents. Alpers now says he thinks the *Helicobacter-*
ulcer link is one of the most outstanding discoveries in this century in gastroenterology: "Many people in the profession feel it should get the Nobel Prize."

"In fact, under many circumstances it makes sense to treat with both antibiotics and antisecretory drugs, because the H-2 antagonist treats symptoms, and the antibiotic eradicates the organism. If it takes four or five days for the ulcer to start to heal while you're treating the organism — and you're hurting those four or five days — that seems crazy."

Although inexpensive, antibiotics are not without problems. Bacteria can develop drug resistance, creating mutant strains that cannot be killed by current pharmacopoeia. (See the related story in this issue.) There is also evidence that some antibiotics may not penetrate far enough into the stomach lining where the bugs are burrowed.

Borén and Normark believe the time is right to go a step beyond antibiotics to develop new treatments that target bacterial adherence, the first step in the infection process. One of the postulates of modern molecular microbiology is that bacteria don’t stick to tissues by chance. They are "destined" to infect specific tissues, says Per Falk, M.D., Ph.D., an instructor in molecular biology and pharmacology.

Finding out why one strain of E. coli prefers the urinary tract while H. pylori prefers the gut is the kind of bench work done in the Department of Molecular Microbiology. Largely because of the microbiologists' efforts, all scientists have a better
understanding of the concept of tropism, the unseen forces that direct microbes to select one type of tissue over another.

Using various strains of Helicobacter provided by gastroenterologist Ray E. Clouse, M.D., associate professor of medicine, and others gathered from as far away as Sweden and Peru, Normark, Borén and Falk began their task of defining how the bacterium attaches to cells in the stomach. A key component of the attachment, the group found, is a carbohydrate receptor that pokes from cells in the stomach lining. They demonstrated that the bacteria recognize this receptor and anchor themselves on cells. Examining the carbohydrate, Borén found that it was the Lewis$^b$ antigen, a carbohydrate known to define blood type.

This critical piece of information helps explain the old epidemiological data showing that ulcers are more common among individuals with type O blood. Lewis$^b$ antigen is found in higher concentrations in people with type O blood. "This suggests that blood group O individuals have more receptors available for Helicobacter attachment than people with type A or type B blood," says Falk.

In addition, the studies showed that human breast milk contains Le$^b$ antigens that can act as natural "anti-adhesive" carbohydrates that interfere with $H. pylori$ attachment to human cells. These carbohydrates could scavenge Helicobacter before it can reach receptors in the stomach, Borén says. The group found variations in the quantity of Le$^b$ antigen in the samples studied, suggesting that some children may be more protected than others against Helicobacter infection depending upon their mother's breast milk. Helicobacter infection is much more common in developing countries, Normark says, so these data indicate that children in Third World countries should be breast fed if possible.

The breast-milk finding could provide nature's blueprints for anti-adhesive drugs. Normark and Borén are working in collaboration with the Swedish pharmaceutical companies Astra and Symbicom to further define how Helicobacter binds to its receptor. Detailed studies of the interaction between the bacterium and its carbohydrate receptor could provide new drugs that would bind to Helicobacter and thereby prevent the bacterium from binding to its natural receptor. In the future, says Borén, it might be possible to put specially designed carbohydrates in baby food or in infant formula to prevent bacterial colonization and infection by blocking the binding regions in the ingested bacteria before they get to the cells.

Such a remedy already appears to be in popular demand. When news of the Helicobacter receptor's discovery made its way around the world last December, many people called the School of Medicine looking for the new drugs. Most of the people calling had type O blood, and they had ulcers.

The Microbe Hunters

Many "forgotten" diseases like tuberculosis and whooping cough are making a surprising comeback. And most of the bacterial or viral pathogens that cause plagues, epidemics or even sporadic outbreaks are underestimated by the public, and sometimes by the medical profession.

At Washington University School of Medicine, a special group of researchers is deadly serious about human pathogens. Nearly 40 investigators from all corners of the Washington University campus form the team known as the Center for Host-Pathogen Interactions.

Led by codirectors Eric J. Brown, M.D., professor of medicine, and Charles M. Rice, III, Ph.D., professor and interim head of molecular microbiology, this diverse team specializes in molecular studies of some of humankind's most lethal microbes. The group has achieved international recognition for unveiling the survival strategies of many different microorganisms, including those responsible for malaria, sepsis, tuberculosis, leishmaniasis, hepatitis C, whooping cough, strep throat, pneumonia, meningitis, influenza, histoplasmosis and herpes, among others.

Researchers in the center also seek ways to apply information learned about microbial survival to the development of new drugs. The center's location in the Medical Center gives its scientists access to clinical tests involving the latest experimental treatments. Such cooperation between clinicians and researchers may lead to a new generation of drugs that target the most vulnerable stages in an organism's life cycle.
The immune system, with its network of backup and fail-safe mechanisms, rarely falters in its main mission — distinguishing “self” from “nonself,” friend from foe. But the system’s unrelenting ability to identify and destroy what is alien frustrates organ transplant surgeons. Their patients, destined to receive a lifelong regimen of anti-rejection drugs, pay a high price for this extraordinarily efficient surveillance system.

Despite the modern success of organ transplants, no simple method exists for tricking a transplant patient’s immune system into gracefully accepting a donor organ. Transplants succeed because powerful anti-rejection drugs suppress the immune system’s ability to respond to all that is foreign — donor tissue cells, cancer cells and disease-causing microorganisms alike. For that reason, overwhelming infection is a leading cause of death in transplant recipients.
The emergence of more potent anti-rejection drugs in the past decade has improved the success of organ transplants. But chronic organ rejection, which can occur for months to years following transplantation, remains a major problem.

"Patients with chronic rejection invariably lose their grafts, and there's nothing we can do for them except try to find another organ and transplant again," says Todd Howard, M.D., assistant professor of surgery and director of the liver and kidney transplant programs at Barnes Hospital. "There is no known therapy and no way to predict which patients will undergo chronic rejection and which patients will be spared."

Researchers at the School of Medicine are investigating the cellular and molecular interactions within the body that allow some patients to have successful organ transplants. Precise manipulation of the immune system's ability to recognize donor tissue without diminishing its capacity to respond to other immunological challenges is their goal. The scientists speculate that inducing a state of "transplant tolerance" in organ recipients would reduce acute and chronic rejection and patients' reliance on immunosuppressive drugs.

The Washington University group, led by T. Mohanakumar, Ph.D., professor of surgery, of pathology and of medicine, recently received a $2 million, four-year program project grant from the National Institute of Allergy and Infectious Diseases to study how the immune system responds to and tolerates transplants. "The eventual loss of an organ is an issue for almost all types of organ transplants," says Mohanakumar. "By investigating ways to induce transplant tolerance in the laboratory, we hope to improve the success of all transplants," he says.

Mohanakumar and Howard are studying tolerance in liver transplant patients; Wayne Flye, M.D., Ph.D., professor of surgery, immunology and of molecular microbiology, and Ted Hansen, Ph.D., professor of genetics, are investigating different ways of inducing transplant tolerance.

**Understanding Tolerance**

Researchers know that a set of genes that orchestrate the production of personal molecular identity markers on the surface of the body's cells plays a crucial role in determining the fate of organ transplants.

This set of genes, called the major histocompatibility complex, or MHC, is unique for each person, except identical twins.

Following an organ transplant, the donor's unique identity markers are detected by a subset of the immune system's white blood cells in the recipient's body called helper T cells. Once alerted, helper T cells signal to B cells and killer T cells. B cells make antibodies to speed the destruction of transplanted tissue and killer T cells attack the graft.

Using blood samples provided by Howard's patients who received liver transplants at Barnes Hospital, Mohanakumar and coworkers in his laboratory are investigating why some transplants are tolerated better than others.

Liver transplant patients provide an opportunity for researchers to study transplant tolerance. Unlike recipients of other organ transplants, liver transplant patients usually do not have a major problem with chronic rejection. Researchers have made that observation only in the past several years as more patients have successfully undergone liver transplants. In 1980, only 30 percent of liver trans-
plant patients survived more than a year following surgery. Now, the one-year survival rate has increased to nearly 80 percent nationwide.

Liver transplant patients still encounter problems with acute rejection, which occurs soon after transplant. But unlike chronic rejection, acute rejection can be treated successfully with anti-rejection drugs. Researchers don't yet know why liver transplant patients are less susceptible to chronic rejection.

"But if we can understand why they are doing so well, then we can apply what we learn to other types of transplant patients," Mohanakumar says. "Perhaps there are ways to induce a similar tolerance in kidney, heart and lung transplant patients."

Preliminary research in his laboratory has uncovered some important hints.

Blood samples examined by Mohanakumar revealed an unusual unresponsiveness by each of the liver transplant recipients to their respective donor antigens during the year after transplantation. When he looked closer, Mohanakumar noted the mysterious disappearance of a subset of killer T cells between five and 12 months after patients received liver transplants. In each instance, the missing killer T cells were those designed to respond specifically to the donor's antigens.

The patients' immune systems each showed evidence of adequate killer T cell function to antigens from other donors. In all cases, helper T cell function remained normal.

"The disappearance of cytotoxic (killer) T cells is unique to liver transplant patients," says Mohanakumar. "This does not happen in kidney, heart or lung transplant patients. We don't know why it happens; that's what we're hoping to learn."

In related studies, he has found that patients with successful long-term liver transplants make antibodies to their own T cells. Mohanakumar hopes to learn whether these particular T cells are involved in recognition or destruction of the donor cells. Either way, the antibodies may play an important role in down-regulating the immune system, he says.

Patients with successful liver transplants also have large amounts of donor MHC in their bloodstream. In samples of blood from 12 patients, 10 had large amounts of the donor MHC in their blood shortly after transplantation. The two patients in whom donor MHC was absent lost their grafts.

"We believe that the development of antibodies against a patient's own donor-reactive T cells and the large quantities of donor MHC antigens in the blood of liver transplant patients may play an important role in inducing specific tolerance to their grafts," Mohanakumar says.

**Training T Cells**

While Mohanakumar endeavors to define the mechanisms of liver transplant tolerance, Flye and Hansen are working to determine the mechanisms of transplant tolerance in animal models.

Flye investigates how tolerance occurs in rats undergoing heart transplants. Before transplantation, he induces tolerance by injecting donor spleen cells into the thymus of rats. T cells mature in the thymus and it is there that immature T cells learn to distinguish what is foreign from what is self.

Flye hopes the injections will educate immature T cells to recognize donor cells as self, thereby eliminating the body's ability to mount a specific immune response to donated organs. Preliminary results look promising. One study compares the success of heart transplants in rats with different MHC makeups that received injections of donor spleen cells and anti-lymphocyte serum (ALS) with other rats that did not. The ALS eliminates mature T cells circulating in the blood.

In rats that did not receive injections, the heart transplants survived about seven days. However, the heart transplants lasted indefinitely in animals that received the injections. Injections of either donor spleen cells alone or anti-lymphocyte serum alone also did not improve graft survival.
"These results may indicate that T cells that would have recognized the donor tissue are being deleted or inactivated as they mature in the thymus," Flye explains. "Only those T cells that do not recognize the donor cells as foreign are surviving."

While these cellular injections worked well for heart transplants, they were not successful in significantly prolonging the survival of kidney or skin grafts. That may be because the donor spleen cells do not carry the necessary, organ-specific antigens responsible for inducing tolerance for kidney and skin grafts. Flye and his coworkers are now working to find donor cells that carry the right antigens.

More research is needed before this therapy can be used in humans. Researchers must find ways to rejuvenate the thymus, an organ that produces virtually all the T cells needed during infancy and childhood. By puberty, the human thymus, unlike that in the rat, has atrophied. However, hormone stimulation can increase T cell traffic through the thymus.

Flye's work gives researchers a better understanding of how the immune system may be regulated to achieve tolerance to a specific organ donor.

**Blocking Recognition**

On a related front, Hansen's laboratory strives to induce transplant tolerance in mice by blocking the interaction between the recipient's T cell receptors and the donor's molecular identity markers, or MHC molecules. Without recognition of the donor MHC, the cascade of immunological events that leads to rejection can be prevented, he says.

Hansen and his coworkers have successfully blocked T cell recognition in mice undergoing skin transplants by injecting synthetic peptides into the animals. The peptides are derived from a subset of the recipient's T cell receptors responsible for recognizing donor MHC molecules.

"If you don't have recognition, you have nothing," Hansen explains. "We're essentially knocking out the brains of the immune system, which is exactly what you want to do."

In preliminary studies, Hansen speculates that the synthetic peptides dramatically prolonged the survival of skin transplants in mice by binding to the donor's MHC molecules, thereby preventing their binding to the donor's T cell receptors.

In order to continually block T cell recognition, the researchers must inject the synthetic peptides into the mice every three days. "That's the trouble with the therapy," Hansen says. "We need massive amounts of peptides to swamp the system."

Hansen and his coworkers are now studying ways to achieve the same effect with a single injection or more widely spaced injections. Such peptide therapies may one day prevent human organ rejection.

Ideally, custom-made peptide cocktails would block an individual's T cell recognition of donor cells. The cocktail would be specific to the donor and not interfere with T cell recognition of other immunological challenges.

"Once you've characterized the MHC differences between a transplant recipient and donor, and you determine which subset of T cells are responsible for recognizing those differences, you could use this therapeutic strategy to slow down or block recognition of organ transplants," Hansen says. "That's the dream."

Together, Mohanakumar, Flye and Hansen's work will help researchers better understand how the immune system is regulated and how it can be manipulated to achieve transplant tolerance. While potential clinical therapies may be years away, the group members realize their work is important in piecing together the puzzle of immunological events that allows some transplanted organs to survive while others fail.

Worldwide, the supply of human donor organs continues to fall short of the demand. If researchers can find a way to induce tolerance, thereby preventing the rejection of organs and the toxic side effects of immunosuppressive drugs, more patients will enjoy the long-term benefits that transplants can offer.
Emerging Resistance

Gozzillabacters Require New Thinking About Antibiotics

by Steve Kohler

In the 50 years since antibiotics revolutionized medicine, the trend in the war against bacteria has run consistently in favor of the humans. Penicillin and the other miracle drugs that followed delivered safe and effective treatment for what had been incurable infections. But the adversary is legion, wily and dangerous. Worse, we are proving to be our own enemy. The advantage may be slipping away, and the implications are alarming.
Beth Owens Schwab, R.N., Barnes Hospital infection control specialist, is among those standing guard against the spread of resistant bacteria.

"During the golden age of antibiotics, we always stayed a step or two ahead of the bacteria," says Gerald Medoff, M.D., professor of medicine and of molecular microbiology and codirector of the division of infectious diseases. Now, there's a problem: Bacteria are developing resistance to existing antibiotics, making previously routine infections difficult or even impossible to treat.

"Most all clinically relevant bacteria have acquired resistance to one or more therapeutically useful drugs," says Daniel Sahm, Ph.D., associate professor of pathology and director of the division of microbiology and serology at Jewish Hospital. There is a new "element of uncertainty in the treatment of infections. The list of bacterial species with completely predictable susceptibility is approaching zero. I can't think of one clinically relevant bacterium that has not been reported to be developing resistance to one or more drugs," he says.

Meanwhile, devising new antibiotics has become more difficult and more expensive. Whole classes of drugs and mechanisms of action have been rendered ineffective by bacteria's adaptations. The microorganisms are "amply provided with ways to survive, and we have relatively little that is novel in the pipeline," according to Wm. Claiborne Dunagan, M.D., assistant professor of medicine.

The problem is not new, Medoff says. Most antibiotics probably mimic elements that exist in the bacteria's natural environment, so bacteria have been adapting to survive the effects of antibiotics for eons. The enemy was preparing to win the war before the first shot of penicillin was fired.

That's just one of the paradoxes involved. Bacterial infections must be treated, but the application of antibiotics — and especially their indiscriminate or inappropriate use — leads to resistance. By their nature, antibiotics work themselves out of a job. Susceptible organisms are killed, but those that are naturally resistant or become resistant then gain an unexpected advantage and a clear field in which to thrive. As long as the antibiotic stays in wide use, this advantage remains. If the pressure is removed, the advantage becomes superfluous and the resistant characteristics may be lost.

As an example of how bacteria respond to evolutionary pressures, consider the virulent bacterium Staphylococcus aureus. According to Sahm, penicillin was originally an effective treatment for infections caused by this organism, but pressure brought by the use of that antibiotic caused strains to emerge that exuded penicillin-neutralizing enzymes. Today, more than 95 percent of all strains of staph are penicillin resistant.

Pharmaceutical houses altered penicillin to form penicillinase resistant penicillin (PRP), and effectiveness was restored. In the past 20 years, however, strains of staph resistant to methicillin and the other PRPs have emerged. Bacteria responded to PRP with a different strategy — they altered the target on which methicillin works. They were able to change via the uptake of foreign DNA from an unknown source, Sahm explains.

Staphylococcus aureus now can be resistant to all known penicillins and cephalosporins. "One of the most common killers of the past is now effectively treated in only one way, only with vancomycin," Sahm says.

What's more alarming is that Enterococcus, the bacterium that Sahm studies, has established a precedent for genetic communication with staphylococci, and the number of enterococci resistant to vancomycin is increasing.

Sahm says, "The scare is that if vancomycin resistance from Enterococcus finds its way into methicillin-resistant staph, we'll be back to the '40s in treatment options. We are only a set of a few genes away from such an untreamtable, virulent organism."

Resistance can occur in one or more of many ways. Most antibiotics derive from natural substances — either directly or in the mechanism by which they work. Bacteria often have "seen" toxins in their environments similar to antibiotics and have developed strategies for defeating them. Spontaneous background mutations also may provide an advantage that remains in place as long as the environmental pressure from an antibiotic is at work.

A larger threat to the effectiveness of antibiotics comes from acquired
resistance, a result of genetic changes in the bacteria. Bacteria can acquire genes from foreign strains via conjugation, the equivalent of bacterial mating. They also can take up naked DNA released into the environment by dying cells of other bacterial species. Or, via transduction, they can become infected by a bacterial virus that carries a genetic payload.

"And," Sahm says, "the natural barriers to genetic exchange are not as substantial as we once thought. Transfer appears possible between a variety of bacterial species and genera; at times it almost seems to be out of control. We're even seeing spontaneous mutations that result in resistance genes that then are transferred to previously susceptible species. Such promiscuity appears to be relatively common as the cauldron of bacterial resistance genes approaches full boil."

Staphylococcus aureus is just one example. Tuberculosis resistant to all conventional treatments has appeared. So far, the spread of this resistant strain appears to have occurred only as it was passed from one individual to another, not as a result of similar mutations.

Physicians know that antibiotic resistance can develop within a tuberculosis patient while he or she is undergoing treatment. Therefore, they routinely treat TB patients with two or three agents to guarantee that all resistant microorganisms are eliminated, Dunagan says. On the East Coast of the U.S., where newer, resistant strains have appeared, five or six antibiotics may be prescribed to ensure that therapy is effective.

In addition, pneumonia-causing Streptococcus pneumoniae has developed resistance. And strains of Escherichia coli, the most common cause of hospital-acquired infections, have become resistant to nearly all standard treatments. Such invincible bugs earn the nickname "Godzilla-bacteria" from researchers who battle them.

Neither is the problem limited to bacteria. According to Sam Stanley, M.D., associate professor of medicine and of molecular microbiology, parasites and viruses are adapting to overcome the agents used to treat them, too. The problem of drug resistance is especially serious in regard to the organism that causes malaria, killer of millions every year. "We can't be complacent," Stanley says, "Ten years ago, we may have had a cheap, effective agent, and no one would have called for a new drug. Today, microorganisms are outstripping our ability to keep up."

**In The House**

Another paradox is that major medical centers — the places at which antibiotic resistance is best understood — are the most common sites for resistant strains to appear. Antibiotics are in wide use there. "In a hospital-confined population, one-quarter to one-third of patients receive antibiotics during their stay. The opportunities for bacteria to acquire resistance and spread are acute," says Dunagan, an infectious diseases specialist.

Vicky Fraser, M.D., assistant professor of medicine in the infectious diseases division, cites the severe illnesses and many infections common in medical centers. "If you're in the hospital for months and months, and you keep getting antibiotics, you may not win. The bacteria may win," says Fraser, who oversees infection control for Barnes Hospital.

At Washington University Medical Center, concerted efforts combat antibiotic resistance. On the front lines, Fraser and four infection control nurses at Barnes aggressively pursue infection control to limit the transmission of bacteria between patients. The nurses teach infection prevention techniques, investigate outbreaks, review policies and study procedures for limiting the spread of infection. Any patient with active tuberculosis, for example, is isolated under negative pressure ventilation that changes the air in the environment six or more times per hour, dilutes bacteria to a safe level and exhausts the air to the outside.

In addition, since 1986 Medoff has had in place a system that controls the use of antibiotics dispensed by hospital pharmacies. Devised primarily as a cost saving discipline, the system also considers that the more an antibiotic is used, the more likely resistance is to develop. Under the guidelines, all antibiotics are first approved for use, purchased under contract, then classed as uncontrolled, controlled (agents to be used for a set period of time before cultures and
device for prescribing antibiotics. The Infectious disease specialist Gerald speci a lists and prescribing clinicians approvals per day weigh such issues as appropriateness of drug choice, dosage, dangerous, "Dunagan adds. Fraser treatment are reviewed) or restricted which approval must be received used for trivial infections and for before dispensation).”

"Penicillin works great against strep against the infection they are fighting. "Penicillin works great against strep throat. But if I use an antibiotic that affects 50 different types, I put pressure on those other bacteria to mutate to survive.”

Antibiotics’ reputation as “miracle drugs” and the memory that penicillin was once prescribed at rates 10 or more times the effective dose without apparent side effects may contribute to a history of antibiotic misuse. “But the old ‘Dose ’em philosophy is no longer appropriate,” Sahm says.

Computers are on guard, too. GermWatcher and GermAlert — expert programs written in the division of medical informatics under the direction of Michael Kahn, M.D., Ph.D., with the support of Barnes Hospital — monitor infections tirelessly.

GermWatcher, the first version of which was created at an expenditure of $300, employs a rule-based “if-then” format to classify the results of cultures run in microbiology laboratories. It follows all the rules of the National Nosocomial Infection Surveillance System (NNISS) established by the Centers for Disease Control and applies them to about 500 cultures a day.

Now a year old, GermWatcher tracks 1,400 organisms, stores final results of 20,000 cultures and has identified 32,000 organism occurrences. Saving information on any infections that deserve tracking, as per the CDC, it alerts infection control personnel. Antibiotic resistance is one reason for an alert. Infections that are not significant are discarded, and if there’s some question, the system can hold a result and wait for a second occurrence.

"Nurses used to have to memorize the huge NNISS book; applying its criteria to microbiology results took half of their workday,” Kahn says. Now the computer does the job in 20 minutes with an accuracy of 96.4 percent, “and it doesn’t get tired or bored,” Kahn says. “Once a significant infection is entered into the database, nurses can monitor it by ward, patient characteristic or by any feature of the organism. When a problem has been identified, the database allows nurses to track it until the problem is resolved.” Kahn says the program soon will be made available to other hospitals that have no infectious disease or infection control specialists.

GermAlert performs similar functions, but serves as a first line of defense by watching preliminary lab results. “If the lab gets an E. coli that has no listings in the ‘susceptible’ column and gentamicin in the ‘resistant’ column, the system immediately issues an alert,” Kahn says. “We get an alert on such things as methicillin-resistant staph, and if the CDC ever reports a vancomycin-resistant strain of staph, then we’ll put that in the system.”

Another program, DrugMatcher, compares antibiotics being administered to the organisms being treated and looks for mismatches. The next step, Kahn says, is to devise an expert system that catches therapies that are too broad. “Broad spectrum antibiotics can be unnecessarily expensive and also promote increases in resistance,” he says.

But in the long term, even the prudent dispensation of antibiotics and precise infection tracking may not guarantee victory. Sahm says new strategies are required.

“The standard approach has been to go to the compost pile and find a mold that produces antibacterial substances, purify the substances and develop those agents for safe therapeutic use,” says Sahm. “Alternatively, we have biochemically manipulated many of the older agents to develop first, second or third generations. In either case, these strategies are time consuming — up to 10 years or more — and they don’t present antimicrobial strategies that our bacterial foes haven’t seen before.”

“A newer strategy involves the use of molecular techniques to study the genetics and physiology of essential bacterial functions and structures, such as their cell wall assembly,” Sahm says. “Then we design agents that interfere directly with the copying and expression of vital DNA instructions. If we can keep bacteria from producing the essential proteins at all, we can hope to avoid the endless struggle of dealing with their impressive ability to constantly change these proteins.”
Cardiovascular surgeons manipulate a double-edged scalpel when they treat complex aortic disease, such as atherosclerotic aneurysms or separations of the thoracic aorta. While they can successfully mend a diseased or torn section of the artery, some of their patients awaken suffering from irreversible spinal cord injury.

Spinal cord injury has been a devastating complication of such extensive operations for more than 30 years, according to Nicholas T. Kouchoukos, M.D., who says up to 40 percent of patients may develop paraplegia following the surgery. Kouchoukos has spent the last decade studying how to minimize the risk of spinal cord injury using hypothermic circulatory arrest. The technique he and his colleagues are currently evaluating involves the induction of hypothermia by a cardiopulmonary bypass machine, which acts as the patient’s heart and lungs, and a heat exchanger, which slowly cools the blood and lowers the patient’s body temperature to 15 C from 37 C.
Hypothermia was induced before heart-lung machines were available by immersing the patient in an icy water bath to lower the body temperature," says Kouchoukos, who is the John M. Shoenberg Professor of Cardiovascular Surgery and surgeon in chief at Jewish Hospital. "It was attempted for some operations on the heart in the 1950s and '60s, but it was a very complicated process. The operations were lengthy, there were bleeding problems and other problems, so it was abandoned."

Spinal cord injury can occur when the spinal cord is deprived of blood. Operations on the descending thoracic aorta and the upper abdominal aorta require that blood flow be interrupted by clamping, sometimes for more than an hour, while the artery is repaired.

Even though hypothermia was technically difficult to implement in surgery, it was discovered early in studies with animals that there were benefits to cooling the spinal cord. Kouchoukos says the challenge at that time was to find a way to apply the technique clinically and safely. Although some surgeons adapted hypothermia for use with operations to repair aortic aneurysms in the chest after heart-lung machines became available, Kouchoukos says the practice was stopped because of rudimentary technology and complications.

Deep hypothermia has been used extensively to protect the brain during cardiac operations in infants and in adults with diseases of the aortic arch. But Kouchoukos was among the first to use deep hypothermia produced by a heart-lung machine to protect the spinal cord. He reported his initial results in 1989. In that study, Kouchoukos applied hypothermic circulatory arrest to five patients who had aneurysms that involved the entire descending thoracic aorta and the upper abdominal aorta and were at high risk for spinal cord injury. None of the patients developed paraplegia.

Previously, he had studied the cooling technique in animals, simulating the complete operative procedure for repair of an aortic aneurysm in a patient. In a study with baboons, nine animals remained at normal temperature for surgical treatment and nine were cooled with cardiopulmonary bypass. Those that remained at normal temperature all developed paraplegia; the animals that were cooled were injury free.

Deep hypothermia has been used extensively to protect the brain during cardiac operations in infants and in adults with diseases of the aortic arch. But Kouchoukos was among the first to use deep hypothermia produced by a heart-lung machine to protect the spinal cord. He reported his initial results in 1989. In that study, Kouchoukos applied hypothermic circulatory arrest to five patients who had aneurysms that involved the entire descending thoracic aorta and the upper abdominal aorta and were at high risk for spinal cord injury. None of the patients developed paraplegia.

Previously, he had studied the cooling technique in animals, simulating the complete operative procedure for repair of an aortic aneurysm in a patient. In a study with baboons, nine animals remained at normal temperature for surgical treatment and nine were cooled with cardiopulmonary bypass. Those that remained at normal temperature all developed paraplegia; the animals that were cooled were injury free.

Since his early work, Kouchoukos and his colleagues have applied deep hypothermia and circulatory arrest to 35 carefully selected patients with various types of severe aortic disease and dissection who were at risk for development of spinal cord injury. Of those patients, 26 had extensive thoracic or thoracic and upper abdominal aneurysms. Three of the 26 developed spinal cord ischemic injury, two developed permanent paralysis, and one had a temporary paralysis. None of the eight patients with aortic dissection and extensive aneurysms (where the risk of spinal cord injury with conventional techniques has been 30 to 40 percent) developed spinal cord injury.

"Initial results suggest that we may be reducing the frequency of this complication," Kouchoukos says. "However, it's too early to make definitive conclusions."

Although the risk of spinal cord injury varies among patients,
Kouchoukos says the primary considerations are the duration of aortic clamping time, the extent of aortic involvement and whether a tear or separation of the artery's layers has occurred. Tears or separations are more complicated to repair than aneurysms.

"The operations that require major resections and are lengthy are associated with some risk," he says. "In certain subgroups of patients, the risk is as high as 40 percent. However, you have to weigh these risks against the risk of not doing the surgery and with possible later rupture of the aorta, which is almost always fatal."

Spinal cord injury also can occur if the critical lumbar and intercostal arteries, which provide blood to the spinal cord and originate from the aorta, are not properly reconnected. Kouchoukos says hypothermia extends the safe period of aortic clamping and gives the surgeon more time to re-establish blood flow to the smaller arteries.

For the benefits it provides, hypothermic circulatory arrest is not without problems. Kouchoukos says one drawback is the amount of time the technique requires — up to four hours, including one hour for cooling the patient and up to two hours for rewarming.

"That means using the heart-lung machine for three or more hours. Twenty years ago we couldn't do that and have many survivors. But the technology associated with the use of cardiopulmonary bypass has improved dramatically in the last 10 years. Today, we have better perfusion systems and better (arterial) grafts which are almost totally impervious to blood, so they don't leak."

Although surgical experience with hypothermia to protect the spinal cord is not extensive, Kouchoukos says more surgeons have begun to use it. "People are accumulating small numbers of cases. The cases where it should be considered aren't that common, so it takes a long time to accumulate enough data to make statistical comparisons."

To complement his clinical findings, Kouchoukos is working with neuroscientists to learn more about the basic mechanisms of injury that occurs when the blood supply is cut off from the spinal cord. He and his associates have borrowed from what neuroscientists already know about nerve cell death in the brain when it is starved of its blood supply.

When the brain is deprived of blood, neurotransmitters, such as glutamate, escape the confines of the cell and leak into the extracellular space. These agents, which become deadly in high concentrations, are known as excitatory neurotoxins and can kill nerve cells. But when hypothermia is applied to cool the brain, it prevents or blunts the release of glutamate and possibly other neurotoxins as well.

In collaboration with Chris Rokkas, M.D., a fellow in the division of cardiothoracic surgery, and Dennis W. Choi, M.D., Ph.D., Andrew B. and Gretchen P. Jones Professor of Neurology and head of the Department of Neurology, an animal model preparation was developed that allows measurement of the extracellular concentration of potentially dangerous neurotransmitters in the spinal cord.

"What we found is that deep hypothermia prevented the release of these neurotransmitters into the extracellular space," Kouchoukos says. "It doesn't necessarily imply a cause and effect, but at least we've shown the same thing in the spinal cord with this preparation that has been shown with the brain."

Choi says the findings are potentially widely applicable: "They have demonstrated the rather powerful ability of hypothermia to protect the spinal cord from ischemic injury, which has potential immediate practical significance. The models that Dr. Kouchoukos and colleagues have set are especially attractive because they provide a ready system for testing other therapeutic strategies. Thus, there is a benefit to their work which goes beyond any individual result. It's very exciting and applicable to real world problems."

Says Kouchoukos, "If we can understand the mechanism of injury, we can then try other interventions, such as drugs, which alone or in conjunction with hypothermia may protect the spinal cord even more effectively. And that's what we're trying to do, to protect the spinal cord so it will function normally when the operation is completed."
Written Prescription —
When The Phone Rings, My Bed Shakes

by Steve Kohler

INTO a cynical world chockablock with ulterior motives and meanness comes Philip Zazove’s straightforward, guileless and inspiring story of caregiving.

Zazove, M.D. ‘78, recently has published When The Phone Rings My Bed Shakes: Memoirs Of A Deaf Doctor (Gallaudet University Press, 1993), in which he recounts experiences as a family physician who cannot hear his patients’ complaints nor his colleagues’ recommendations. Latenight emergency calls require that an electronic device attached to the telephone shake him awake.

From birth, Zazove has been unable to hear music or warning shout, birdsong or dramatic performance, teacher’s instruction or family member’s kind word. He has cause to be bitter or small, considering the hand he was dealt. Instead, this memoir shows, his own difficulty has prompted Zazove to seek the central humanity in himself and especially in others. He has become the kind of doctor most would choose if they could.

Not that Zazove writes self-servingly about overcoming hardship or about how deeply he cares for his patients. He is a good enough writer to show his readers what he wants them to believe, not tell them what he wants them to think.

Zazove (who, for reasons he does not understand, can communicate using an amplified telephone) says that learning to write in a lay style tough to overcome the weight of opinion, some from teachers who did not share his belief that he could become a doctor and more from medical school professors who did not think that family practice was a reasonable specialty for him. His inability to hear has never stopped him, although “other people have wanted it to,” Zazove says.

Originally, Zazove conceived the book as a means of showing others with impaired hearing that anything they sought was possible to attain. In that sense, the book was born as a promise to a teacher while the author was just a senior in high school in Chicago. At that time, he had already made the decision to become an “old-fashioned doctor.”

But since its publication, Zazove says he has come to see the book more as a vehicle for educating hearing people regarding what it is like to be deaf.

Because he has never heard the proper pronunciation of the word “anxious,” even at age 41, he takes a gentle lesson from his wife in how to say it so that others will understand. In the operating room, with all players behind masks where he cannot read their lips, Zazove has no
Deafness has made me more attuned to 'the person' inside each of the people I deal with. His hearing loss, he says, has helped make him more "him."

To treat his patients effectively, Zazove reads not only lips but body language, watching intently for clues concerning what his patients really mean when they tell him what's bothering them. And he recognizes that everyone is up against obstacles: poverty, cancer, prejudice or some other force.

Zazove lovingly shows his readers the people he treats. We meet the pregnant, apathetic teen who loses her baby but never reveals the secret of what has destroyed her emotions. The reader senses Zazove's frustration as he tries to win her confidence in order to treat the whole person, but fails.

He uses magic tricks — sponge balls pulled from ears — to gain the trust of youngsters who must be coaxed into cooperating. His expertise is stretched, but ultimately successful, when a patient presents with an uncommon case of borrelia. And Zazove's open mind wins the devotion of the pregnant daughter of an underworld figure who becomes something of a thorn in the physician's side before she is determined to have lost her child.

Some of medicine's less-than-prettty side is presented here, but Zazove insists that the patient examples he selected are representative of what every family practitioner sees, not chosen for shock value. In fact, he says his manuscript was rejected by many publishers because it was not "horrific" enough.

What Zazove finds compelling about the practice of medicine is the humanity shared by all of his patients, and he wants his reader to be involved along with him. Even his practice's pain in the neck, an elderly hypochondriac who tracks down the doctor in the grocery store and at an accident scene, is painted with the author's compassionate brush.

When Barbara's career in Utah sours after eight years, the Zazove family makes the difficult decision to leave the satisfying practice and move to Michigan for a life of more academic medicine. In Ann Arbor, both Philip and Barbara Zazove serve on the faculty at the University of Michigan. He splits his time between seeing patients, teaching, research and administrative duties.

Zazove still misses the people from the practice he built in Utah. But he no longer fears that pressure on physicians will end the era of the family practitioner who serves people from their cradles to their graves. "In the past two years, there has been a dramatic shift in healthcare. Now family practitioners are the doctors of the future," Zazove says. "I'm excited about the new emphasis on family practice, with all of its inherent benefits." Zazove also can take comfort in knowing that he has indeed set a powerful example for other deaf people and has instructed hearing people in some of the implications of deafness.

Editor's Note: Philip Zazove's next book, a mystery featuring a deaf protagonist, is in the word processor and 90 percent complete.
Concerted Effort: 
One Student’s Stand On Sex Education Policy

by Craig Carmichael

OVER a burger and fries, I discussed our society’s approach to sex education with a friend. We were amazed that the school district in our small Midwestern town had purchased an aggressive sex education curriculum that begins in kindergarten with boys and girls in the same classroom naming the “private” parts of the body in order to become comfortable talking about sex. I pointed out that my five-year-old nephew takes baths with his sister and doesn’t know the difference between her breast and her arm. Nonetheless, under this system, children would discuss sexuality all during grade school.

It was not an approach with which I agreed. “I wish there were something I could do,” I said. “I edit a student column in the state medical journal, but if I start talking about abstinence and old-fashioned values in the current political arena, I might end up doing my residency in Siberia. Besides, what difference can I make?” I had seen firsthand the repercussions that position of a rebel, but I think that if you can’t stand up for what you believe in, then you have to wonder what purpose your life can serve.”

The next morning I was at the medical library, deep in articles on sex education. I was surprised to read about how abstinence-based curricula with names like Sex Respect, Facing Reality, Teen S.T.A.R., and others had reduced the pregnancy rate for students.

Participants in Sex Respect in 26 public schools had a five percent pregnancy rate two years after participation in the program, compared to a nine percent rate among a control group of students not enrolled in the program. When Sex Respect was tried in a St. Louis district, elementary school pregnancies fell from 10 a year to none, and middle school pregnancies dropped from 40 a year to 10. Follow-up on a program created at Emory University to help low-income eighth graders choose not to have sex showed that these students were one-fifth as likely to have started having sex as their peers.

Perhaps more amazing was that when Emory University surveyed 1,000 sexually active teenagers, asking them what they most wanted information about, 84 percent put as their number-one choice that they most wanted to learn how to say...
"no" without hurting the other person's feelings.

Still, we refuse to teach children how to avoid being overwhelmed by society's sexual pressures, and our Surgeon General says, "We taught them what to do in the front seat (of a car). Now it's time to teach them what to do in the back seat." While she was director of the state department of health in Arkansas, the state went from having the fourth highest rate of pregnancy in the country to the second highest, and rates of STD infections increased as well. Nevertheless, abstinence-based programs like those listed above are finding it harder to find funding.

Even if condom programs were successful and teenagers used condoms every time they had sex, STDs and pregnancies might not decrease significantly. Women who rely on condoms for birth control have a 15 percent chance of becoming pregnant every year, due in part to the eight percent rate at which condoms fail. Condoms are even less effective against STDs. In a study of three New York City clinics, 21 percent of female patients with STDs reported that they had been using condoms regularly.

These findings made it easy to write an article for the state medical journal, and, to my amazement, six physicians wrote to show me their support. Heartened by this unanticipated acceptance, I lost any objectivity which I may have possessed and decided to attempt the impossible — I asked the medical student section of the AMA to support abstinence-based sex education.

I submitted the resolution and called a high-ranking AMA member to see what he thought. "The AMA already has a policy about sex education, and I don't know that we want to re-open some of these issues." Then he dropped the bombshell, "We have to consider what is best for the AMA." Call me crazy, but it seemed to me that what is best for the AMA is to do what is best for the health of the American people. However, my hopes began to sink, because I knew the powers-that-be were aligning against me.

Needless to say, the resolution was not popular. When I stood at the microphone during the reference committee hearing, (the first of two presentations of the resolution) I heard a great deal of laughing and commotion behind me. When I turned around to see what was up, I was amazed to find that about 30 people were standing in line behind the microphones to address my resolution. My friend Sam said "Uh oh," and pointed to a member of the governing council who stood resolutely behind the "con" microphone.

My stomach laden with butterflies, I turned back toward the mike and started to present the arguments that I had formulated. I was halfway through the first one when the reference committee chairperson called time. I watched as student after student addressed my resolution while I had no means of explaining myself. It felt like I was shouting into the wind. I knew that people did not understand my intentions nor my reasoning, but the lines at the microphones were so long that I could not address even one issue.

I was so frustrated that I didn't sleep at all but spent most of the time pacing the halls.

I was amazed to find that about 30 people were standing in line behind the microphones to address my resolution. My friend Sam said "Uh oh," and pointed to a member of the governing council who stood resolutely behind the "con" microphone.

My stomach laden with butterflies, I turned back toward the mike and started to present the arguments that I had formulated. I was halfway through the first one when the reference committee chairperson called time. I watched as student after student addressed my resolution while I had no means of explaining myself. It felt like I was shouting into the wind. I knew that people did not understand my intentions nor my reasoning, but the lines at the microphones were so long that I could not address even one issue.

I was so frustrated that I didn't sleep at all but spent most of the time pacing the halls.

left in which to explain myself, because that was all the time I would be allotted before a vote. I also knew I needed to read about the intricacies of parliamentary procedure, so that I could rebut any unwarranted "con" arguments.

The next day, the big moment arrived. I raced through the 60-second speech I had practiced repeatedly during the night. It must have worked, because several students applauded and only a few stood behind the microphones.

When the final vote was called, no one was more surprised than I to see more than 100 delegates vote for the resolution and only one vote against it. For me, it was one of those moments you wish you could live over and over again — when you have fought a battle for a cause that you have believed in, and you win against the odds. The resolution supporting abstinence-based sex education is now AMA medical student policy, and physician members will vote in June on whether to approve it as AMA policy at large. The story is being carried by at least four magazines, and a letter writing campaign is underway. All I did was make a small effort. I don't possess any special talent, knowledge or experience, but I was able to make a change in my own small way. I remain amazed at how big an impact one small but concerted effort can make.

Ed Note: Craig Carmichael is a second-year medical student from Illinois. The opinions expressed herein are those of the author, not necessarily shared by Washington University School of Medicine, Washington University Medical Center, nor the policy of any of these entities. Letters concerning the resolution are being accepted at Box 799, Pekin IL 61555.
**New Distinguished Alumni Honorees Chosen**

Four alumni have been chosen this year as honorees for the Distinguished Alumni Scholarship Program in recognition of their outstanding contributions to teaching, research, and patient care at the School of Medicine. Nicholas T. Kouchoukos, M.D. ’61, John M. Shoenberg Professor of Cardiothoracic Surgery, vice chair of the Department of Surgery, and chief of surgery and cardiothoracic surgery at Jewish Hospital; Ira J. Kodner, M.D. ’67, associate professor of surgery and director of the division of colon and rectal surgery at Jewish Hospital; Gerald Medoff, M.D. ’62, codirector of infectious diseases and vice chair of clinical affairs for the Department of Medicine; and Penelope G. Shackleford, M.D. ’68, professor of pediatrics and associate professor of molecular microbiology, were selected as the 1994-95 honorees.

Created by the Washington University Medical Center Alumni Association, the Distinguished Alumni Scholarship Program is the school’s major merit scholarship funded through annual gifts from alumni, former residents, and friends and a matching grant from the school. For the past five years, four outstanding medical students have been selected each year to receive a four-year, full-tuition scholarship named for one of the honored alumni. To date, 20 students have benefited from this program.

**Mattson On Board**

William R. Mattson, Jr., has joined the School of Medicine’s National Council.

Mattson’s firm, The Mattson Jack Group, specializes in new business development, product planning and management, business management and financial planning and analysis, with an emphasis on health care products and expertise in university collaborations. Mattson previously has been employed at Searle Pharmaceuticals, its parent Monsanto Company, and Abbott Labs.

The National Council comprises prominent men and women from a broad assortment of endeavors to assist executive vice chancellor and dean William A. Peck, M.D., in steering the school. The council meets twice each year to consider the medical school’s direction and to offer advice and counsel.

---

**Alumni honorees and student recipients include:**

<table>
<thead>
<tr>
<th>HONOREES</th>
<th>STUDENTS</th>
<th>YEAR AWARDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eugene Bricker, M.D. ’34</td>
<td>Gregory Esselman</td>
<td>1989-’90</td>
</tr>
<tr>
<td>Alexis F. Hartmann, Sr., M.D. ’21</td>
<td>Kirk Gasper</td>
<td>1989-’90</td>
</tr>
<tr>
<td>Carl V. Moore, M.D. ’32</td>
<td>Corina Norrbom</td>
<td>1990-’91</td>
</tr>
<tr>
<td>Mildred Trotter, Ph.D. ’24</td>
<td>Naomlevine</td>
<td>1989-’90</td>
</tr>
<tr>
<td>Justin J. Cordonnier, M.D. ’28</td>
<td>Thomas Daly</td>
<td>1990-’91</td>
</tr>
<tr>
<td>Paul O. Hagemann, M.D. ’34</td>
<td>Kimberly Allman</td>
<td>1990-’91</td>
</tr>
<tr>
<td>Edward H. Reinhard, M.D. ’39</td>
<td>Martha Terry</td>
<td>1991-’92</td>
</tr>
<tr>
<td>Frederick C. Reynolds, M.D. ’34</td>
<td>David Hunstad</td>
<td>1991-’92</td>
</tr>
<tr>
<td>John C. Herweg, M.D. ’45</td>
<td>William Lyons</td>
<td>1991-’92</td>
</tr>
<tr>
<td>Virgil Loebl, Jr., M.D. ’44</td>
<td>David Miller</td>
<td>1991-’92</td>
</tr>
<tr>
<td>George Sato, M.D. ’52</td>
<td>Hyman R. Senturia, M.D. ’53</td>
<td>1991-’92</td>
</tr>
<tr>
<td>David Goldring, M.D. ’40</td>
<td>I. Jerome Flance, M.D. ’35</td>
<td>1992-’93</td>
</tr>
<tr>
<td>Charles W. Parker, M.D. ’53</td>
<td>Jessica Ternberg, Ph.D. ’53</td>
<td>1992-’93</td>
</tr>
<tr>
<td>Jessie L. Ternberg, M.D. ’53</td>
<td>Leonard Berg, M.D. ’49</td>
<td>1993-’94</td>
</tr>
<tr>
<td>John Kissane, M.D. ’52</td>
<td>Robert C. Drews, M.D. ’55</td>
<td>1993-’94</td>
</tr>
<tr>
<td>J. Neal Middelkamp, M.D. ’48</td>
<td>Louis Kuchnir</td>
<td>1993-’94</td>
</tr>
</tbody>
</table>

A special reception in November brought together the students and alumni honorees (some for the first time) for an evening. Enjoying conversation are: Jessie L. Ternberg, Ph.D., M.D. ’53, and Damla Karsan.
Reunion Speakers Named

BARRY Siegel, M.D., president of the Washington University Medical Center Alumni Association, has recruited 12 distinguished speakers for the Reunion '94 Scientific Program. Many of the presenters are members of the reunion classes. They include:

Thursday afternoon, May 12:
Robert C. Kolodny, M.D. '69
Jonathan Mann, M.D. '74
Penelope G. Shackelford, M.D. '68
Steven L. Teitelbaum, M.D. '64

Friday afternoon, May 13:
Brent T. Allen, M.D. '79
J. Raymond Fletcher, M.D. '64
Charles L. Rich, M.D. '69
Jessie L. Ternberg, Ph.D., M.D. '53

Saturday morning, May 14:
Fred L. Brown, president and CEO of Barnes Jewish Christian Health System
David Citron, M.D. '44
Ronald G. Evens, M.D. '64
Elbert P. Trulock, Ill, M.D., FHS

Continuing medical education credit will be available for those attending.

Recent Bequests To The School Of Medicine

TWO major bequests from St. Louis residents and longtime supporters of Washington University were among those recently received by the School of Medicine.

Mrs. Jane K. Pelton gave more than $450,000 through her will to the School of Medicine. She was a 1922 graduate of Washington University and one of the first women to receive a master's degree in architecture from the University.

Her bequest provides for the operation, support and maintenance of the Irene Walter Johnson Rehabilitation Institute. Before her death, she also supported lipid research and the Department of Neurology at Washington University and endowed the Kuhn-Pelton Kidney Unit at Barnes Hospital, as well as scholarships in the School of Architecture.

Mr. Sam J. Golman, a non-alumnus of Washington University, made two major gifts through his bequest. His first gift of $1 million establishes the Virginia E. and Sam J. Golman Professorship of Oncology in the Department of Internal Medicine. The second gift of $500,000 supports the J.J. Flance (M.D. '35) Professorship of Medicine in the Department of Internal Medicine in memory of Mr. and Mrs. Golman. This professorship is named for Jerome Flance, M.D., longtime physician of Mr. Golman and clinical professor of medicine at Washington University School of Medicine. Mr. Golman was co-founder of Golman Department Stores in Festus, Crystal City and Flat River, Missouri.

Murphey Fund Enables Diabetes Research

Support provided by the Ruth Shaw Murphey Diabetes Research Fund is enabling several avenues of research into diabetes.

The fund honors Ruth Shaw Murphey, LA '46, and was established on her birthday in 1992 with an initial gift of $100,000 from her husband, attorney Richard R. Murphey, Jr., LA '47. A second, similar contribution followed on Ruth Murphey's birthday in 1993.

Murphey says the fund was established as "a birthday present for a lady whose worldly needs were otherwise provided for." But the unrestricted gifts came only after considerable research. "Both of us..."
graduated from Washington University, but we haven’t been back,” he says. “Juvenile onset diabetes has been a force in Ruth’s life for more than 30 years, and we looked for a good place to invest with that in mind. Washington University was one of the top places in which such research is done. Pride in the school is one thing, but from our point of view, results were the driving force.”

Murphey says he was convinced that the School of Medicine would apply the gift in a “result-oriented, focused way.” According to David M. Kipnis, M.D., Distinguished University Professor of Medicine, who oversees the fund, several lines of inquiry are supported by the gifts.

In one, researchers look for new human pancreatic islet genes that might be contributors to the inherited susceptibility of both insulin dependent and non-insulin dependent diabetes. The second project seeks to understand more completely the mechanisms by which the body processes proinsulin into proinsulin processed intermediates and then into insulin. Secretory abnormalities may be inherited in a pattern, and the enzymes involved may be in some way altered in Type II diabetes.

Kipnis says that the Murphys’ gifts have generated considerable excitement among his colleagues, and that, with more than 1,000 patients enrolled, the diabetes registry makes it possible to carry out meaningful clinical, epidemiological and genetic studies.

**WUMCAA Allocates Funds**

THE Executive Council of the Washington University Medical Center Alumni Association (WUMCAA) has allocated financial support for fiscal 1994 to the following programs and activities:

- $140,000 to the Distinguished Alumni Scholarship Program, which provides four-year, full-tuition scholarships in the names of distinguished alumni faculty to four incoming students each year (a total of 16 are supported). WUMCAA provides $10,000 toward each yearly scholarship award, and the School of Medicine adds funds to bring the award to the current tuition amount.
- $25,000 to a Continuing Medical Education, which supports postgraduate education opportunities for physicians.
- $5,000 to the three academic societies, each with a mix of approximately 100 medical students and 70 faculty members. Of this amount, $3,000 ($1,000 to each society) is given in honor of the three student-selected Teachers of the Year. The societies meet four times a year for social and educational events which provide unique opportunities for students and faculty to communicate informally.
- $750 each for the student activity funds of the first-year class and the second-year class, for social and recreational events.
- $1,600 to the Young Scientist Training Program with the School of Medicine and the St. Louis City Public Schools, which provides paid summer research positions in School of Medicine labs for eight outstanding WUMS students and a local school medical students.
- $1,516 to match the Class of ’92 gift to Medical Student Scholarships.

**Students teach classes on prenatal care, counsel expectant mothers about sound nutritional and personal habits, participate in a labor coaching and mentoring program and make home visits.**

- $3,350 to the Reproductive Health Education Project, a joint effort between approximately 60 WUMS students and a local school district.
- $5,000 to the Young Scientist Program, a collaboration between the School of Medicine and the St. Louis City Public Schools, which provides paid summer research positions in School of Medicine labs for eight outstanding junior students.

**Honor Roll Changes**

TWO errors affecting alumni of the medical school crept into the 1992-’93 Honor Roll of Donors, published by the University’s Office of Alumni and Development Programs to recognize those who made gifts. George L. Wulff, M.D. ’33, accidentally was listed as having given to Arts and Sciences, when in fact he supported the School of Medicine. The name of Allan H. Rappaport, M.D. ’72, was inadvertently misspelled.
'30s

Robert S. Smith, M.D. '33, writes that though he received his degree in 1933, he thinks of himself as a member of the class of '31, with which he began. The two-year discrepancy is attributable to his having gone to Oxford for two years as a Rhodes Scholar. He practiced in Idaho from 1936 to 1971 with the exception of three years during World War II. His professional career ended in 1971 with a severe stroke. Since then he has traveled, painted the western scene and published three books: Idaho Surgeon (1974), Doctors and Patents (1976) and Life After Stroke (1986).

Carl Peter Birk, M.D. '34, has been retired for three years from his practice in Decatur IL, where he served the community for 51 years. He and his wife, Martha S. Birk, OT '35, have three children, six grandchildren and one great-grandson.

Clara Maupin Burke, NU '34, is enjoying retirement at Leisure World, a community for retired persons in Laguna Hills CA. She says she doesn't have time to do all the things she would like.

'40s

Burte Guterman, M.D. '43 March, continues to serve the School of Medicine as a member of the Boston area Eliot Society Committee. In that capacity, he calls the 250 medical alumni living in the region to encourage their participation in the Eliot Society.

Bruce W. Armstrong, M.D. '44, has made plans to attend the reunion of his class and writes that since leaving the U.S. Navy in 1948, he has worked for three medical schools and seen each of his five children graduate from college, three of them with advanced degrees. For several years he has been in practice at Carson Tahoe Hospital, Carson City NV.

Wesley Fee, M.D. '44, Robert Hodge, M.D. '44, and Guy Callaway, M.D. '44

Wesley Fee, M.D. '44, Robert Hodge, M.D. '44, and Guy Callaway, M.D. '44, continue to share a friendship that began during their days in medical school. Each returned to his hometown to practice medicine, but in retirement they travel together extensively.

Florence Marshall, NU '47, retired from more than 14 years of teaching at the School of Nursing at Southern Illinois University in Edwardsville in August 1993. She taught a course at Jewish Hospital College of Nursing during the fall of 1993 and reports having enjoyed being on the Kinghighway campus again.

James C. Hawkins, M.D. '49, retired in early 1991 from Veterans Administration Hospital in Tucson. After spending time looking for a place to live in the Midwest, Hawkins says the weather drove him back to Tucson in December of 1992. "Since then, we've built a new home and we travel and play. It's tough, but somebody has to do it," he writes.

'50s

Hubert C. Huebl, M.D. '56, is in the practice of general surgery with Dearborn Associates in Dearborn MI.

Genevieve Mason, NU '57, retired from Barnes Hospital in April 1993, but her life of ease lasted only one week before she accepted the job of patient care manager of the operating rooms and post-anesthesia care unit at St. Louis University's Anheuser-Busch Eye Institute, a new eye hospital. She also has been installed as president of the American Society of Ophthalmic Registered Nurses.

'60s

Carolyn Bauer Robinowitz, M.D. '64, writes that 1993 was a busy year that included her work as chief operating officer of the American Psychiatric Association and her interest in the issues of psychiatric education. She teaches at three medical schools, serves as president elect of the Association for Academic Psychiatry and received the 1994 Bows Award of the American College of Psychiatrists.

Rebecca F. Collins, Ph.D., NU '68, completed her Ph.D. in nursing at the University of South Carolina in 1992 and serves as dean of the nursing division at Greenville Technical College. She is especially interested in bioethics and public policy and wrote her dissertation on moral conflicts confronted by critical care nurses.

'70s

Dennis A. Hall, HA '73, has been named president and CEO of Baptist Health System in Birmingham AL. Hall had been president of Montclair Baptist Medical Center, one of the system's flagship hospitals. Hall now oversees a system that includes nine hospitals with 2,003 beds and 1,418 physicians, along with a broad assortment of outreach, nursing and seniors' programs.

Jo-Ellyn M. Ryall, M.D. '75, has been elected the first speaker of the House of Delegates of the American Medical Women's
ASSOCIATION at that group's meeting in New York on November 5, 1993.

Curt H. Hagedorn, M.D. '76, is the recipient of the Elsevier Initiative Award from the American Gastroenterological Association. The grant of $25,000 is made annually to researchers taking novel approaches in gastroenterology research. Hagedorn, an associate professor at Emory University School of Medicine, will use the grant to develop hepatitis C antiviral agents by identifying DNA molecules that bind viral DNA and thereby disrupt the processes essential to viral replication.

Stuart R. Schlanger, M.D. '77, is in the practice of internal medicine in Omaha and is an associate professor of medicine at both Creighton Medical School and the University of Nebraska Medical School. He writes that he feels "very strongly that it was the excellent medical education I received (at Washington University) that has, to a large degree, been instrumental in the success I am now enjoying."

'80s

Charles Kim Jones, M.D. '81, and his wife, Susan, both practice family medicine in Pauls Valley OK, where they have been for more than nine years. The couple has five children: Laura, aged 10; Blaise, eight; Olivia, four; Maribeth, two and Luke, one.

Raymond J. Tesi, M.D. '82, and Claudia Jane Morgan, Ph.D. '82, are moving to Tulane University to join the faculty of the medical school there after five years on the faculty at Ohio State University School of Medicine. Morgan will continue her basic science research in the mechanisms of inflammation and studies of the mechanisms of chemotherapeutic agents. Tesi will direct extra-renal transplantation with a responsibility to expand the solid organ transplant program at Tulane. Write to them at 1698 Robert Street, New Orleans LA 70115.

Jay Diamond, PT '85, reports that he and Erin O'Reilly became parents on December 23, 1993, when Jesse Rae Francis O'Reilly Diamond was born at home. Diamond says, "He has a ravenous appetite, changes his own diapers and takes out the garbage. He anxiously awaits moving the lawn once the weather turns warmer."

Lyn McDivitt Duncan, M.D. '86, and her husband, Timothy, have recently moved to Cambridge MA, where she is on the faculty at Harvard Medical School.

Cynthia L. Vehe, M.D. '86, has joined the Department of Internal Medicine at Group Health Como Medical Center in St. Paul MN. Group Health is a member of the HealthPartners family of health plans, the largest managed healthcare organization in the Twin Cities, with more than 580,000 members.

IN MEMORIAM

Willard M. Allen, M.D., former head of the Department of Obstetrics and Gynecology, and Dorothy D. Allen, his wife, were killed in a traffic accident August 2, 1993, in Terry County PA. The couple were residents of Glenwood MD; he was 88 and she was 89. Allen served as department head from 1940 to 1971, coming to the medical school from the University of Rochester. In 1935, he won the Eli Lilly Award in biological chemistry for the isolation of progesterone, a female hormone. Allen retired from Washington University in 1971. Among those surviving Allen are a daughter, a brother, two sisters, four grandchildren and three great-grandchildren.

Vern H. Anderson, M.D. '34, died December 29, 1993, in Idaho. He was 84.

Shirley Collier Craig, NU '45, passed away on September 5, 1993, in Indian Harbour Beach FL, after a long fight with lung cancer.

Joseph C. Edwards, M.D., FHS in internal medicine and a former member of the faculty, died January 9, 1994, at his home in University City, apparently from heart failure. He was 84.

Edwards was a cardiologist in St. Louis for more than 50 years and in 1960 wrote the book, Management of Hypertensive Disease that became a highly regarded reference.

His survivors include his wife of 52 years, two sons, a daughter, 15 grandchildren and a great-grandchild.

Paul Lefkowitz, M.D. '32, died November 12, 1993, in Fort Lauderdale FL. He was 87.

Lefkowitz practiced general medicine, with an emphasis in ear, nose and throat, for many years in Rockland County NY. In 1954, he and a colleague began an anesthesia practice.

He is survived by his wife, three sons, one daughter, three brothers, two sisters and eight grandchildren.

Severo Ochoa, M.D., former member of the faculty and winner of the Nobel Prize in Physiology or Medicine in 1959, died November 1, 1993, in Madrid, Spain. He was 88 and succumbed to pneumonia.

Ochoa, who first worked in this country in Washington University School of Medicine's pharmacology department, won the Nobel Prize for his discovery of an enzyme that synthesizes RNA under laboratory conditions. The prize was shared with Arthur Kornberg, M.D.

Said to have been a consummate researcher who sought the truth for truth's sake, Ochoa entered Madrid University Medical School at the age of 17. He never practiced medicine, preferring the complexities of basic biochemistry.

Ochoa's wife, Carmen, died in 1986. He was buried in Luarca, a fishing port on the north coast of Spain, where he was born.
Cardiology fellow John Murphy, M.D., part of a teaching team that also includes Mark E. Frisse, M.D., and Nilesh Jain, employs the Medical Library's new LiveBoard. Under the direction of John Schnase, Ph.D., and the Advanced Technology Group, the board's large interactive display brings the power of the computer to groups. Washington University medical school is the first to employ LiveBoard technology as a teaching tool.
Researchers looking for new ways to fight bacterial infections have discovered a method of inhibiting "chaperone" proteins responsible for transporting the elements that allow bacteria to stick to the hosts they infect. In this representation from X-ray crystallographic data, the purple "ribbon" is the transport protein. The multicolored molecular structure associated with the chaperone forms a blueprint for compounds that prevent the production of "sticky hairs," leaving the bacteria bald and effectively abolishing their infectiousness. The image is courtesy of Scott Hultgren, Ph.D., assistant professor of molecular microbiology.