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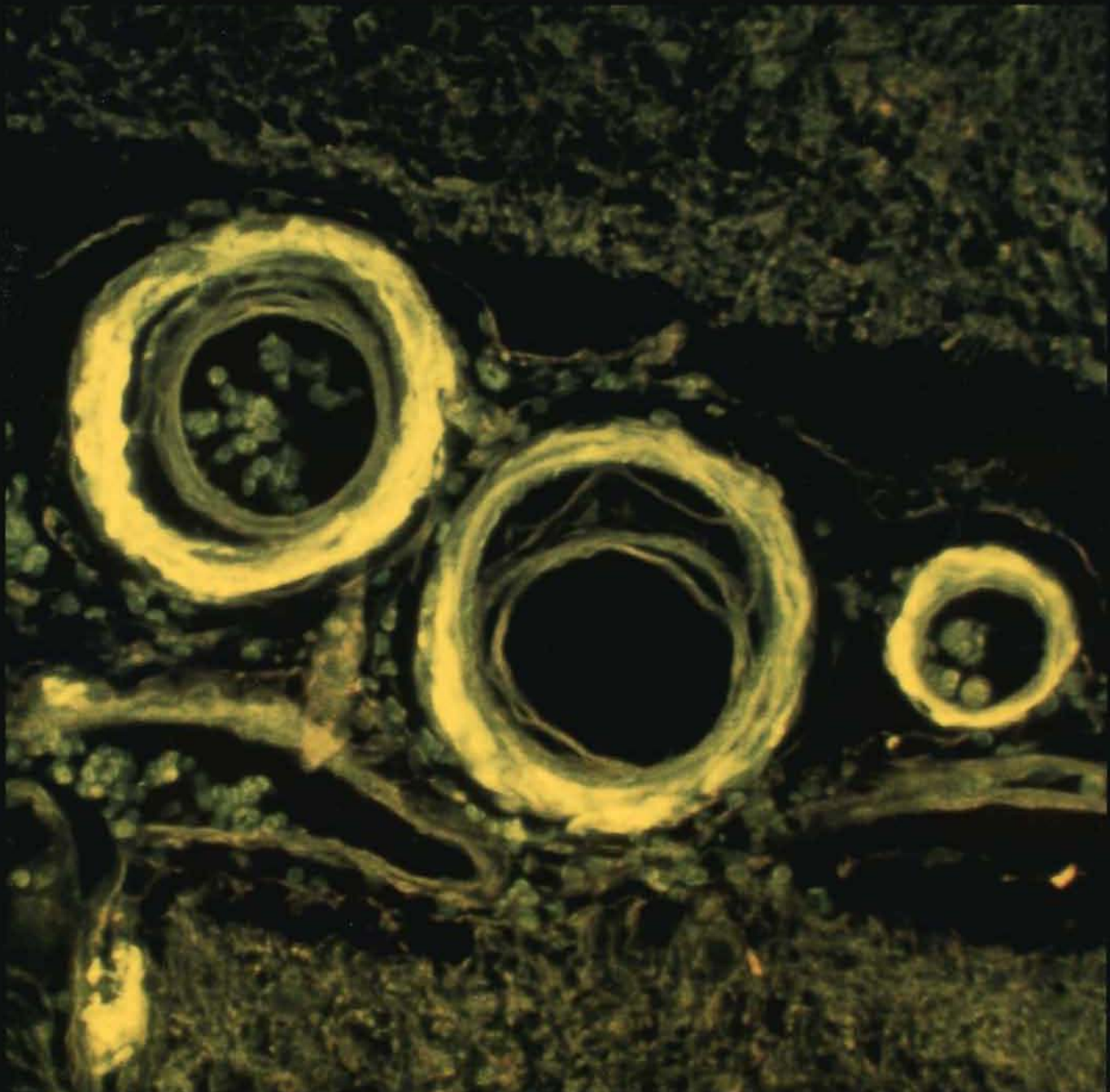
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Outlook

Washington University School of Medicine

Spring 1997



Education Reform • Alzheimer's Disease • Attacking AIDS



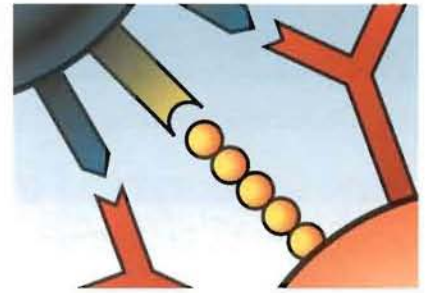
A postural problem known as winging of the scapula is explained by Robert H. Deusinger, PhD, assistant professor in the Program in Physical Therapy, right, to Yolanda Curry, a student at Vashon High School, center, and Christina Rios, a student at Central High School. Curry and Rios were among 137 students from 10 St. Louis-area high schools who attended the 1997 Health Professions Fair at the School of Medicine in February. The event, which introduces students to a variety of health and science careers, was sponsored by Diversity Programs.

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Outlook

Washington University School of Medicine



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THE COVER

A histologic section of cerebral cortex from an Alzheimer brain has been stained to reveal bright yellow fluorescence in the arterial walls. This is caused by abnormal deposits of the protein beta amyloid which contributes to the development of senile plaques in the brain, a characteristic of Alzheimer's disease. For more on Alzheimer's disease and the work taking place in the Alzheimer's Disease Research Center, turn to the story on page 16. *Slide courtesy of Daniel W. McKeel, Jr., MD, and the Washington University ADRC Neuropathology Core Laboratory.*



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New Leadership For The Department Of Medicine

GUSTAV Schonfeld, MD, has been named Adolphus Busch Professor and head of the Department of Medicine at the School of Medicine.

He replaces John Atkinson, MD, professor of medicine and molecular microbiology, who held the position since 1992 and has returned to full-time teaching, research and clinical activities.

Formerly the William B. Kountz Professor of Medicine, Schonfeld has been director of the Department of Medicine's division of atherosclerosis, nutrition and lipid research since 1972. He is a 1956 graduate of Washington University and a 1960 graduate of the School of Medicine.

An active and recognized leader within the Washington University community, Schonfeld is an internationally respected expert on lipid metabolism. His research has shown that the concentration, composition, structure and metabolism of lipoproteins are affected by changes in diet, and by hormonal and genetic factors. These studies were instrumental in the design of low-cholesterol diets in use today.

Schonfeld directed the St. Louis portion of the multicenter Coronary Primary Prevention Trial, which in 1984 released indisputable evidence that lowering cholesterol reduces the risk of heart disease.

During Atkinson's tenure as department head, many outstanding faculty were recruited, educational efforts were enhanced, and clinical services were reorganized and upgraded. Atkinson oversaw the creation of the division of general medical sciences, and under his leadership the department assumed responsibility for emergency services.

Atkinson is a former Howard Hughes investigator and is well known for his research on the complement system, a group of proteins critical to the immune response. He has received numerous honors and awards and recently was elected into the Institute of Medicine of the National Academy of Sciences. ●

Beverly To Head Molecular Microbiology

STEPHEN M. Beverly, PhD, has been named head of the medical school's Department of Molecular Microbiology and will occupy the newly endowed Marvin A. Brennecke Chair in Molecular Microbiology.

Beverly comes from Harvard Medical School, where he was the Hsien Wu and Daisy Yen Wu Professor of Biological Chemistry and Molecular Pharmacology and acting department chair.

One of Beverly's priorities will be to create a multidisciplinary center in microbial pathogenesis that will bring together faculty with similar interests.

Beverly is widely recognized for his work on *Leishmania*, a microscopic parasite that infects more than 10 million people in tropical countries. Transmitted by biting sand flies, the organism causes massive ulceration of the skin, mucous membranes and internal organs. Beverly studies the genes and proteins that allow *Leishmania* to spend part of its life cycle in the sand fly

and part inside human macrophages, the white blood cells that normally kill harmful microbes.

The gift for the chair was provided by Marvin A. Brennecke, MD, who graduated from the medical school in 1930 and became a plantation physician in Hawaii. He left a bequest to the university when he died in October 1994.

Brennecke grew up in Jackson MO. After spending two years in medical school at the University of

Missouri in Columbia, he transferred to Washington University, where his education was financed by fifty \$100 notes signed by the people of Jackson and collected by an officer of the local bank. He obtained his medical degree in 1930.

After graduation, Brennecke served a one-year internship at Missouri Baptist Hospital. Then he served a preceptorship in Hawaii with Jay M. Kuhns, MD, who graduated from the School of Medicine in 1915. In 1933, Brennecke became the Territory of Hawaii Government Physician for the Koloa District. He was a United States Public Health Officer from 1933 to 1958 and medical director of Waimea Hospital in Waimea, Kauai, from 1942 to 1946. He entered a group practice in the Waimea Clinic, Inc., in 1963 and retired in 1975.

The Washington University Medical Center Alumni Association honored Brennecke with the 1985 Distinguished Service Award for his many years of service to the people of Hawaii. ●



Stephen M. Beverly, PhD

Four Faculty Members Elected AAAS Fellows

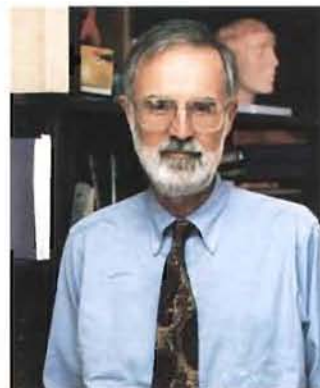
FOUR School of Medicine faculty have been named fellows of the American Association for the Advancement of Science (AAAS). The rank of fellow is the highest awarded by the AAAS, the world's largest federation of scientists, with 144,000 members.

The new fellows are: George W. Gokel, PhD, professor of molecular biology and pharmacology; Marcus E. Raichle, MD, professor of radiology, neurology and neurobiology; Sondra Schlesinger, PhD, professor of molecular microbiology; and Robert D. Schreiber, PhD, Alumni Professor of Pathology and professor of molecular microbiology.

Gokel, who directs the Bioorganic Chemistry Program, is a macrocyclic chemist who studies compounds made of rings of nine or more atoms. In the late 1970s, he synthesized the first lariat-shaped macrocyclic compound. He now incorporates these lariat ethers into synthetic models of biological systems that can insert into membrane, providing channels through which small ions can travel. The research explores the chemical interactions that must occur in the ion channels



George W. Gokel, PhD



Marcus E. Raichle, MD



Robert D. Schreiber, PhD



Sondra Schlesinger, PhD

brain activity as a person performs given mental tasks. By analyzing PET, and more recently, MRI data, Raichle and colleagues are mapping the functional organization of the human brain. Their studies of language processing and other functions have revealed that the brain uses different routes for new tasks and tasks that are familiar.

Schlesinger studies the structure and replication of the Sindbis virus with the hope of developing it into an agent for gene therapy. Her lab is interested in the structure of the Sindbis virus and in its replication. She also is studying ways in which the virus commands a host cell to switch from making its own proteins to making viral proteins.

Schreiber has been a leader in determining the mechanism of action of sev-

eral immune system proteins, known as cytokines, and has developed new techniques to study the physiologic roles of these proteins in the body.

He and his colleagues have helped to define the signaling mechanisms used by a particular cytokine, known as interferon-gamma, and have significantly enhanced understanding of the mechanisms used by other cytokines. ●

that are present on all cells and that are involved in the generation of nerve impulses.

Raichle heads a pioneering team of scientists that investigates brain function using positron emission tomography (PET) and functional magnetic resonance imaging (MRI). Developed at Washington University in the 1970s, PET allows researchers to construct images of

Peck Elected To Chair AAMC Council Of Deans

WILLIAM A. Peck, MD, executive vice chancellor for medical affairs and dean of the School of Medicine, was elected chair of the Council of Deans for the Association of American Medical Colleges (AAMC).

"It is a great privilege to occupy this position," Peck says. "These are very challenging times for our

nation's medical colleges; our goal for the year is to enhance the academic mission of these great institutions."

The AAMC is a professional organization made up of representatives from academic medicine. The AAMC's Council of Deans identifies issues affecting academic medicine and develops strategies to achieve the various missions of medical schools.

Peck serves in the dual position of dean and vice chancellor for medical affairs at Washington University. He also is an internist who is internationally recognized for his work on osteoporosis, a progressive bone disease that affects more than 25 million Americans. ●

Students Launch Community Clinic



Will Ross, MD, left, questions patient Billy Marshall during his initial examination at the Saturday Neighborhood Health Center, which recently opened in Forest Park Southeast. Medical students Benjamin Verdine, back, and Neal Sikka were among a team of six medical students who first proposed the clinic more than a year ago.

THE School of Medicine, working with the Family Care Health Center, has opened a free health care clinic in the Forest Park Southeast neighborhood.

The walk-in Saturday Neighborhood Health Center, which is open from 9 a.m. to noon on Saturdays at the Forest Park Southeast Family Care Health Center at 4352 Manchester, provides medical services in an area where many people lack health insurance and have limited access to health care. A team of six School of Medicine students first proposed the clinic more than a year ago and has been working on the details.

The students, Neal Sikka, Stephen Skjei, Edward Song, Jeanne VanCleave, Benjamin Verdine and Michael Wei, formed the Student Organized Clinic Committee (SOCC) during their first year of medical school. The members of SOCC did their own fundraising, and they also received financial support from the school's alumni association and the dean's office.

With an attending physician from the School of Medicine on duty at all times, the clinic is fully equipped to treat common medical problems such as asthma attacks, sprains and upper respiratory infections. In addition, a student from the George Warren Brown School of Social Work helps link patients to services such as Medicaid. The clinic serves only adults age 18 and above.

The clinic staff includes seven medical student volunteers who assist the attending physician by taking patient histories and performing physical exams. Students also provide information on preventive medicine and screen for diseases such as diabetes and high blood pressure. The attending physician then sees the patient and plans a course of treatment.

Response from medical school faculty and students has been strong. To date, 44 faculty members have offered to serve as attending physicians at the clinic, and more than 150 students have volunteered to serve a shift. ●

Center For Clinical Studies Opens

THE School of Medicine has opened a Center for Clinical Studies, a resource for both industry and faculty investigators who conduct clinical trials of investigational drugs and devices. The center also signed its first contract, a \$1.2 million agreement with G.D. Searle & Co., a wholly owned subsidiary of Monsanto Co.

The center's purpose is twofold, says center director Daniel P. Schuster, MD, professor of medicine and radiology. It will serve as a resource for companies conducting clinical studies by helping to expedite contact with faculty investigators and subjects, consulting on trial design and providing core facilities.

The center also will help faculty investigators negotiate contracts, gain approval from the Human Studies Committee, recruit patients and coordinate projects. The center's services are open to investigators who secure contracts independently or through the center, says Schuster.

The School of Medicine currently conducts about \$11 million worth of clinical trials annually. The figure has nearly doubled since 1992, and Schuster says the Center for Clinical Studies will foster continued growth.

The center recently signed a \$1.2 million master agreement to conduct clinical trials with Searle, which is based in Skokie IL. The company develops drugs in several specialties, including cardiovascular diseases, oncology, women's health, arthritis and sleep disorders.

As part of the agreement, Searle is supporting a clinical fellowship and start-up costs for an information systems office. One of the center's goals, says Schuster, is to provide new opportunities for training clinical investigators. He also hopes the master agreement will serve as a model for other companies. ●

Recognizable Graduates

THE Program in Physical Therapy honored outstanding students and alumni at its graduation ceremony last December.

Among the 77 master's degree candidates honored were Stacy Burkhardt, who received the



Director's Award, which recognizes an individual who excels in academics, shows superior performance in the clinic and contributes positively to class leadership; Rekha Ramanathan, who received the Beatrice Schulz Award, which is named for the first director of the program and recognizes a graduate who excels in clinical performance; and Barbara Shiplett, who received the Steven J. Rose Research Award, named for Steven Rose, who directed the program from 1979-1988. The award is given to an individual interested in research.

Alumni honored were Dick Roettger, St. Louis, a 1962 graduate of the program who has practiced physical therapy for 34 years; Michael Mueller, PhD, an assistant professor of the program who in 1992 was the first graduate of the doctoral program, Interdisciplinary Program in Movement Science at the School of Medicine; and Anne Short, St. Louis, who was a member of the first class to graduate from Washington University with a bachelor's degree in physical therapy in 1948. Short also served as the first chief of physical therapy at the Irene Walter Johnson Institute of Rehabilitation in 1959. ●

U.S. News Ranks Medical School And HAP

THE School of Medicine was ranked No. 5 in the nation among research-oriented medical schools, and its Health Administration Program ranked No. 12 in the 1997 *U.S. News & World Report* rankings.

In the magazine's eighth annual guide to *America's Best Graduate Schools*, the School of Medicine was ranked behind Harvard University, Johns Hopkins University, Duke University and the University of California-San Francisco.

"It is an honor to be listed among the top five medical schools

in the country," says William A. Peck, MD, executive vice chancellor for medical affairs and dean of the medical school. "The rankings reinforce what we within the Medical Center know to be true, that we have faculty members who are leaders in their respective fields guiding brilliant students who are the world's future medical and scientific leaders."

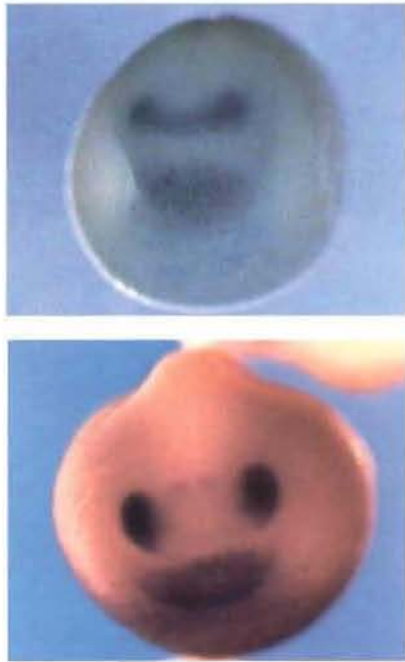
Of the Health Administration Program's ranking, James O. Hepner, PhD, program director, says, "Washington University's Health Administration takes great pride in consistently ranking in the top 10 percent of university graduate health administration programs. For the past 50 years, we have prepared many outstanding health care executives." ●

Student Achievers



Roy R. Peterson, PhD, professor emeritus of anatomy and neurobiology, right, autographs a copy of the *Netter Atlas of Human Anatomy* for second-year medical student Albert Kim. Kim received the Roy Peterson Award in Anatomy at the 1995-96 student awards luncheon in December. Kim was among 24 first-, second- and third-year medical students receiving awards at the event. Other awardees were: Irene Hong McAtee, Nancy Chen, Michelle L. Hermiston, Andrea Stonecipher, Gabriel Soto, Amanda Cashen, David Miller, Amy E. Bane, C. Todd Vedder, Laxmeesh Nayak, Esi Marie Morgan, Ericka Hayes, Elias Dagnew, Patrick Yue, Xinna Kong, Heather L. McGuire, Melanie Everitt-Watson, Neal Kumar Sikka, Geoffrey A. Kerchner, Denise Dewald, Jennifer Sue Gold, Rashmi Mehrotra and Michele Lili Jones.

An Eye For Development



Expression of the *ET* gene in frog embryos reveals how a single eye field becomes two eyes. The upper panel shows an embryo with *ET* expression in two bands. In the lower panel, the single eye band has become two spots.

RESearchers at the medical school have solved a centuries-old puzzle: Do both eyes develop from a single precursor or does each eye develop from a separate structure?

Yi Rao, Ph.D., assistant professor of anatomy and neurobiology, explored eye development after he discovered a gene he named *ET*, which is expressed early in embryonic development. The gene produces a protein belonging to a newly identified family of transcription factors, called T domain proteins, which bind to other genes and turn them on.

The molecular marker made it possible to locate the part of the embryo that develops eyes. By tracking the gene's product, the researchers were able to see the eye field of frogs change from a band into two spots over the course of a few hours.

They also wondered why two eye spots form. "We found that an inhibitory signal shuts off *ET* expression in the middle of the eye field," Rao says.

The signal came from the prechordal mesoderm, which lies beneath the center of the eye field. When the researchers removed the tissue, the eye field formed but it did not divide into two, so the resulting tadpole was cyclopic. Similar experiments showed that the same mechanism operates in chick embryos.

Two recent discoveries suggest the mesodermal signal could be made by a gene called *sonic hedgehog*, which is expressed in prechordal mesoderm and is known to regulate nervous system development. ●

Heart Therapy Via Fiber Optics

FIBER optics and a new laser are being used to perform heart surgery on patients with chronic chest pain.

Thoralf M. Sundt, MD, assistant professor of cardiothoracic surgery, and Joseph G. Rogers, MD, assistant professor of medicine, were the first to use the fiber-optic laser technology in the United States.

They are testing the safety and effectiveness of the new laser, called the TMR System.

"These patients have end-stage coronary heart disease that gives them severe chest pain," Sundt says. "Some can't even bear to walk across a room."

Sundt says three months after surgery nearly all of the patients had less severe angina than previously reported and their tolerance for exercise had improved.

Transmyocardial revascularization, or TMR, is used to relieve this debilitating form of angina. Surgeons use a laser to drill holes in the heart to help improve blood flow around clogged arteries that are beyond repair from standard, conventional therapies such as balloon angioplasty and bypass surgery.

The TMR System offers a more delicate and maneuverable fiber-optic alternative than that currently available. Also, it soon may be deployed through small, "keyhole" incisions in the chest, Sundt says. Eventually, the versatile cables may be inserted through an artery in the leg and guided to the heart through the body, similar to having heart catheterization. ●

1996 Support From NIH



In 1996, the School of Medicine achieved third place among all U.S. medical schools in funds received from the National Institutes of Health. When NIH funds to schools' affiliated hospitals are added, Harvard Medical School ranks No. 1 and Washington University, No. 8.

An Intoxicating Finding: Fatty Acid Ethyl Esters

SCHOOL of Medicine researchers may have answered a question that has lingered ever since humans started smashing grapes: Why does alcohol make people drunk? The researchers discovered that a compound produced by alcohol-soaked brain cells can potentially inhibit the release of neurotransmitters, which is what happens in human brains after five or six beers.

Richard Gross, MD, PhD, professor of medicine, and Rose Gubitosi-Klug, an MD/PhD student, have linked potentially intoxicating changes in brain chemistry to a group of compounds called fatty acid ethyl esters. The compounds, lipid molecules that cells manufacture by combining ethanol and fatty acids, apparently speed up the release of potassium ions from brain cells. In the brain, an increased flow of potassium would inhibit the release of neurotransmitters, says Gubitosi-Klug. A slow-down in neurotransmitter release could lead to slurred



speech, clumsiness, slow reflexes and a loss of inhibitions in intoxicated people, she says.

The researchers achieved their results with a concentration of alcohol relevant to actual drinkers. They treated hippocampal rat cells and insect cells genetically engineered to carry potassium channels with either

0.1 percent alcohol, the alcohol plus some fatty acids or ready-made fatty acid ethyl esters. The straight alcohol solution had no effect on the cells, but the fatty acid ethyl esters and the combination of alcohol and fatty acids greatly stimulated the flow of potassium from each type of cell.

An increased flow of potassium would interfere with communication between brain cells by making it difficult for cells to absorb enough calcium to trigger the release of neurotransmitters. In the hippocampus, curbing the release of neurotransmitters could lead to short-term memory loss, a common complication of drunkenness.

Gross, who also is professor of chemistry and molecular biology and pharmacology, and Gubitosi-Klug say understanding the biochemical pathway of intoxication may eventually lead to new treatments for alcohol addiction. ●

Cutting Chemotherapy-Related Infections

RESearchers here have shortened the time during which high-dose chemotherapy patients are most vulnerable to potentially deadly infections. Through blood transfusions laced with growth factors, they cut the initial period when patients experience severely low counts of infection-fighting white cells to six days from three weeks.

Though high doses of toxic chemotherapy agents effectively kill cancer cells, they decimate many important factors in blood that normally protect the body and fight infection. Some of the most important infection-fighting white cells, called neutrophils, are killed by the billions during the first weeks of chemotherapy.

Such a compromise is dangerous and potentially fatal. As a result, more than 5,000 cancer patients a year in the United States must undergo stem cell transplants to survive chemotherapy. Stem cells are neophyte blood cells that can help strengthen the body's ability to fight infection. Even so, mortality from severe, opportunistic infections during the initial stages of treatment may still reach 5 percent. Up to 10 percent of chemotherapy patients develop a collection of blood infections called sepsis, and all require some form of antibiotic treatment, says Douglas R. Adkins, MD, assistant professor of medicine and a co-investigator in the study.

In an evaluation of 10 high-dose chemotherapy patients under-

going stem cell transplants, Adkins and his colleagues transfused concentrations of neutrophils that strengthened the patients against infection. The transfusions were laced with growth factors, natural body proteins that help regulate the number of blood cells in circulation. When given in high concentrations, growth factors can help neutrophils survive longer, boosting their numbers, Adkins says.

Stem cells may be harvested from bone marrow, but the researchers opted for a second technique, called pheresis, in which the cells are obtained from blood. These peripheral blood stem cells were collected from 30 healthy donors. ●

HOPE *in the face of* AIDS

*Medical School
Programs Take
Extraordinary
Steps To Help
Women And
Children Fight
HIV*

by CHRIS WOOLSTON



Kyanna White appears unconcerned about her future. The four-month-old gurgles in her mother's arms and looks around the room with big, alert eyes. Her mother, Paris Collins, gazes tenderly at her daughter and tickles Kyanna's chin.

Collins, 24, is infected with HIV, the virus that causes AIDS. Although Kyanna's first blood test showed no sign of the virus, it is too soon to say if she is HIV-negative. "They're going to test her again soon, and I pray," Collins says. "God only gives you what you can handle. I think He knows I couldn't handle losing my child."

The scene — an HIV-infected mother holding a baby and hoping for the best — has played out many times at the School of Medicine. In 1996 alone, 23 HIV-infected women who were referred to the medical school gave birth to 23 infants. That's 23 chances for an infant to be born with little hope of reaching his or her 10th birthday.

So far, doctors have given mothers the best possible news: None of the 23 infants has tested positive for HIV. Some will need to be tested again, but researchers already are excited about the possibility of a perfect streak of HIV-negative infants.

Such success seemed impossible just a few years ago. In 1994, the virus struck 44 percent of infants born to HIV-infected mothers referred to the School of Medicine. At that rate, at least 10 of the babies born in 1996 would have been infected.

PROGRAMMED FOR SUCCESS

The mothers and infants in 1996 had two advantages that did not exist in 1994: The Helena Hatch Special Care Center for Women with HIV and Project ARK (AIDS/HIV Resources for Kids). The programs take extraordinary steps to help women and children fight HIV. Together, the Helena Hatch Center and Project ARK

have given families like Paris Collins and her daughter Kyanna unprecedented hope in the face of AIDS.

The programs have much in common. Each takes a comprehensive approach to health care by providing social workers and nutritionists as well as doctors and medication. Doctors from the programs work closely together, sometimes sharing the same room when a mother and her child come in for a check-up.

So when an entire year goes by without an HIV-positive infant, researchers from both programs share in the excitement. "We're delighted," says Gregory A. Storch, MD, professor of pediatrics and medical director of Project ARK, a cooperative network of St. Louis physicians who provide primary care for children with HIV.

"We have some women who are very sick, and we have some women who are very poor," says Victoria Fraser, MD, assistant professor of medicine and medical director of the Helena Hatch Center. "We would have been happy if we could have reduced the rate of transmission to 10 or 15 percent." A year-long transmission rate of zero percent was beyond anyone's expectations, she says.

And while 1996 was a banner year, 1995 also boasted positive results. In that year, only two out of 22 newborns treated at the medical school had the virus, and the mothers of those two children did not go through the Helena Hatch program. So far, not one HIV-infected woman who has received medication, comprehensive prenatal care and social support through the Helena Hatch Center has given birth to an infected baby. "It's a dramatic, amazingly great health care benefit and something that works," Fraser says.

It's easy to see why Fraser and Storch are enthusiastic about their programs. All they have to do is remember the state of AIDS care in St. Louis a few years ago. In 1994, women with AIDS or HIV infection rarely got the medicines and medical examinations that they needed. Services were scattered throughout

the city, and many women lacked the resources to make multiple doctor visits. Even as powerful new AIDS drugs arrived, women in St. Louis kept getting sick and passing the virus to their children.

"In the past, most of the HIV services were geared toward gay men, particularly gay white men," Fraser says. "Many women either didn't seek medical care, or, if they got medical care, they didn't stick with it because it was too directed at one specific group." HIV clinics were not equipped to handle the needs of women, Fraser says. "They didn't have the facilities to do pelvic exams, pap smears, to check for sexually transmitted diseases or provide birth control. Women were really disenfranchised."

Infected babies became the hallmark of the system. In 1994, the virus struck eight out of 18 babies born to HIV-infected mothers referred to the medical school, for a transmission rate of 44 percent — far exceeding the national average of 25 percent.

Researchers here knew that many of the infants could have been saved. A national study had shown that aggressive therapy with the anti-HIV drug AZT could reduce the transmission rate to 8 percent. Doctors had the tools to protect infants, if only they could reach the mothers.

ONE-STOP HEALTH CARE

Fraser saw a need for new type of health care clinic — a one-stop shop where HIV-infected women could get their medications and medical exams. The federal government awarded her a Special Project of National Significance grant in 1994, and the Helena Hatch Special Care Center started running at full speed in early 1995.

Today, the clinic treats more than 200 women from St. Louis, eastern Missouri and southern Illinois. Women who visit the clinic see an infectious disease specialist — either Fraser or Mary M. Horgan, MD,

assistant professor of medicine — who measures their virus levels and prescribes medication. Nurse practitioner Katherine Williamson provides gynecological care and checks for cervical cancer, a common problem for women with HIV infection. Peer counselors who have HIV share advice and personal stories with other patients. The care is not limited to the clinic, however. Social workers from the center make home visits and help the patients find food, work and a decent place to live.

Care shifts into an even higher gear when a woman becomes pregnant. “We see them every month, we chase them around, we do pill counts, we have all of these nurses and social workers providing extraordinary medical care — it’s more medical care than I got when I was pregnant,” Fraser says. Treatment becomes intense during labor. Specially trained members of the Department of Obstetrics and Gynecology deliver the infant while the mother receives AZT intravenously.

If any pregnant patient doubts that the Helena Hatch Center is a different kind of clinic, all she has to do is miss an appointment. “If they don’t make their appointment, our staff members are like bulldogs,” says Karen Meredith, director of the center. “They will get that woman in and encourage her to take her AZT, which might not happen if she were attending a very busy prenatal center somewhere else.”

Women with infants have a special incentive to visit the Helena Hatch Center. Staff members from Project ARK work alongside the center’s staff so the whole family can be treated at once. “Before the Helena Hatch Center, moms would be quite conscientious about bringing us their babies, but the moms wouldn’t be getting any care,” Storch says.

The doctors, nurses and social workers at Project ARK see children of varying ages and stages of infection, so they must attack HIV in different ways. They feed newborns an AZT syrup and test their blood for HIV. The test is repeated several



Victoria Fraser, MD, says if the Helena Hatch Center is forced to close its doors, HIV-positive babies may become the norm again in St. Louis.

times during the infant’s first four months of life. Even when tests are negative, the children receive antibiotics to help fight the infections that can kill children with AIDS. If they still show no signs of the virus after two years, the children “graduate” from the program.

When infants are born with HIV infection, Storch and Kathleen McGann, MD, assistant professor of medicine and co-medical director of Project ARK, try to fight the virus with a combination of drugs. Still, some children show symptoms within a few months and die well before their second birthdays. Storch and McGann are following other infected children who are 5 or 6 years old and still look and act perfectly healthy.

The doctors say it has been some time since they have held an infected newborn. “Our clinic is changing right before our eyes,” Storch says. “Our youngest infected baby is 20 months old.” No one knows for sure how the medical school has managed 20 months without an infected newborn. Perhaps the prenatal care offered by the Helena Hatch Center is the key, or it could be the careful but aggressive use of AZT or a combination of

both. But members of the Helena Hatch Center and Project ARK know they would not want to fight AIDS and HIV infection without each other’s program.

Unfortunately, Project ARK may soon be left to fight alone. The \$600,000 annual federal grant that runs the Helena Hatch Center will end in 1999. Unless the center can find another source of funding, it will have to close its doors in two years. “That would be terrible,” says Storch. “We’ve been there before. We’ve worked with these families at a time when there wasn’t a women’s clinic, and despite real efforts, it was difficult to keep these women under care.”

“It’ll be very scary if we can’t keep this program going,” Fraser adds. “I’m afraid we’ll start having a lot of HIV-positive babies born again.”

For now, the Helena Hatch Center seems too boisterous to be in any danger of dying. Children scatter toys across the playroom. Nurses and social workers pass each other in the hallways, and mothers hold infants in the waiting rooms. Paris Collins grabs Kyanna by both hands and helps her stand on a table. “She’s fighting for her life, but I’ve been blessed,” Collins says. “She hasn’t fallen sick or anything. I know everything is going to be OK.” ●



Editor’s Note: With this issue we begin

Community Connection, a periodic feature spotlighting programs sponsored by the School of Medicine. An integral part of Washington University’s fundamental mission and vision is to reach out to individuals in the community and provide help to those in need. The Helena Hatch Special Care Center for Women with HIV and Project ARK are two of the many outreach programs that help Washington University fulfill its goal to deliver superior health care and enhance the community with its commitment to service.

MEDICAL EDUCATION AT THE CROSSROADS

Curriculum Changes Will Prepare Students And Medical School For The Future

by Kleila Carlson

Flexibility, diversity, communication, integration. These are some of the key elements of the modernized, customized curriculum that will be unveiled this fall at the School of Medicine.

Eight years of discussion and almost four years of legwork and contemplation by administrators, faculty and students went into the Medical Education 2000 Project, which will be phased in over the

next three years. Officials describe the revised program of study as "contemporary," and say it will enable the school to meet the challenges of the future while preserving the excellent educational foundation upon which it was built.

"We are not going to alter the basic philosophy of how we run the education program here," says Bruce Dowton, MD, associate dean for medical education, who spearheaded

the project. "But I think we've crafted a plan which redefines some of our priorities, recognizes new technologies for education and contextualizes the way the curriculum might evolve into our culture."

Dowton, who has spent 3 1/2 years in the trenches tailoring changes to the existing curriculum, says recent pressures on the national, local and regulatory fronts dictated that something be done. The two

biggest challenges facing all medical schools, he notes, are financial and sociological.

"The increased penetration of managed care into the health care

decades, and we can't just keep on adding to the curriculum without regard to priority and relevance," says Dowton. "We've got to step back and rethink what is really core



Bruce Dowton, MD, left, with medical students Heidi Weilbach, seated, and standing from left, Mike Kappelman, Erik Wallace and Ramsey Ellis. Dowton is showing the students the program for instructional materials for the genetics course that he and Jeffrey I. Gordon, MD, teach first-year medical students.

marketplace has eroded the clinical profit margin, which historically has supported much of the unfunded research and education taking place at medical schools," says Dowton. "And as the marketplace changes, so too, does the way in which health care is provided: to outpatient community-based settings from inpatient intensive or inpatient hospital-based clinical settings."

To respond to the changes in health care and health care delivery, Dowton says the medical school needs a curriculum that offers students more flexibility and more educational opportunities in ambulatory settings. On top of that, he says, the school must decide how to deal with the explosion of basic biomedical information in the first two years of medical school, and how to enhance clinical experiences for students in the Medical Scientist Training Program, one of the oldest and most respected in the country.

"The amount of basic biomedical, scientific information has burgeoned enormously over the last two

and how we can achieve that core without sacrificing the richness and the depth of what a research institution like Washington University has to offer students."

The recent reconfiguration of the hospitals that partner with Washington University in teaching its medical students is another factor in the education equation. In the long term, Dowton says the BJC Health System will provide a valuable opportunity for exposure along the continuum of health care delivery, from rural cottage hospitals and clinics to tertiary through quaternary care. "The opportunity to design a medical student education program that takes advantage of the wider BJC system is a potential attraction, where most of our teaching has historically been done in a tertiary care environment," he says. "This will better prepare students for the practice of medicine."

The Proposal

The plan being proposed maintains the existing two years of basic pre-clinical study followed by two years of clinical experience. But it affords students greater flexibility than before in creating and planning their medical education.

"We want increased flexibility to be our hallmark of the first year," says Dowton. "We want a program that promotes flexible opportunities for students to have some choice, but to be rigorous, nonetheless, in how they approach those offerings."

Under the proposed plan, students who have strong backgrounds in biomedical sciences would have the opportunity to bypass the core molecular foundations of medicine course of the first year and take advanced or graduate-level courses. Also, courses that previously have been taught in a very separate way and at different times of the year, such as pharmacology and pathology, will become more coordinated as students study organ systems and learn disease perspectives from the clinician, pathologist and pharmacologist in a cohesive manner.

"The faculty would jointly decide how they are going to do it," Dowton says of how the courses would be planned. "We don't look to complete integration — it wouldn't be a single course. But we would be looking to closely coordinate what goes on between departments."

On top of the medical biology core curriculum of the first year, a program of so-called "selectives" will be offered so students can explore areas they find interesting. They may elect to participate in a basic science journal club in cell biology or to examine how molecular genetic diagnostics are performed in the laboratory. They also could opt to

PLANNING DOMAINS FOR CURRICULUM	I	II	III	IV
Medical Biology	☉			
Human Pathobiology		☉		
The Physician for the Patient and Society	☉	☉	☉	☉
Core Clinical Experiences			☉	
Selective and Elective Opportunities	☉			☉
Evaluation and Outcomes	☉	☉	☉	☉
Health Promotion, Disease Prevention and Delivery of Health Care	☉	☉	☉	☉
Perpetuation of Learning	☉	☉	☉	☉
Environment for Education	☉	☉	☉	☉
Governance of Education	☉	☉	☉	☉

This matrix outlines the 10 core planning domains and assigns the content of each domain to relevant time periods of the four-year curriculum (Year I, II, III & IV).

pursue humanities, literature and medicine, or ethics relating to privacy of medical writings.

Communication will be key to the project's success, Downton says. "We will promote communication at every level - from faculty to students, from students to faculty, among students and among faculty within and between courses — by using an information systems approach," he says. "We have designed an interface that will allow anyone with the right software who is on the campus-wide network to get into curricular material."

Downton says another important feature of the revised curriculum is that it incorporates an appreciation of students' different learning aptitudes. "Our students bring a rich diversity of ways in which they learn," he says. "Some people learn better in group settings; some people learn better by self-study. The idea that our curriculum would promote a more flexible way in which students get at materials and learn is an attractive feature. Part of that involves freeing up time for them to be able to do things in the way that works for them best."

Students Speak Up

Students seem to agree. At present, first-year students study anatomy, biochemistry, cell biology, histology, medical genetics, microbiology, neurosciences and physiology, along with a humanities course and an elective. They describe the curriculum as "time-intensive" and say it leaves them few hours in the day to study.

"The curriculum here is good, but it's not flexible. And for those who don't learn well from lecture it's difficult to decide whether to attend lecture or spend the time studying," says Ramsey Ellis, medical education representative for the first-year class.

Ellis says students are excited about the proposed changes. One course offering she and others are particularly enthused about is clinical interviewing skills, which prepares students to work with patients in their third- and fourth-year clinical clerkships. The first- and second-year course, which was introduced two years ago, teaches students how to take a patient history, complete a physical examination, write up findings and present cases orally in a clinical setting.

"Students get more practice in taking histories and doing physicals so that they can enter their third year (clinical clerkships) with confidence," she says.

Like the first year, the second year will feature organ-based teaching. It will differ from past second-years, however, in that it will be divided into short modules. At the outset, introductory pathology and pharmacology will be discussed, followed by four or five six-week modules on organ systems that have been coordinated between the teaching clinical faculty and the pathology and pharmacology faculty.

"The second year has traditionally been a series of yearlong courses, which the proposal would eliminate," says Downton. "There would be no more yearlong, cumulative exams. The idea being that students would complete each of these modular units, with five to six weeks of class time, and then they would have exams for that segment."

Downton says many aspects of the proposal already have been tested among students and faculty in pilot programs over the last several years. One recently integrated course that has been particularly successful is "Diseases of the Nervous System," which was previously known as

neuropathophysiology. The second-year course, which Downton describes as a "gold standard," has been coordinated between physiology, pathology and pharmacology.

Second-year medical student Larry Bercutt had the course last semester and says students benefit by integrating or coordinating disciplines.

"It helps us learn," says Bercutt, who is second-year class president. "When we're looking at an organ or disease process and we see and hear about it from all the different medical perspectives — clinical, pathological and pharmacological — it helps us integrate the material.

"We had lab sessions with a clinician and pathologist together — before they were two sessions at different times of the year and in separate laboratories. Here, we got to integrate what the clinician sees, what the pathologist sees and how both fit together in making a diagnosis."

Repositioning For Patient Care

Integration and flexibility will not stop with the first and second years, but will be continuing themes through the mandatory clinical clerkships which occur in the third year of medical school, says Dorothy A. Andriole, MD, assistant dean for student affairs and medical education.

Andriole says the proposed third-year curriculum would continue to include a three-month internal medicine rotation, ultimately with a four-week block in an ambulatory setting for every medical student. Currently, about one-third of students have an opportunity during the course of their internal medicine rotation to spend a month in ambulatory medicine. But as contacts with practicing physicians increase, Andriole anticipates that all students would have such an opportunity.

"Students need the opportunity to be at the forefront of diagnosis,

seeing patients when they first present with medical problems," she says. "Due to the tertiary nature of the care we deliver at Barnes-Jewish Hospital, pure inpatient rotations increasingly result in students being exposed to only the sickest patients with the most complex illnesses. Students simply may not encounter patients with common or minor medical problems, or healthy patients with fairly major problems. This has been one of the challenges that has stimulated us to re-evaluate the curriculum."



Dorothy A. Andriole, MD, speaks to a group of third-year medical students who are currently performing their surgery clerkship.

The blocks of time that students spend in the required disciplines are also likely to be revised. Andriole says students generally benefit most from a minimum of three-to-four weeks at one site to get to know the practicing physicians and residents, the patients and the environment in which they are working. Currently, clerkships in neurology, neurosurgery, otolaryngology and ophthalmology are three weeks or less.

"We have looked at designing a curriculum based only on four-week rotations — 12 separate four-week rotations over the course of the 48 weeks required for clinical clerkships," she says. "At the same time, we have been interested in looking at ways to incorporate a family prac-

tice rotation into our mandatory curriculum, as this is a field that is of interest to more and more of our medical students."

Some changes have been implemented over the last several years. Clerkships in surgery and internal medicine, which previously included rotations of varied lengths, from three to six weeks, now consist of three four-week rotations. The surgery curriculum also has been broadened and expanded so that it will integrate surgical disciplines in related fields such as otolaryngology, ophthalmology and anesthesiology, as well as general surgery.

Likewise, rotations in pediatrics and obstetrics and gynecology will be combined into a single 12-week maternal child medicine block, Andriole says. It will include experiences in women's health, obstetrics, newborn medicine and pediatrics.

Andriole says the proposed changes mean a better defined third-year curriculum for all medical students. "It provides a more cohesive experience of uniform quality and an opportunity within the constraints of the mandatory third year for students to have some flexibility in exploring specialty choice options and to have increased exposure to ambulatory care," she says. "It also provides a better opportunity for the faculty to more thoroughly evaluate students and provide them with ongoing feedback as we get to know them better by having them at fewer sites but for longer periods of time."

Most students take the fourth year of medical school, which is broken up into four-week rotations, to explore possible specialty choices or disciplines not included in the mandatory third-year rotation, such as dermatology, radiology and radiation oncology, Andriole says. About 15 percent of students do not go on to complete a fourth year because they are in the MSTP.

"The fourth year is as individual as the student," says Andriole. "I don't know two fourth-year students with the same schedule. The students have a required number of weeks to spend on campus, but there is tremendous flexibility in the scope

and design of the rotations. It is one of the very attractive features of the curriculum that they do have this flexibility."

Andriole and Dowton say that "change for the sake of change" is not what is taking place at the

School of Medicine; rather it is an attempt to respond to the realities of a changing medical field.

"It's not as revolutionary as a lot of schools have done in the last 10

years," Dowton says of the proposed curriculum. "I believe it's good that it's not that way. It's methodical, it's respectful of the good things here at Washington University and at the same time promotes creativity in other areas." ●

Integrating Courses One Step At A Time

The second-year course, "Diseases of the Nervous System," was inspired by course masters Alan L. Pearlman, MD, and Kevin A. Roth, MD, PhD, and is the first truly integrated systems course to be taught at the School of Medicine.

Pearlman is professor of neurology and neurological surgery and of cell biology and physiology, and Roth is associate professor of pathology and of molecular biology and pharmacology. Together, with the help of Douglas F. Covey, PhD, professor of molecular biology and pharmacology, they have taken what used to be the course in neuropathophysiology and blended it with neuropathology, clinical neurology and neuropharmacology.

"This is a process that has been going on for four or five years now," says Roth. "Part of the integration had to do with Alan's and my appreciation of the fact that we were teaching common topics from different points of view.

And in the spirit of Washington University and its multidisciplinary approach, we really made an effort to not look at our individual courses as separate entities, but to ask ourselves what the students were getting on the whole."

The monthlong course features a series of lectures from neurologists, neurosurgeons, neuropathologists, neuropharmacologists and infectious diseases faculty. In addition to the lectures, there are laboratory and clinical correlation sessions in which case

vignettes are discussed by clinicians in neurology, neurosurgery or infectious diseases, along with neuropathologists who present the pathology that is directly relevant to the case material.

"It's a very close tying of a clinical discussion and a pathological presentation, so the cementing takes place at one time," says Pearlman. "It's easier for the students to have most of the material about a given topic at the

kind of integrated course and that really is a boon to the students."

Roth says students have been asking for more integration in neurology on their course evaluations.

"Repeatedly, we would get comments about redundancy," he says. "So now that we are encouraged to have fewer lecture hours and a more varied teaching style, this fit in perfectly. Now, if I want to talk about degenerative diseases, I don't have to give a 15-minute introduction into the clinical

presentation of Alzheimer's disease because they just heard that in the previous hour. I save myself time so I can concentrate on the topics that weren't covered."

Pearlman and Roth estimate that by integrating course material they have reduced their total number of lecture hours by about 25 percent and created both a more efficient way of presenting information and more time for small group sessions.

"I would encourage other course masters to do it," says Pearlman. "It's very gratifying, and the students certainly appreciate our efforts. The faculty who have taken part, the clinicians and pathologists, enjoy being in the same room discussing the same case."

"The neuroscience community here is quite strong and cooperative, and that has made this integration very easy to do," adds Roth. "There has to be a critical mass and a commitment by the course directors to do the melding for this to be a success." ●

by Kleila Carlson



At the conclusion of the course, *Diseases of the Nervous System*, students meet with course masters to discuss subject material and suggest improvements. Seated from left are second-year student Jennifer Smith, and course masters Kevin A. Roth, MD, PhD, and Alan L. Pearlman, MD. Standing from left are second-year students Karen Woolf, Maria Dans and Julie Schwarz. Course master Douglas F. Covey, PhD, is not pictured.

same time so they can integrate and cross-fertilize."

Covey says the biggest advantage the format offers is the opportunity to eliminate redundancy.

"If you are going to talk about treatment of disorders you must go back and describe the disorder and talk about the basic pharmacology of the drugs you are going to use, so there is a necessity to repeat a lot of material," he says. "That is eliminated in this

WORKING AGAINST THE

The Alzheimer's Disease Research Center Races To Find Causes And Cures

Like the lives it affects, the Alzheimer's Disease Research Center at Washington University is in a race against time.

Just two decades ago, Alzheimer's disease was rarely diagnosed. Now, scientists know it afflicts 4 million Americans — a number that will increase dramatically as the population ages — and is the leading cause of dementia and the fourth leading cause of death among adults.

When the Alzheimer's Disease Research Center (ADRC) was established here in 1985 by the National Institutes of Health, it was one of only 10 designated centers to facilitate in-depth research on

Alzheimer's disease and related disorders. There are now 27 Alzheimer's Disease Centers across the United States.

"This disease is an enormous problem in society today and it's only going to get worse," says Eugene M. Johnson, Jr., PhD, ADRC co-director. "Curing Alzheimer's disease is going to make traveling to the moon look like a cakewalk; it's a very difficult scientific and clinical problem that involves many people with different areas of expertise and perspectives."

Bringing together clinical researchers and basic scientists to focus on questions about the relationship of aging and Alzheimer's disease has been the ADRC's primary role since it was established under the direction of Leonard Berg, MD, professor of neurology. That focus will continue when Berg steps down on May 1, 1997, and his responsibilities are assumed by Johnson, who is Norman J. Stupp Professor of Neurology, and John C. Morris, MD, associate professor of neurology and assistant professor of pathology.

"Leonard Berg has been able to attract a lot of very talented people to the problem of Alzheimer's dis-

ease," says Johnson, who also is professor of molecular biology and pharmacology. "He has been able to maintain their interest and enthusiasm as well as show them how they can interact together to accomplish something that could not otherwise be done."

"Our challenge now is to maintain the momentum, create new initiatives, and expand our activities to try and attract other investigators to Alzheimer's and neurodegenerative disease-related research."

Early, Accurate Detection

The ADRC grew from the program project award Healthy Aging and Senile Dementia (HASD), which Morris has been involved in since it was first funded in 1984. For several years prior to that, Berg had been studying older volunteers in a forerunner program known as the Memory and Aging Project, or MAP. Morris now directs MAP and also is the principal investigator of HASD, which is one of the major grants within the ADRC that carries on clinical research, focusing on

THE CLOCK

by *Meila Carlson & Joanna B. Downer*

healthy aging and mild dementia of the Alzheimer type. Within the HASD, the yearly progress of some 1,200 volunteers — both healthy and demented — has been followed through clinical, psychometric and other studies.

"We are increasingly interested in the aging of healthy people because as we become better able to recognize Alzheimer's in its earliest stages, we need to know what is normal cognition for a 75-year-old, an 85-year-old or a 95-year-old," says Morris. "So, healthy participants remain an important aspect of our studies."

The program project has set international standards for evaluating patients with Alzheimer's disease. Through it, researchers

developed a widely accepted system for staging the severity of dementia in Alzheimer's disease known as the Clinical Dementia Rating (CDR). The system, which allows comparisons of research subjects at different centers, is accurate even for patients

in the initial stages of the disease. It uses clinical interview and examination together with biochemical and imaging tests to rule out other causes and make a diagnosis of Alzheimer's.

The Washington University team was the first to validate its criteria through autopsy studies.

"When we first started this work, it was said that there was no way to make a diagnosis of Alzheimer's during life, and that when a diagnosis was made it was in error 35 percent to 40 percent of the time," recalls Berg. "The reviewers for our grant proposal were skeptical that we could make the diagnosis with confidence, but we were correct on every one of the first 50 research subjects

that were autopsied after we had diagnosed them. For a while, we were running at 100 percent accuracy; our current accuracy rate is about 95 percent."

By carefully mapping the clinical progression of Alzheimer's over the course of the disease, Berg says the ADRC has provided researchers with insight into the natural history of the disease — information that is

critical when planning clinical trials to prove the effectiveness of new medications.

"Washington University is known around the world for its ability to identify people in the mildest stages of the disease with confidence and to map their natural history over time with the use of our staging instrument, the CDR," he says.

Morris says it is a goal of the ADRC to maintain that identity. "Our ability to distinguish cognitively healthy adults from people in the earliest stages of Alzheimer's is going to become even more important, because increasing numbers of therapeutic agents are becoming available for Alzheimer's disease," says Morris. "If we can identify the disease in its earliest stages, then that is the time we'd like to intervene."

Morris says this involves examining Alzheimer's on both a human scale and a microscopic scale, melding interdisciplinary efforts to identify causes and cures. Currently, more than 15 departments and divisions at Washington University work under the umbrella of the ADRC. "Because we are looking at a disease of the brain, a tremendous number of fundamental questions about how the brain works become apparent and can be addressed in a variety of ways, ranging from molecular, cellular, systems and clinical levels," he adds.



Eugene M. Johnson, Jr., PhD

Looking To The Genes

Johnson says basic scientists working under the wing of the ADRC are advancing fundamental knowledge that is or may be related directly to neurodegenerative disorders and their causes and cures.

One of the most exciting fields of research is human genetics; Alison M. Goate, PhD, associate professor of psychiatry, discovered the first gene responsible for familial Alzheimer's in 1991. To date, three chromosomes with genetic mutations have been related to familial Alzheimer's. The mutations have been found to produce disease in almost all individuals when they reach the appropriate ages.

"Right now, much of the basic science of Alzheimer's disease is being driven by the enormous insights provided by genetics in the last several years," says Johnson. "I think the challenge in the future will be to translate this kind of basic science insight into practical strategies to retard the process of disease development.

"To reverse the disease or cure Alzheimer's may be too grandiose an expectation. But I am optimistic that we will find ways to slow the progression of the disease, particularly through genetic tests or biochemical tests that would identify



John C. Morris, MD

people who have the disease but who are not yet symptomatic."

In addition to human genetics, Johnson says advances in transgenic and gene knockout technologies have led to new ways to learn about Alzheimer's at the smallest levels. Until recently, researchers had few alternatives to verify proposed mechanisms of dementia or to try new therapies.

"To have animals that present many of the neuropathological hallmarks of Alzheimer's allows us to test ideas about how to halt development of the disease, and likely re-energizes researchers who are afraid to leap from cell culture to expensive human clinical trials," says Johnson.

"Developing treatments that

slow the progression of disease by 50 percent, and administering them before symptoms appear, would add many cognitively healthy years to a person's life," he adds.

Meeting Its Mission

The ADRC's clinical and research missions are complemented by education and outreach programs which occur at nursing homes, private organizations, schools and conferences for professionals and the public. The ADRC also publishes its own newsletter, *Horizons*.

Kathy Mann Koepke, PhD, executive director of the ADRC and director of its education core, says the ADRC reaches isolated or



Theresa Brayford, MHS, OTR/C, left, helps Katie Wynne glue together two sides of a bookmark. Wynne participates in the Memory and Aging Project Satellite activity group that meets weekly at Metropolitan Village in north St. Louis. The activity group was started last fall by Janet Acocks as part of a project for her master's degree in occupational therapy. Acocks died on Feb. 20, 1997, from an asthma attack.

underrepresented populations through outreach programs, such as the Memory and Aging Project Satellite that meets weekly at Metropolitan Village in north St. Louis.

The project, which was designed to identify persons with dementia, provides diagnosis and connects participants with social service agencies. It is run by Dorothy Edwards, PhD, assistant professor of occupational therapy.

Another program, operated in collaboration with the University of Iowa, links rural health care providers with information and expertise from large centers, such as the School of Medicine. This is accomplished through electronic media, including the Internet, and teleconferencing.

Mann Koepke also manages an on-line e-mail discussion group and Internet site at <http://www.biostat.wustl.edu>. The discussion group, started in 1994, has attracted worldwide attention and led to similar projects in England, Russia and Israel.

Mann Koepke says the goal is to educate people that Alzheimer's is not an inevitable part of aging and that treatment may be available.

Johnson says time is of the essence. "Age-related neurodegenerative diseases are a time bomb in our society," he says. "In many ways we are working against the clock. The Baby Boomers are on their way. We need to move forward with a greater sense of urgency than ever to try to translate these basic science discoveries into things that are going to have an impact on this devastating and very complicated disease." ●

Editor's Note: Joanna Downer is a graduate student in chemistry who works in the laboratory of Michael J. Welch, PhD. For information about taking part in an Alzheimer's study, call 286-2683. For web site information on the ADRC Neuropathology Core Laboratory, contact URL <http://www.biostat.wustl.edu/adrc/adrc2.html>

Berg MAPs The Course For Alzheimer's Disease Research

by JOANNA B. DOWNER

Leonard Berg's interest in aging and neurodegenerative diseases began in 1972 with the study of symptomatic hydrocephalus, an adult version of what is called "water on the brain" in infants. He organized a study group of interested Washington University researchers to develop clinical criteria to distinguish reversible hydrocephalus from cerebral atrophy.

Sometime later, he says, neurologists began to realize that cerebral atrophy was actually Alzheimer's disease and was very common. "We saw a lot more of what would prove to be Alzheimer's than hydrocephalus, and it was closely related to aging," says Berg, MD, professor of neurology and director of the Alzheimer's Disease Research Center (ADRC). "So, we focused on the larger public health problem, Alzheimer's disease."

Berg's study group evolved into the Memory and Aging Project (MAP), a clinical research team that evaluates older healthy subjects and persons with mild dementia of the Alzheimer's type. The research was so successful that it was eventually expanded into a program project called Healthy Aging and Senile Dementia (HASD), which was funded by the National Institute on Aging in 1984 and directed by Berg until this year.

Although Berg will step down as ADRC director on May 1, he plans to continue his clinical research on the natural history of Alzheimer's disease. "One of my ongoing projects under HASD focuses on healthy aging and Alzheimer's disease in the very old — people in their 80s, 90s and past 100," he says. "I'm also working on a major manuscript comparing the changes in the brain and clinical manifestations of Alzheimer's across the age span, from the mid-40s to over 100."

Berg, who was honored for his contributions to Alzheimer's research with a symposium at the Eric P. Newman Education Center in April, says there will be many advances in the future. "There will be more discoveries in genetics and in the biochemical abnormalities that result from genetic mutations, and how they lead to disease. This will result in improved drug designs to prevent or delay Alzheimer's," he says.

"Functional imaging techniques will be important to compare mental processing in healthy young and older adults, and those with Alzheimer's," he continues. "All of this research will help us to answer the question all Alzheimer's researchers ask: Is Alzheimer's an exaggeration of the normal aging process or a different kind of brain disturbance?" ●



Leonard Berg, MD, talks with Mary K. Witte, 87, of St. Louis, during her annual visit to the ADRC. Witte has participated in the center's clinical research programs as a control subject for 17 years.

Igniting Immunity

Researchers Find That Antibody Pr

Circulating throughout the human body are many immune cell and protein "Paul Reverses" that call out an initial alarm in defense against infection. But recently, one voice has been heard above the rest, growing louder and carrying farther than before. The voice is that of a well-known family of proteins, called the complement system, which researchers have learned plays a key role in rallying the body's defensive forces into action.

The complement system, in part, induces the antibody response, which is one of the two main branches of the immune system. Protein combinations of antibodies and complement are one of the main guardians against disease. However, a debate over whether complement actually prompts antibody production has gone on for decades.

"Scientists have known for a long time that the complement system contributes to the development

of various immune functions," says Hector D. Molina, MD, assistant professor of medicine in the division of rheumatology. "Now, we understand more about its role in boosting production of antibodies — a crucial element in immune protection."

Through his research, Molina describes the complement system as a fuse for the explosive actions of B cells, the body's antibody-producing cells, and subsequently for a full-force immune response. He reported the findings in the April 1996 *Proceedings of the National Academy of Sciences*. With the help of a live mouse model, the work may also have an impact on the understanding of autoimmune diseases and other disorders in humans and clarify the ability to develop resistance to infection, Molina says.

The complement system is essential for the overall efficiency of immune defenses. First recognized in the late 19th century, the system was named for its ability to work with antibodies to kill foreign invaders. Initially, scientists thought it simply

complemented the actions of B cells as they initiated the body's antigen-specific immune response. Specific antigens, or invaders, elicit different immune responses from the body, and complement was thought to tailor and focus the body's pinpoint chemical defenses. These actions are indeed the case, but Molina has helped clarify the science.

"B cells are in charge of antibody production, but for certain antigens, a robust response from B cells relies heavily on proper function of the complement system," Molina says. "Whether the complement system is properly activated seems to determine whether bacteria or other microbes are properly recognized and eliminated from the body, or are poorly recognized and allowed to proliferate and cause disease."

The response is part warfare and part ballet. Complement proteins, which are distributed between blood plasma and cell surfaces, attach to invading microorganisms to help recruit circulating immune cells.

by GEORGE CORSIGLIA

Antibody Production Takes Its Cue From Complement

The circulating cells, which include neutrophils and macrophages — the scavengers of the immune system — join in the effort to kill invaders. New evidence from Molina's work shows that B cells are cued in a similar fashion, making complement an even more versatile component of the immune system.

A New Model

Since its discovery, the complement system has been shown to interact with a variety of immune system components to coordinate the most definitive and potent host responses to infection. The system itself is actually a series of more than 20 related proteins that work in a cascading, chain reaction to fight infection and disease. Another key talent is complement's ability to distinguish between "self" and "non-self" — the essence of immunity. Such vital distinctions allow the body to destroy harmful bacteria,

microbes and parasites, and separate invading antigens from host tissues and cells.

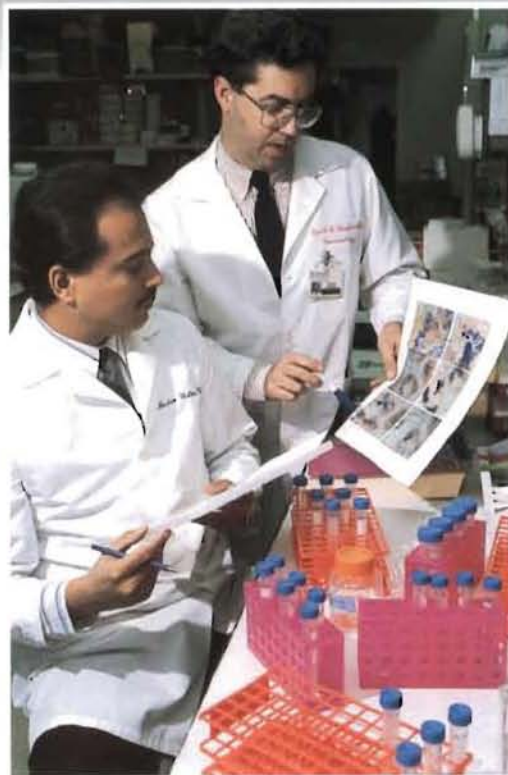
Molina and his colleagues used genetically altered mice to study the role of complement proteins in regulating B cells. By removing a specific gene, the scientists bred mice deficient in the receptors on B cells that recognize activated complement proteins. These complement receptors serve as important docking mechanisms; they allow B cells to link with foreign antigens tagged with complement proteins. Once the connection is made, the B cells' ability to produce antibodies is enhanced.

Removing, or "knocking out," genes in such experiments is like pulling a fuse from a fuse box; certain functions may shut down as a result. In Molina's initial experiments, the genetically altered mice failed to produce antibodies against a specific antigen-laced vaccine. Without the complement gene in place, a major pillar of their immune systems failed to develop.

"In the absence of the complement receptors on B cells, there is not an adequate immune response to specific antibodies," Molina says. "This demonstrates that activation of the antibody portion of the immune system is dependent on the complement system. And without antibody production, other facets of the immune system may not be activated, and infection will prevail."

The genetically altered mice differ from their normal litter mates in one major way: They lack two specific complement receptors normally present on B cells, Complement Receptor 1 (CR-1) and Complement Receptor 2 (CR-2). In the genetic blueprint for mice, a single gene encodes for both CR-1 and CR-2, providing a clear target for the gene deletion experiment.

Molina and his colleagues also established that CR-1 and/or CR-2 work together with the major class of communication molecules in B cells called membrane immunoglobulin. Binding of foreign antigens to membrane immunoglobulin signals



Studies by Hector D. Molina, MD, left, and David D. Chaplin, MD, PhD, show that the complement system plays an important role in boosting production of antibodies, a crucial element in immune protection.

the activation of B cells. In turn, the signal initiates a complex chain reaction that ultimately leads to B cell proliferation and the secretion of antibodies.

"The experiments revealed that in specific circumstances, membrane immunoglobulin works in tandem with the complement receptors to

activate a robust immune response from B cells," Molina says. "When CR-1 and CR-2 are missing, the process falters. So it is clear that not only do these receptors help stimulate production of antibody, they also help enhance the efficiency of the B cell response to certain antigens."

Resisting Infection

Molina's work, conducted with collaborators from the University of Colorado and the Monsanto Co., may help explain the complement system's role in the body's ability to develop resistance to certain infections. Scientists refer to resistance as adaptive immunity.

In separate observations, the same genetically altered mice that lacked complement receptors also had difficulty developing adaptive immunity. In humans, the malfunction would be similar to never becoming immune to the chicken

pox. Most people suffer through the infection once, but if there were no adaptive immunity to build resistance, the pox virus, among many other microorganisms, would overwhelm them again and again.

CR-1 and CR-2 are important factors in adaptive immunity; they are thought to help the body store copies of old, infectious foes. The copies, called immune complexes, are essentially static displays of dead antigens combined with the antibodies originally used to kill them.

For safe keeping, the body retains the immune complexes to remember how its enemies look and feel — and to remember what it took to kill them. If the body recognizes an antigen it has destroyed before, immune complexes serve as templates for mass producing the appropriate antibody response. One theory of adaptive immunity holds that immune complexes are stored throughout life in the spleen and lymph nodes.

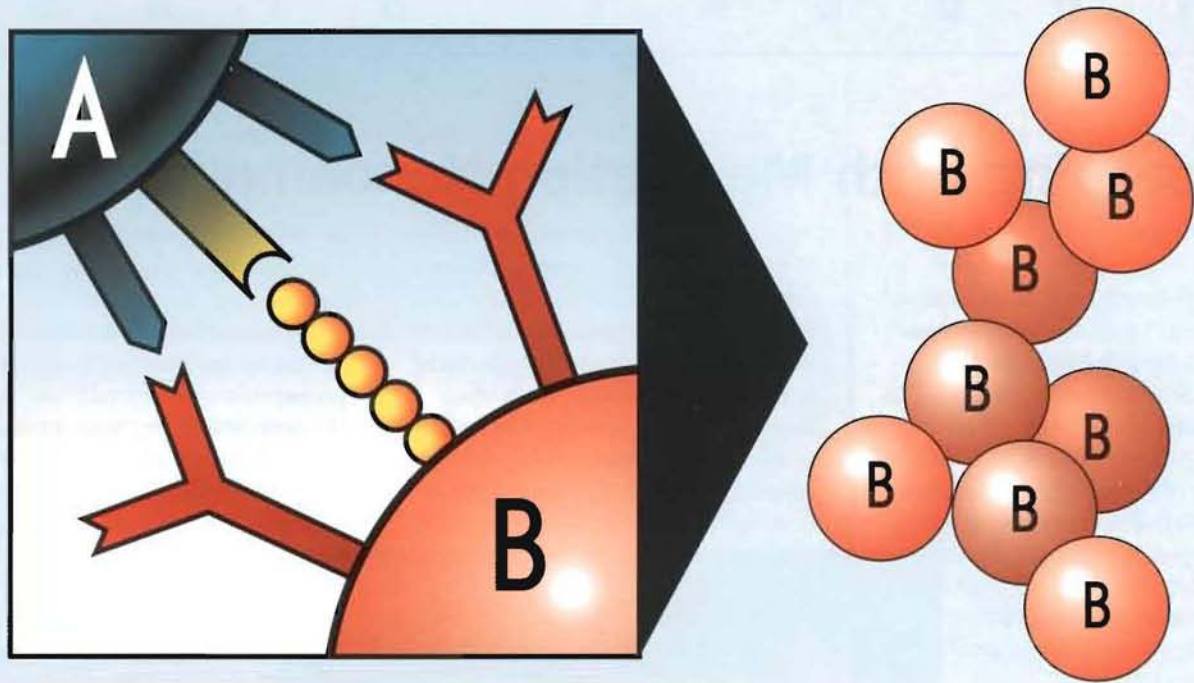
"We found that the CR-1/CR-2-deficient mice could not store immune complexes in the spleen," says David D. Chaplin, MD, PhD, professor of medicine and director of the division of allergy and immunology. Chaplin, who also is associate investigator of the Howard Hughes Medical Institute, co-authored the initial report with Molina.

"These immune complexes contain hundreds of copies of the foreign antigen together with antibodies that recognize the antigen. These complexes give signals that enable cells in the spleen to become activated," Chaplin says. "Without CR-1 and CR-2, the activation fails."

By storing immune complexes, the spleen and lymph nodes act as a



The top photo shows active immune complex trapping in the spleen of a normal mouse capable of developing resistance to infections. The photo beneath it displays the spleen of a genetically altered mouse that has no complement receptors on its B cells and is incapable of trapping immune complexes.



On healthy B cells, complement receptors connect with the complement proteins that tag invading antigens. These connections (represented in yellow) help hasten the immune response and activate cell machinery that prompts mass production of infection-fighting B cells. Antigen receptors (also called membrane immunoglobulin) are featured in red. These receptors also connect with antigens (blue) to help fight infection.

collective armory for the body's immune arsenal. The organs have similar functions in filtering the blood and lymph fluid, respectively, removing bacteria, microbes and fragments of microbes that enter the body.

The immune complexes stored in the organs help to "educate" naive B cells after the cells are manufactured in the bone marrow and circulated. In this role, the spleen and lymph nodes help replenish the immune system with a continual supply of battle-ready B cells and other immune cells.

"It is thought that the immune complexes can persist in the spleen for long periods of time," Chaplin says. "Dr. Molina also has identified one of the signals that is required for the spleen to have its normal function and to trigger the adaptive immune response. In the mice born without complement receptors, a crucial part of this immune network is lost."

In a healthy spleen, CR-1 and CR-2 can be found on the surfaces of cells that are responsible for storing immune complexes. The cells use complement receptors like clamps to anchor immune complexes.

If the clamps are missing, then the immune complexes will not be retained. Without the immunologic anchors in place, the body loses its main reference tool for fighting infection. As a result, antigens that have entered the body before will never be recognized and disposed of efficiently, Chaplin says.

Autoimmune Disease

A better understanding of adaptive immunity and how immune complexes survive and act to regulate immune function would improve the understanding of autoimmune diseases such as lupus, as well as other disorders triggered by complement receptor deficiency, Chaplin says.

Some studies show that patients with lupus have very low levels of complement receptors on their B cells and other important immune cells, he says.

"Mice born without CR-1 and CR-2 may prove useful in the study of autoimmune disease in humans," says Chaplin. "Humans also have

CR-1 and CR-2 on their B cells, and some studies have suggested that their function may be disturbed in cases of lupus."

There is one significant obstacle, Molina adds: In mice, CR-1 and CR-2 are encoded by one gene; in humans, CR-1 and CR-2 are encoded by two distinct but related genes.

"We are designing experiments that will help replicate more specifics of the human disease in mice — even though their genetic makeup in this area is so different," Molina says. "It will require more work with mice, but we are ready to begin this new set of experiments."

Immunology research is complicated by the intricate interrelationships among the many arms of the immune system, the researchers say, but a more precise understanding of the complement system's role may trigger a new cascade of discovery.

"This is a time of explosive growth in our knowledge of the natural functions of the complement system," Molina says. "These mouse models may soon help us decipher precisely how this complex system works." ●

Dispensing With Medication Noncompliance

by Sam Sliselman WUMS IV

AS A fourth-year medical student, I am beginning to realize the magnitude of the problem of noncompliance with medications by patients. Many patients come to the hospital without a list of their medications. Some patients arrive at clinics or the emergency department carrying shoe boxes filled with medication bottles of various shapes, sizes, expiration dates and names of prescribing physicians. Others mix their medications into one bottle to save space.

It is rare that I see patients with a clear, concise medication list stating proper medication names, doses and dosing intervals. Maybe the patients I've seen really do take their medications as instructed by their physician. But based on the confusion I've witnessed during my clinical rotations, this seems unlikely.

Often, my initial impulse is to blame the patient, but I have to remind myself that I, too, could be accused of mixing medications to save space. My own grandfather calls me to ask if he should take the ampicillin left over from pneumonia he had four years ago for his cough. I can't blame him since it seemed to work last time; it may even work again.

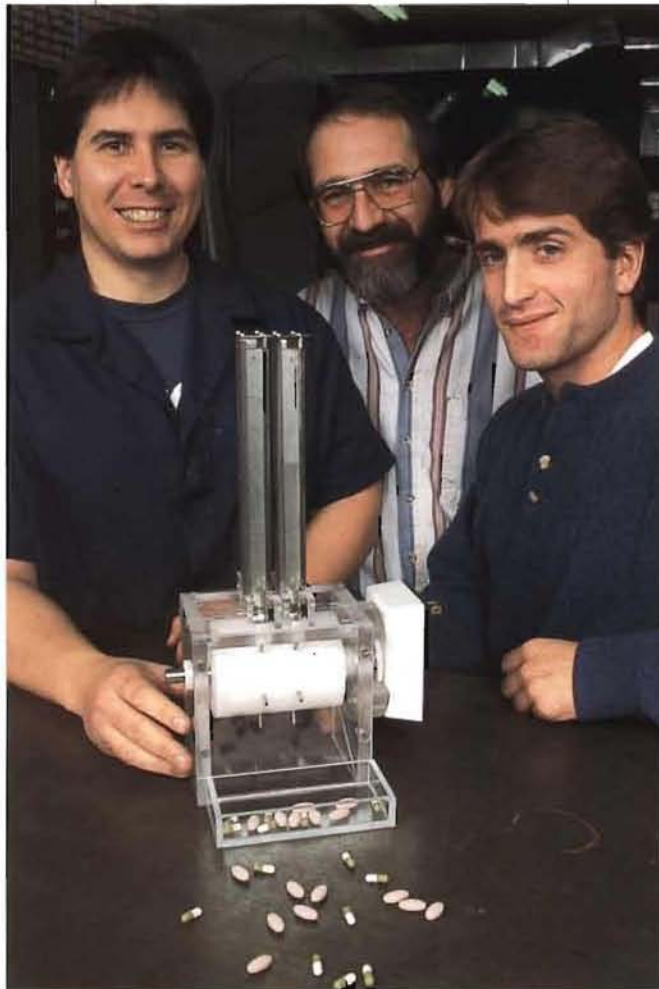
Regardless of the reason for noncompliance, it is evident that what a patient is prescribed to take and what a patient takes often differ drastically. One study by James Cooper, MD, of the University of Kentucky, concluded that approximately 70 percent of

noncompliance is intentional. Patients choose alternative medication regimens for many reasons, such as negative side effects which often accompany antibiotics, and/or lack of a noticeable benefit, which is common with anti-hypertensive

human error. People simply forget, or they are confused about the roles of various medications and their proper dosing regimens. Even with the best intentions, from a patient's perspective, full compliance is often nearly impossible. Prescription of multiple medications with unfamiliar, complex names, taken one to four times daily for uncertain purposes, predisposes them to frequent dosing errors.

Many geriatric patients also have limited eyesight, which makes reading prescription labels difficult; decreased manual dexterity also can make childproof caps patient-proof. In addition, geriatric patients often are faced with increasing numbers of medications, which in general leads to an exponential increase in the dosing error rate.

Many studies focus on noncompliance among geriatric patients, but it is a problem of all age groups. Studies estimate non-compliance rates ranging from 41 to 67 percent. One study, by Deborah Omori, MD, of Brooke Army Medical Center in San Antonio, found that 32 percent of the patients surveyed started or stopped taking certain medications unintentionally; 18 percent took the wrong dosage or at the wrong interval. The study was based solely on patient report — no pills were actually counted — so the issue of forgetfulness was not factored in. Regardless of the statistics, adhering to dosing regimens is a problem that applies to



Fourth-year medical student Sam Sliselman, right, with the prototype of the pill dispenser he designed. John Kreitler, center, School of Medicine Machine Shop manager, and machinist Dennis Tapella developed and built the prototype.

therapies. There is no simple solution for cognitive noncompliance aside from better communication between patients and physicians.

The remaining 30 percent of noncompliance is largely due to

anyone who is taking or caring for someone who is taking multiple medications. Noncompliance alone accounts for a substantial number of emergency department visits and hospital admissions.

Many reminder techniques are used including pill boxes in which pills for each day of the week are stored. Some patients find these useful. Others, however, complain that adding and removing pills from the box is difficult because they have poor dexterity and/or large hands. Some have overcome this problem by using egg cartons labeled with the days of the week.

There are also expensive digital, automated medication dispensers, such as those produced by Pioneer Medical Systems and CompuMed. However, suggested retail for the product by CompuMed is \$795. Medicaid will pay for the dispenser, but for the majority of older patients the price is prohibitive. In addition, it has far more features than most patients need.

To my knowledge, there is no simple pill dispensing device in the price range of \$20 to \$50. From my experience, such a device should:

- Reliably dispense between five and 10 different pills at proper dosing intervals;
- Alert the patient once pills have been dispensed;
- Be compact and portable.

For improved health care at home, the pill dispenser must be useful to patients of all ages. If they grew accustomed to carrying their dispensers to emergency departments or clinics, the device also would help physicians determine patients' actual dosing regimens.

I presented a potential design for a pill dispenser to John Kreidler, machine shop manager at the School of Medicine. With design

modifications to keep production costs below the \$800 grant allocated by Washington University, he produced an elegant prototype that successfully dispenses two pills at variable dosing intervals. The prototype resembles two adjacent, inverted Pez™ candy dispensers.

Designed to deliver a vitamin and an antibiotic, the dispenser is driven by the rotating face of a 24-hour Kmart™ light timer. One revolution of the timer face causes one revolution of the central drum. Pins are placed in the drum at various locations to govern the dosing interval determined by either the

The questions that now face us are: Is the design worth manufacturing, and could it be sold for between \$20 and \$50 while still providing a profit?

If the design were to be manufactured, a number of modifications would be desirable. Among them:

- Extension of the central drum and cartridge sites would allow dispensing of multiple pills at the manufacturer's discretion;

- Cartridges should be adjustable to various pill shapes. Ideally, pill manufacturers would either alter their pill shapes or sell their medications in prefabricated cartridges;

- Battery power would facilitate portability;

- The dispenser could be made tamper-proof, with pills accessible only by the patient or pharmacist, which would potentially limit

over-dosing or other medication misuse.

With my internship rapidly approaching, I will not be able to pursue the development of our pill dispenser as I would like. I am hopeful, however, that another interested party who reads this article may be able to carry on its development. There's nothing I would like more than to one day see such a dispenser accompany a patient of mine into the emergency department. ●

Editor's Note: Sam Sliselman is from Pawling NY, and will begin an internship in emergency medicine in July. He thanks Carl M. Rovainen, PhD, professor of cell biology and physiology at the medical school, and Harold J. Brandon, PhD, affiliate professor in the Department of Mechanical Engineering, and Robert Morley, Jr., associate professor in the Department of Electrical Engineering, on the Hilltop Campus, for assistance with this project.

“Regardless of the reason for noncompliance, it is evident that what a patient is prescribed to take and what a patient takes often differ drastically.”

patient, primary caregiver or pharmacist. The pins could potentially be placed to dispense pills every hour of the day, if necessary.

The main difficulty with the design was the dispensing of pills of various shapes and sizes. We solved that problem, in part, by customizing cartridges to fit specific pill shapes. The cartridges are loaded similar to the bullets in a rifle, with a constant tension spring applying pressure to the pills to maintain their orientation. As each pin of the central drum passes through the cartridge, one pill is dispensed.

To alert patients that it's time to take their medication, we designed a circuit to trigger an auditory or visual alarm after the pill or pills are dispensed. The patient then depresses a reset button to ready the dispenser for the next pill.

The design is basic and simple.

Doc Jones — Earning The Title

by Steve Kohler

FOR the capable and talented physician lucky enough to have a long and successful career, there are awards, citations and memberships designed to honor commitment, contributions and service. Agencies are in place to recognize teaching, research, humanitarianism and dedication to every field of endeavor.

Outside of formal societies and professional organizations with their structured processes of recognition, however, one elusive title is given to only the best and most beloved physicians. There is no applying for this honor and no campaigning to win it. Few ever achieve the elusive status required. Carrying the title requires a certain bearing

and implies a special standing. This simple award — in one sense among the highest a physician can attain — is the nickname “Doc.”

The nickname was first bestowed upon Asa Jones, MD '42, during his time in the United States Army. Now, it has been in place for so long and is so universal that he has taken to using it himself, even signing his personal correspondence to friends, “Old Doc Jones.”

Among all of the personal and professional attributes required to

earn a physician the nickname, it may be selfless commitment to others that is most important. If that is the case, then Asa Jones came by his “Doc” honestly.

During his army service, Jones and his wife, Dorothy, assumed complete parental responsibility for their nephew, Robert K. Monge. The

“In his life, he fractured bones 72 times. I cared for him each time,” Doc Jones says simply. In addition to providing that care, Doc and Dorothy Jones saw to it that Robert aimed high and achieved his full potential, and the three became a family.

Doc Jones downplays the diffi-

culties faced by a family like theirs: “Dorothy made him do everything for himself that he possibly could, so it wasn't really a burden,” he says. And he cites Dorothy's training as a physical therapist as being instrumental in the family's approach to the handicap.

Robert matured to become a brilliant student at the University of

Virginia, to drive an automobile and eventually to hold a responsible position as a CPA, Jones says. He went on fishing and hunting trips with his adoptive father, and enjoyed wide experience of the world, including a close friendship with Woody Hayes, the legendary Ohio State football coach. Robert served as national president of the organization, Able Disabled, and often called upon Hayes as a motivational speaker for the group.



Asa Jones, MD, second from right, and his wife, Dorothy, have created The Asa C. and Dorothy W. Jones Professorship, an endowed chair currently held by Keith Bridwell, MD, right. In addition, the Jones' estate will be dedicated in its entirety to the Department of Orthopaedic Surgery, headed by Richard Gelberman, left, creating a second endowed chair in the department and otherwise supporting education.

child had been born to Dorothy's sister, who found herself unable to manage his care. Robert was born with the condition osteogenesis imperfecta (OI), a collagen disorder characterized by brittle, easily fractured bones. Of several types and variants, OI affects those who have it in many ways. Robert's condition influenced him profoundly, preventing him from reaching his full stature and from walking, requiring that he employ a wheeled cart as a means of locomotion.

Despite the high expectations placed on him and the closeness of the family, Robert nonetheless surprised Doc and Dorothy when he announced that he would not accompany the family to retire in Arkansas but would instead stay in Ohio to marry. At the time that Doc and Dorothy left for Arkansas, Robert was having a new house built for himself and his wife.

As appropriate as Doc's specialty of orthopaedics was to the care of Robert, his adopted son's condition had nothing to do with

the selection of the specialty. At age 4, Asa Jones himself visited the School of Medicine for a hip disease. He was treated by eminent orthopaedist Nathaniel Alison, who went on to

Harvard and Northwestern University. From that day, Doc Jones says, "I wanted to be a surgeon like Doctor Alison."

Doc Jones' affiliation with the university reaches even farther back than that early care. He was born on the Medical Campus, and his grandfather was a law professor on the Hilltop Campus. But perhaps the most telling relationship between the Jones family and the university was the one that grew up between Doc Jones and J. Albert Key, MD, an early and eminent professor of orthopaedics.

While he was studying at the School of Medicine, Jones' interest in orthopaedics led him to seek an elective in the subject. Obstacles to that course of study were quickly eliminated by Key, who continued to mentor Jones throughout his education and early career, though Jones never studied under him formally.

"He was brilliant, a great teacher," Jones says of his mentor. "He knew all of medicine — pathology, internal medicine — and at conventions when we would play

stump the experts, he was impossible to defeat."

Jones encountered Key again during the younger physician's stint in the armed forces. Key, who was consulting for the army at the time, was a diabetic and presented with a gangrenous great toe that required removal. Jones suggested that Key go to Barnes Hospital for the surgery, but Key was happy with Jones' service. After deliberation, the army okayed Jones to operate on the civilian, and the surgery was

Today, Jones' fondness for the School of Medicine frequently brings him back to the St. Louis campus from his Arkansas home.

performed. "I suppose I didn't do him any harm. He lived another 13 or 14 years," Jones says. Jones went on to a private practice in orthopaedic surgery in Ohio that lasted 29 years.

Today, Jones' fondness for the School of Medicine frequently brings him back to the St. Louis campus from his Arkansas home. He interrupts his beloved turkey and deer hunting trips and fishing excursions to Canada to attend grand rounds and orthopaedic seminars as well as social get-togethers with his colleagues. In fact, his interest in his field remains so strong that it takes him to Little Rock every week, where he sits in on teaching seminars at the University of Arkansas' medical campus. Jones says he may be better informed and is certainly better read today than when he was actively practicing, because he has more time.

Richard Gelberman, MD, head of the Department of Orthopaedic Surgery, says Jones is highly aware of issues in orthopaedics today and is an "insightful commentator."

Gelberman says, "He recognizes quality, and I believe he is excited about the future of orthopaedic surgery here. I have the greatest admiration for him."

In generous recognition of that commitment to orthopaedic surgery at the School of Medicine, Doc and Dorothy Jones four years ago established The Asa C. and Dorothy W. Jones Challenge designed to bring in 100 new members to the medical Eliot Society. The challenge

matched gifts up to a total of \$100,000 and successfully attracted 103 new Eliot members in 1992.

Since then, the Jones' have created The Asa C. and Dorothy W. Jones Professorship, an endowed chair currently held by Keith Bridwell,

MD, the Department of Orthopaedic Surgery's senior spine surgeon. In addition, the Jones' estate will be dedicated in its entirety to the department, creating a second endowed chair in the department and otherwise supporting education. "Asa Jones has been an outstanding supporter of orthopaedic surgery at Washington University," says Gelberman. "He wants to see us become a national leader, and he's willing to help us achieve that excellence. If we are going to attract and keep the best orthopaedic surgeons in the land, this is the kind of support that is necessary."

In addition to supporting his colleagues, Asa Jones' commitment and generosity will ensure — quite unwittingly — that he wears his title in perpetuity, forever recognized in the classrooms of his beloved school by the short but powerful nickname that cements his position among the elite few of his profession: "Doc." ●

Final Plans Take Shape For 1997 Reunion

Reunion '97 will get under way with registration at noon on Thursday, May 8, at the Eric P. Newman Education Center. A number of reunion class members will present scientific program sessions, which will be held on Thursday and Friday afternoons and Saturday morning. Returning alumni will have the opportunity to attend two events at the education center on Thursday night: the welcoming cocktail party and a reading sponsored by the WUMS literary magazine, the "Hippocrene," featuring nationally-known writer and poet John Stone, MD, from the reunion Class of 1962.

The Bernard Becker Medical Library will be the site of an "Info Expo" on Friday morning, with demonstrations, tours and Internet classes available. At the same time, medical student guides will lead tours of the medical school, and Gary Rachelefsky, MD, from the reunion Class of 1967, will lecture at the Department of Pediatrics Grand Rounds.

Class dinners will be held Friday night at the reunion hotel, the Ritz-Carlton, where all Saturday events will take place. William A. Peck, MD, executive vice chancellor for medical affairs and dean, will speak at breakfast on Saturday, followed by the final scientific program session. Entertainment will be provided by a stellar cast of reunion class members who will perform music, magic, and share their away-from-medicine interests and talents at the "Docs Off-Duty" luncheon Saturday.

The reunion closes with the awards banquet on Saturday night. Award recipients include: John M. Eisenberg, MD, Helen Hofsommer Glaser, MD, and Kenneth R. Smith, MD, who will receive Alumni

Achievement awards; John O. Holloszy, MD, Ira J. Kodner, MD, and Robert K. Royce, MD, who will receive Alumni/Faculty awards; and Arthur Z. Eisen, MD, and John M. Kissane, MD, who will receive Distinguished Service Awards. ●

Alumni Association Supports Student Projects

The Executive Council of the Washington University Medical Center Alumni Association has allocated financial support to a number of student activities and community service projects for fiscal 1997.

The allocations include:

- **Student Support Services** — \$1,945 — which helps students maintain a healthy lifestyle while coping with the demands of medical school through team building and training in areas such as stress reduction, diet and substance abuse.

- **American Medical Students Association** — \$2,094 — for two projects: the State Legislation Action Project to educate students about political awareness and issues important to health policy and the environment, and the Medical Spanish Project to teach students how to conduct patient interviews and physical exams in Spanish.

- **American Medical Association Student Section** — \$3,000 — to expand several of its community education programs (hypertension screening, organ donor awareness, bone marrow donor) and other services.

- **American Medical Women's Association** — \$1,750 — to assist students in attending the National AMWA Conference.

- **Drug Education Project** — \$1,000 — in which medical students educate approximately 1,500 fifth- and sixth-graders in public schools about the effects of drugs.

- **Medical Aspects of Domestic Violence Awareness Project** — \$400 — to assist 20 students in attending a conference sponsored by the Missouri Coalition Against Domestic Violence.

- **Perinatal Project** — \$2,300 — for resource materials which students use to teach classes on prenatal care, counsel expectant mothers, and participate in a labor coaching and mentoring program in a public health setting.

- **Asian-Pacific Community Fair** — \$1,350 — to provide the Asian population in St. Louis with culturally appropriate health promotion and disease prevention information and services.

- **Students Teaching AIDS to Students Project** — \$1,202 — in which medical students work with middle and high school students to educate them about HIV/AIDS and to decrease behaviors which would put them at risk.

- **Student Organized Clinic in Forest Park Southeast Neighborhood** — \$5,657 — which provides no-cost, basic medical services and preventive medical care to people who lack financial resources or health insurance. ●

Interest-Free Loan Fund Established

In honor of its 50th reunion, the medical school class of 1947 has initiated a gift drive to support a revolving loan fund for current medical students. The effort is chaired by William M. Landau, MD. Other volunteers who have been involved in contacting class members include: Theodore Bryan, MD, Sidney Goldring, MD, and George Sato, MD.

Currently, 46 percent of the class has contributed nearly \$25,000. The interest-free funds will be made available to medical students. ●

'20s

Myrtle Hornbuckle Miller, NU '25, of Sebastopol CA, now 92 years old, enjoyed a long career in public health teaching and nursing. After receiving her diploma in nursing from Washington University, she earned a BS in public health nursing from the University of Minnesota and a MS in education from San Francisco University.

'40s

Ole Slind, MD '40, is retired and living in Sun City AZ.

Seymour Brown, MD '40, retired for the third time in 1994. His family is fine and he and wife Rose delight in their first grandchild, Natalya, now almost 2.

Edward Kowert, MD '43, is taking violin lessons in his retirement, and says that he is "not quite as good as Jack Benny."

Ruth Kauffman Johnson, MD '48, has retired after 47 years in family medicine at Versailles MO.

Dolores Shoulders Moore, PT '48, writes from Champaign IL: "My husband, Dean, has been given a clean bill of health; youngest grandson Tyler is doing OK. I'd love to know what happened to the 'Round Robin' of the Class of '48."

Stanley London, MD '49, has been named an Honor Member of the St. Louis Metropolitan Medical Society. He was a 1993 inductee of Washington University's Sports Hall of Fame. A general surgeon, he has served as the team physician for the St. Louis Cardinals baseball team for the past 28 years.

Margaret Lorraine Farkas, NU '49, retired in 1996 after doing school nursing for 10 years. Her husband, Joe, died in 1971. She lives in Houston and enjoys her three married daughters and six grandchildren, as well as her mission work which has taken her to Romania, Venezuela, Mexico and Germany.

'50s

Elaine Kennard Syers, NU '50, has moved with her husband, the Rev. Paul Syers, to Brazil where she teaches health, Christian education and Portuguese grammar in a Bible institute.

Oscar T. Pinsker, MD '51, is co-chairman of the Health Commission of LINC of Kansas City, a state volunteer organization for improving social services in western Missouri.

Amos Lieberman, MD '52, retired two years ago. He still keeps some contact with medicine but is enjoying himself doing things he was previously too busy to do.

John Sandson, MD '53, received the Marion Ropes Award for physician achievement from the Arthritis Foundation in Boston in October 1996. He is dean emeritus of the Boston University School of Medicine.

Merlin Kilbury Jr., MD, HS '53, retired six years ago from his private practice of general surgery. He had taught at the Tumor Clinic at the University of Arkansas School of Medicine for 20 years.

William D. Sawyer, MD '54, president of the China Medical Board in New York, received the White Magnolia Honor Award and Medal in September 1996 in ceremonies in Shanghai. The award was presented in recognition of Sawyer's efforts in the educational programs of Shanghai Medical University and his support of the development of research and educational programs in medicine, nursing and public health at the university. The award is named for the city flower of Shanghai, and is the highest award the municipality confers on foreign friends.

John Hard, MD '54, is the medical director of the Coastal Group, insurers against malpractice for hospitals and physicians, in Birmingham AL.

Donald H. Tilson Jr., MD '55, still enjoys working full-time in Portland OR. He says that the major event of the year for their fracture clinic will be computerizing medical records. He predicts it will be "more legible, but much slower."

Miles C. Whitener, MD '55, is one of the 1996 Honor Members of the St. Louis Metropolitan Medical Society. He retired in 1993 as vice president of medical affairs at Missouri Baptist Hospital.

Ruth Schneider Dickey, NU '55, writes from San Diego that she retired in February 1996. She and her husband, Wayne, have six grandchildren. Her class gets together annually; last October they enjoyed a reunion in Albuquerque.

Dale Dunnihoo, MD '56, Ph.D., is included in *Marquis Who's Who in Medicine and Healthcare 1997-1998*. He retired from his positions as professor of obstetrics and gynecology and professor of family practice and comprehensive medicine at Louisiana State University School of Medicine in Shreveport.

Carolyn Warner Scholten, NU '56, is back in Denver after caring for her 100-plus-year-old mother for more than five years. She had brain surgery in August 1996 that was successful and she is now enjoying being a full-time sculptor in wood and stone.

'60s

Gabriel Zatlin, MD '60, is a member of the Institute for Urban Family Health and a faculty member of the Beth Israel Hospital Family Practice Residency in New York. He was recently named to *Who's Who in Health Care*.

Louise D. Yurko, PT '60, is president of Carteret Physical Therapy Associates, Inc. She is also president of the North Carolina Physical Therapy Association and winner of the North Carolina State Chapter Olive Wortman Service Award.

Marjorie Moore, PT '62, received her MSPTR in pediatrics from St. Louis University in January 1995. She is enjoying life with husband, Jack, in Town & Country MO and in Boca Grande FL.

Richard S. Epstein, MD '64, became chair of the ethics committee of the American Psychiatric Association in May 1996. His book chapter, "*Professional Ethics and Boundaries of the Clinical Relationship*," was published in the textbook *Psychiatry* by W.B. Saunders Co.

W. Mark Wheeler III, MD '64, writes, "I just rode my bicycle across the US to resettle in my wife's family home in Maine. Exciting times. Three of our four children live on the East Coast now."

Karen O'Sullivan Wegener, NU '65, is program director for behavioral health services at Freeman Hospital in Joplin MO. While her three daughters were growing up she worked part-time; since 1982 she has been in full-time nursing, mostly in psychiatric nursing administration. She and her husband, Ron, enjoy traveling.

Sharon Koch-Parrish, Ed.D, NU '64 and '69, completed an advanced nurse practitioner program in adult health at the University of Florida in August 1996.

Henry Massie, MD '67, is currently president of the Northern California Regional Organization of Child and Adolescent Psychiatry (of the American Academy of Child and Adolescent Psychiatry.)

Gary Rachelefsky, MD '67, is president-elect of the American Academy of Allergy, Asthma and Immunology. He and his wife, Gail, have been married 30 years; daughter Holly has been married two years, Cara is a graduate student (MBA) at UCLA, and Lindsay, 17, will enroll at Columbia College next fall.

Michael Treister, MD '67, is the newly-appointed chairman of the Department of Surgery at

St. Elizabeth's Hospital and secretary of the medical staff at St. Mary of Nazareth Hospital Center in Chicago.

William Neubauer, MD '69, is chief of surgery at St. Joseph's Hospital in Tucson.

'70s

Bruce D. Fisher, MD '70, writes, "It was a great thrill to deliver the keynote address, 'The Physician as Human Being,' at the orientation of the freshman class of the Robert Wood Johnson Medical School (University of Medicine & Dentistry of New Jersey) in August 1996."

John Black, MD '73 and Toby Black, OT '71, write that their son, Lee, is a freshman at Washington University. Daughter Sandy is a junior at West Kentucky University in Bowling Green.

Donald Graham, MD '74, is the president of the Sangamon County (IL) Medical Society.

Scott C. Fleischman, MD '74, is alive and well in Phoenix, "practicing diagnostic radiology and living!"

M. Susan Cigelman, PT '76, received her doctorate in educational administration- higher education from Drake University in August 1996. She was recently appointed to the Commission on Accreditation in Physical Therapy Education.

Loretta Oglick Marx, PT '76, received her master's in health services administration from the University of Washington in June 1996 — 20 years after graduating from physical therapy school.

Steven A. Brody, MD '77, was named Doctor of the Year in 1995 by the *San Diego Medical Journal*. The medical director in reproductive endocrinology and *in vitro* fertilization at Alvarado Hospital Medical Center, he is also assistant clinical professor in the division of endocrinology and metabolism at the University of California, San Diego School of Medicine.

Robert Kulesher, HA '77, is an administrator at the extended care pavilion, Medical Center of Delaware.

Jonathan Horstmann, MD '77, is in private practice and teaching medical students at Loma Linda Medical School - Family Practice.

Capt. Gary Lammert, MD '77, is head of emergency medicine at the Naval Hospital in Jacksonville FL.

Cmdr. Donald Rosenbaum, HA '77, is chief of the Department of Orthopaedic Surgery at Jacksonville Naval Hospital, Jacksonville FL.

Carol G. and John D. Stull, MDs '78, write: "Carol continues an active OB/GYN practice in Evansville IN, while John is completing a master's degree in public health at the Harvard School of Public Health. We have three children: Katie, 15, Laura, 13 and Jonathan, 10."

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

Donald Opila, MD '79, has been appointed medical director of St. Joseph's Hospital Physician Hospital Organization (PHO) in Phoenix.

Harper Jackson, HA '79, is serving as chairman of the board of directors of the HAP Alumni Association. His term ends in 1998.

Robert Chaplin, MD, HS '79, has moved to the radiology department of the University of Pennsylvania. His wife, Marjorie Bowman, MD, was recruited to begin the Department of Family Practice-Community Medicine.

Joan M. (Gabel) Yue, PT '79, married Alexander Yue on June 29, 1996, and is now living and practicing as a rehab coordinator in Minnesota.

'80s

Joel Jahraus, MD '80, is associate program director of the University of Minnesota/HSM family practice residency in Minneapolis.

Steven Calvin, MD '80, became co-director of the program for human rights in medicine at the University of Minnesota in 1995.

Keith Henry, HS '81, celebrated 10 years as the director of the HIV Clinic and Program at St. Paul Ramsey Medical Center.

George Roberts, HA '81, is CEO of Henderson Memorial Hospital in Henderson TX. He and wife, Leslie, have one child, Claire, 3 1/2, and are expecting a second in March 1997.

Myron Tanenbaum, MD '81, and **Monica Tanenbaum, MD**, live and practice in Miami. They have three children: Geoffrey, 10, Laura, 8 and Rebecca, 5.

David J. Kraus, MD '82, moved to South Bend IN, and is chairman of radiation oncology, subsection at St. Joseph's Medical Center. He is listed in this year's *Best Physicians in America, Midwest Region*. He reports that he is still single.

Thomas Chelimsky, MD '83, is having a great time directing the Autonomic Laboratory and the Pain Center at Case Western Reserve University and University Hospitals of Cleveland. He would love to hear from classmates.

Theresa Vogel Crouch, MD, HS '83, married an Englishman in 1991 and works for the United States Air Force as a diagnostic radiologist at RAF Lakenheath, England.

Joseph Francis Jr., MD '84, is chief medical officer of the MidSouth Healthcare Network, Department of Veterans Affairs.

Ronald Wainz, MD '84, is in private practice in Toledo OH. He and his wife, Sherry, have two children: Michael, 4 and Rachel, 2.

Chris Dahlberg, PT '84, participated in the United States Amateur Golf Tournament in 1994 and in the British Amateur in Liverpool, England, in 1995. The Dahlborgs have three children, ages 5, 3 and 1.

Theresa Vicroy, MD '84, is in private practice of internal medicine in Houston. She and Robert Graham expected their third child in January 1997.

Gary R. Collin, MD '85, won the 1996 Hume-Miller Award from the Virginia Surgical Society.

Thomas S. Chang, MD '85, reports, "My wife, Joan, and I welcomed our second daughter, Erica Keesun Chang, into the world on April 6, 1996."

Leslie Steven Szeles, MD '85, is practicing ENT in Kalamazoo MI. Daughter Alexandra Marie is 2 1/2; "new" this year is Elizabeth Ilona, born Sept. 16, 1996.

Diana Gray, MD, HS '85, is on the full-time faculty of Washington University School of Medicine as an assistant professor in the Department of Obstetrics and Gynecology.

LeAnn Larson, MD '85, and John Murry have enjoyed their move to Cleveland and are awaiting their second child in April. LeAnn says, "Part-time is great!"

Neal Frenkel, MD '88, HS, wife Lauri, daughter Jennie, 2 and son Jacob, 5 months, wish everyone a happy and healthy 1997 from their home in Atlanta.

Kim Quayle, MD '88, is working in pediatric emergency medicine at St. Louis Children's Hospital, where she is also medical director of transport services. She and Darin have two children: Emily, 3 and Samantha, 1.

Margaret Scholl, PT '88, is working part-time after the birth of their son, Matthew, in May 1996.

Nancy Cho Landay MD '89, is in her second year of private practice in Andover MA, having fin-

ished her training in general surgery and spent a year on staff at Beth Israel Hospital in Boston. She writes, "Bruce and I are proud parents of 8-month-old twins, Samuel and Sophia."

'90s

Jerome R. Freund, MD '90, enjoys serving a small community in southeast rural Ohio. He is the team doctor for a local high school football team as well as medical director of a local nursing home.

Steven R. Wright, PT '90, has been self-employed for some time and is the owner of an outpatient orthopaedic clinic, "Progressive Physical Therapy of Illinois," in Frankfort.

Dexter E. Arrington, MD '90, recently became board certified in obstetrics and gynecology and practices at the Southwest Center for Women's Health in Chicago.

Joe Graziano, PT '91, writes, "Theresa and I were married in July in a small ceremony with our families. We are living in Washington State."

Robert L. McNamara, MD '91, is an instructor in epidemiology and cardiology at Johns Hopkins. The McNamaras have a new daughter, Katelyn, born Sept. 4, 1996.

Richard Shelton Jr., MD '91, married Sharon Harris in September 1995. He is clinical director of HealthNet Community Health Centers in Indianapolis.

Steven Stein, MD '92, recently finished his anesthesiology residency in Denver and is now "paying back time to the United States Air Force at Wilford Hall Medical Center in San Antonio."

Sharon S. Lum, MD '92, and Ahmed Abou-Zamzam, MD, are proud parents of a baby girl, Aida Lang An, born May 28, 1996. They live in Portland.

John Chongwoo Shin, MD '92, is a fellow in cornea/external disease/refractive surgery at the University of Wisconsin in Madison.

Marc Bernstein, MD '92, was married to Holly Ellen Lowy, GR '95 on Aug. 10, 1996. He is at WU as a GI fellow.

Linda R. Citchen, OT '92, is a staff occupational therapist for Total Rehab Services. She lives in the St. Louis area.

Stan Breaux, HA '93, and Mariya have a new son, Steven Michael, born Feb. 2, 1996.

Mindy Borisoff, HA '93, has accepted a position at Mount Sinai Medical Center in New York as the senior manager of managed care.

David and Robin Councilman, MDs '93, have completed their residencies in family practice at Hennepin County Medical Center in Minneapolis. They will continue to work with the family practice department there. Last March, they became the proud parents of Dana Lynn Councilman.

Lynda S. Kohl, PT '93, is engaged to be married to Geoffrey Hymans on May 10, 1997. She lives in Tacoma WA, and works in the rehab unit at St. Joseph Medical Center.

James Lin, MD '93, is in a general surgery residency at Detroit Ford Memorial Hospital. He and Fawn have a 3-year-old daughter, Tiffany.

Daniel T. Layish, MD, HS '93, has received the American College of Chest Physicians Young Investigator Award. He will complete a fellowship in pulmonary/critical care and sleep medicine at Duke University Medical Center in July, and then join the Central Florida Pulmonary Group in Orlando.

Kristina D. Bate, OT '95, is employed at Baptist Rehabilitation in Germantown TN. She recently married Noah Bate, a graduate student at the University of Memphis.

Victoria Akins, MD '94, is a third-year resident at St. Louis Children's Hospital, planning a hematology/oncology fellowship.

IN MEMORY

Paul C. Hodges, MD '18, died in Green Bay WI, on Dec. 27, 1996, just 10 days before his 104th birthday. He was the oldest surviving alumnus of the School of Medicine. His distinguished career in radiology included eight years in China on the faculty at the Peking Union Medical College of the Rockefeller Foundation and 31 years at the University of Chicago, where he was chairman of the Department of Radiology. Following mandatory retirement from Chicago at age 65, he returned to the Orient as visiting professor at the National Defense Medical Center in Taiwan. In 1964, he was recruited to help reorganize radiology at the University of Florida in Gainesville, where he worked for another 17 years. He contributed significantly to the development of innovative technologic advancements, to the definition of radiologic aspects of numerous diseases and to the training of many leaders in his field. Two of his inventions, an X-ray film-viewer and an automatic film exposure instrument, the phototimer, still are used. Just prior to his 100th birthday, the Radiological Society of North America dedicated the scientific program of their scientific assembly and annual meeting in his honor. Hodges was the son of a physician and is survived by a son who is a physician and a daughter.

Ellsworth A. Westrup, MD '37, a family physician in Webster Groves MO, for 50 years, died June 14, 1996, after a brief illness. His wife, Jeanne, and two sons survive.

Robert Rainey, MD '47, died in St. Louis June 8, 1996. He had practiced general surgery and occupational medicine for many years and had been a faculty member of Washington University School of Medicine. He is survived by his wife, Sharon, and two daughters.

Wilmier M. Talbert Jr., MD '56, died June 26, 1996, in Long

Beach CA. Both an anatomic and clinical pathologist, he was a member of the Long Beach Memorial Medical Center Department of Pathology for 25 years. He was clinical professor of pathology at the University of California at Irvine, where he was awarded the John Budd Golden Scope Award for teaching. He is survived by his wife, Cecilia Ossowski Talbert, two daughters and two sons.

August W. Geise, MD '56, died of cancer on Jan. 14, 1997, at the age of 66. He practiced neurosurgery in St. Louis for 30 years. He was a past president of the Neurosurgical Society of America, the St. Louis Medical Society, the State Board of Registration for the Healing Arts and the Washington University Medical Center Alumni Association. In addition to his wife, Caroline, he is survived by three children.

Arlen Morrison, MD '58, died Aug. 5, 1996, of amyotrophic lateral sclerosis. He had been in the private practice of cardiology for more than 30 years in the St. Louis area and was an emeritus faculty member of Washington University School of Medicine. Among his survivors are his wife, Lenora, four sons and one daughter.

Rodger B. Smith, MD, HS, died of cancer on Nov. 8, 1996. He was an otolaryngologist in Mason City IA.

H. James Davidson Jr., MD '68, died June 16, 1996, in Tacoma WA, at the age of 54. He had practiced full time emergency medicine at Tacoma General, Lakewood and Allenmore hospitals, for 23 years. He was board certified in emergency medicine and had served as director of the emergency room and director of the Emergency Department. He was a member of the Washington State Medical Association. He is survived by his wife, Madeline; daughters, Jenny, Bonnie Trent and Anne Marie; and his mother, Gladys. ●



Celebrating Survival: Lenabell Bell shares birthday cake at her 80th birthday party with two of the School of Medicine physicians who have treated her for sickle cell anemia over the course of 40 years. Morey A. Blinder, MD, right, assistant professor of medicine and of pathology, is her current physician, and Hugh Chaplin, Jr., MD, left, professor emeritus of medicine and of pathology, first treated Bell in the late 1950s. Bell, who has been involved in numerous School of Medicine sickle cell studies during the last four decades, is the only surviving patient from a sickle cell research project that started in 1956. The March 3 party took place in the Clinical Sciences Research Building.

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Jazz For What Ails You, The Soulard Sessions, the first compact disc recorded by Code Blue, a seven-piece jazz combo at the Medical Center, has just been released. The 72-minute CD features 11 selections and is available at the Washington University Medical Bookstore in Olin Residence Hall and at Borders Books in St. Louis. Code Blue members, above, include: back row, from left, Bob Knapp, trumpet; Mark Anson, bass; Kevin Kilimann, piano; and Mark Overton, tenor sax; front row, from left, David McGregor, alto sax; and Stu Ottolini, trombone. Jim St. Pierre, drums, is not pictured. Code Blue, formed in 1994, is an offshoot of the Hot Docs, a 20-piece big band dance orchestra that was formed at the Medical Center 16 years ago. Both groups perform throughout the St. Louis and Medical Center communities and are made up of medical students, faculty, graduate students, house staff, fellows and others affiliated with Washington University Medical Center. They play music for dancing, listening or dining. For booking information, contact Mark Overton at (314) 865-0698 or (314) 362-1662.