

OUTLOOK



After the fallout



Drs. Martin Silverman (right) and Stephen Hughes have developed a photoreceptor transplant technique that may one day restore sight to the blind.

OUTLOOK

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Studies of atomic bomb survivors show that low-level radiation may be more dangerous than was previously thought. Illustration from John Fraser/Image Bank.

New compounds block replication of both AIDS and leukemia viruses

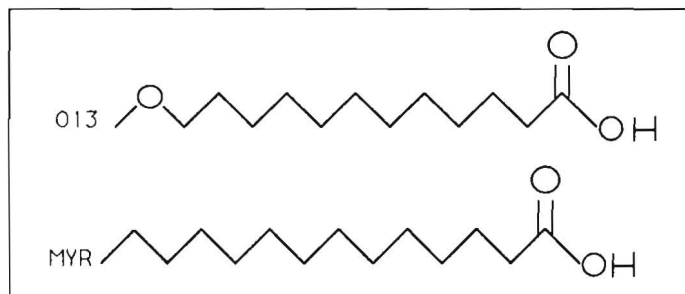
A newly developed class of compounds has proven to effectively inhibit replication of the AIDS virus in cultured human white blood cells and might hold promise as a new therapeutic approach to this disease, according to researchers at the School of Medicine. The scientists' findings appear in a recent issue of *The Proceedings of the National Academy of Sciences*, a highly regarded research journal.

"While these results are exciting, it's important to point out that the studies described in the report were limited only to testing in cell cultures. We must temper our enthusiasm until more is known," says Jeffrey I. Gordon, M.D., principal investigator and professor of medicine and of biochemistry and molecular biophysics, who directed the research. "Considerably more work has to be done with cultured cells and in animals before we completely understand how these compounds work and whether or not they will be useful in treating viral illnesses such as AIDS."

The new compounds resemble myristic acid, a rare, naturally occurring fatty acid that appears to be key to the replication of some viruses, for example the AIDS virus. After infecting a cell, viruses commandeer the cell's protein-producing machinery and use it to produce their own protein building blocks. Myristic acid must be linked to some of these proteins in order for them to be incorporated into an in-

tact virus. Thus, viral replication is dependent on linkage of myristic acid to viral proteins.

Scientists in Gordon's lab have been studying the enzyme N-myristoyltransferase, which links myristic acid to specific viral and cellular proteins. The new compounds they have syn-



This new AIDS-inhibiting compound (top figure) resembles myristic acid (bottom drawing) except for an additional oxygen in the seventh position of the molecule.

thesized are structurally similar to myristic acid, yet have different chemical and physical properties. The enzyme "recognizes" the novel compounds and transfers them to some cellular and viral proteins. Treatment of cells with these myristic acid analogs significantly reduces viral replication. At optimal concentrations, one myristic acid analog reduced HIV replication in vitro by approximately 90 percent with no significant toxicity. These results are quite similar to those seen when AZT, the "gold standard" among AIDS drugs, was used in the same experimental model.

The research team showed that members of this class of fatty acid analogs also inhibit the replication of another retrovirus—the Moloney murine

leukemia virus—which causes leukemia in mice. While one analog worked most effectively against HIV, a different one was more successful against the Moloney virus. The analogs are produced by substituting sulfur and oxygen for native atoms at various locations in the myristic acid molecule.

"At the very least," Gordon says, "these analogs will be useful tools to help us understand the role of fatty acids in viral replication. They might

also prove to have significant clinical potential."

The idea for these compounds came from an analysis of how N-myristoyltransferase works, and specifically from the observations of an M.D./Ph.D. graduate student in Gordon's lab, Robert O. Heukeroth. Testing of the compounds was done together with Lee Ratner, M.D., Ph.D., and Marty Bryant, M.D., Ph.D., at Washington University and Steve Adams, Ph.D., at Monsanto.

This research has been supported by The National Institutes of Health and by Monsanto through the Washington University/Monsanto Joint Research Agreement. ■

Rothman receives coveted Javits award from U.S. Congress

Steven M. Rothman, M.D., associate professor of pediatric neurology, has received a Javits Neuroscience Investigator Award from the U.S. Congress.

Rothman is the 12th Washington University faculty member to receive the prestigious award, which will provide more than \$1.1 million in research funding over the next seven years. Javits Awards, given to scientists who have submitted regular research grant applications for competitive review, encourage research and training in communicative and neurological disorders.

Rothman's research deals with excitatory amino acids, especially glutamate, a common amino acid found in high concentrations in the brain. Glutamate is important in the formation of brain peptides and proteins and also acts as a neurotransmitter that, by exciting nerve cells, mediates the transfer of information from one cell to another.

Research by John Olney, M.D., professor of psychiatry and neuropathology at Washington University, also has demonstrated that excess glutamate can kill nerve cells. Because of its role as a neurotoxin, glutamate may be linked to a number of neurodegenerative diseases, including Alzheimer's Disease, epilepsy and stroke.

Rothman is particularly interested in glutamate as it affects cell death, development

and communication. The Javits Award will enable him to investigate the mechanism of glutamate neurotoxicity and how it relates to nerve cell death caused by oxygen deficiency, and the effect of prolonged glutamate release on the structure and function of developing nerve cells. He also will try to determine what factors control the release of glutamate in its function as a neurotransmitter.



Steven M. Rothman, M.D.

Congress gives the Javits Awards in honor of the late Sen. Jacob K. Javits of New York, on recommendation of the National Advisory Neurological and Communicative Disorders and Stroke Council of the National Institutes of Health. Javits was a victim of amyotrophic lateral sclerosis (ALS), more commonly known as Lou Gehrig's disease. ALS is a degenerative neuromuscular disorder that attacks the nerve cells that control muscles.

The awards program began in 1983, and recipients are chosen three times a year. ■

Medical School recycling effort puts mounds of computer paper and piles of pop cans to good use

The success is apparent in the statistics: 71,000 kilowatt hours of electricity conserved, 3,100 barrels of oil saved, 160 trees left standing and 819 dollars earned. Those are the numbers posted by the School of Medicine's fledgling recycling program during its first six months of operation in just one department.

Under the direction of Paul P. Hipps, Ph.D., and Jo Louise Seltzer, Ph.D., and with the cooperation of many others, the recycling program removes white paper and aluminum cans from the school's waste stream. It also conserves much of the energy that would have been required to process new paper and aluminum, saves the trees and the ore that would have been used, and earns cash from the sale of the waste.

Among the concerns driving the project is an awareness that the country may well run out of landfill space within the decade. According to one estimate, the number of dumps in the nation has declined from 9,000 in 1984 to 6,000 today; by 1993, 2,000 more will be filled up and closed. Hipps says, "Landfills are all but gone, and though incineration is necessary for some items, we ought not to be burning or burying paper and aluminum." Indeed, this country throws away enough aluminum in three months' time to completely rebuild the nation's fleet of commercial aircraft. All of it could be recycled at a savings of 95 percent of the energy required to produce more.

Two elements have been fundamental to the program's early

success, Seltzer and Hipps say. First has been widespread enthusiasm for the plan. When Seltzer approached David M. Kipnis, M.D., chairman of the Department of Medicine, he lent the project his immediate support. Robert J. Hickok, assistant vice chancellor for medical affairs and chief facilities officer, supported the program by approving the use of environmental safety personnel and resources. But perhaps most important has been the cooperation of those who contribute daily by carefully disposing of their waste.

The limitations on what can be recycled are kept as simple as possible: white paper and computer paper, yes; gummed or glued paper, colored paper and glossy paper, no. The recycling process requires that the "raw" materials be as pure and homogeneous as possible, Hipps explains. It's interesting to note that computer paper, with its long fibers for durability, has a value 2.5 times that of notebook paper or even bond paper. Hipps and Seltzer are therefore delighted that those at the school's computer center have expressed an interest in becoming involved in the program.

But they'll have to wait their turn. On December 1, the Department of Psychiatry was added to the voluntary program, and Hipps and Seltzer plan to include interested departments at the rate of one every two months.

Seltzer and Hipps hope Washington University continues to set the pace. Expansion into other areas of the University, cardboard recycling and,



Paper is the single largest source of garbage in the U.S. Recycling paper not only saves trees, but also saves room in the nation's landfills.

by 1992, the inclusion of glass and plastic are planned. "We want to provide a model for others to follow," Seltzer says. "And once people get in the habit of recycling in the office, they become more interested in recycling at home. That's a legitimate function of a university, and it's also a clean and efficient way to do some real good." ■

Dacey appointed new head of neurological surgery

Ralph G. Dacey Jr., M.D., is the School of Medicine's new professor and head of neurological surgery and co-head of the Department of Neurology and Neurological Surgery.

Dacey replaced Sidney Goldring, M.D., who headed the department since 1974. Goldring, a specialist in the surgical treatment of epilepsy, retired from administrative duties as department head and

blood vessels in the brain, and their responses to various types of injury or disease. These responses are especially relevant to vasospasm, or constriction of blood vessels, which is the primary cause of morbidity and mortality in stroke, due to rupture of intracranial aneurysms.

Currently, Dacey is investigating cellular changes that occur in these blood vessels with age and hypertension. His work is funded through a five-year grant of more than

\$400,000 from the National Heart, Lung and Blood Institute of the National Institutes of Health.

Dacey received the doctor of medicine degree in 1974 from the University of Virginia. He completed a residency in medicine at Strong Memorial Hospital in Rochester, N.Y., and a residency in neurosurgery at the University of Virginia. His training also included a year as a postdoctoral fellow in physiology at the University of Virginia as an American College

of Surgeons Schering Scholar. He was a faculty member at the University of Washington and the University of Virginia before joining the University of North Carolina faculty.

He is a diplomate of the American Board of Neurological Surgery and the American Board of Internal Medicine, a fellow of the American College of Surgeons and the Stroke Council of the American Heart Association, and a member of the Neurology A Study Section of the NIH. ■



Ralph G. Dacey Jr., M.D.

will concentrate full time on patient care and research activities.

Dacey came to Washington University from the University of North Carolina at Chapel Hill, where he was professor and chief of the division of neurological surgery since 1987. In addition to his School of Medicine post, Dacey serves as neurosurgeon-in-chief at Barnes Hospital, and on the staffs at Children's and Jewish hospitals.

Dacey's major clinical interest is in the treatment of cerebral aneurysms, arteriovenous malformations and basal skull tumors. His research focuses on cerebral arterioles, minute

Preventing AIDS in drug abusers

The National Institute on Drug Abuse has awarded \$3.5 million to the School of Medicine for research designed to improve drug abuse treatment in order to prevent the spread of HIV infection among IV drug users in the St. Louis area.

The four-and-a-half year grant will support researchers from the Department of Psychiatry in an effort that is unprecedented locally: to persuade IV drug users to get treatment by providing 300 new treatment slots at a drug-free program and a methadone maintenance clinic. This will significantly reduce waiting lists for drug treatment in the inner city. In addition, the project will provide street outreach in high risk areas to educate the community on ways to reduce the risk for HIV infection and to distribute vouchers for drug treatment.

"At last we, as researchers, have the opportunity to work

directly with St. Louis area treatment programs to help the intravenous drug user," says epidemiologist Linda B. Cottler, Ph.D., principal investigator of the study. "Minority drug users need particular attention because they often are less likely to enter treatment." Cottler, an assistant professor of epidemiology in psychiatry,



Linda B. Cottler, Ph.D., with bleach used to sterilize hypodermic needles.

will head the collaborative effort involving Washington University faculty in psychiatry and pediatrics, two area substance abuse treatment programs—BASIC and West End Clinic—and the Metropolitan AIDS Program.

Researchers will work with the staff at these centers to make program improvements that until now have been impossible, largely due to lack of funds. Over time, the investigators will evaluate street outreach and improvements in the treatment programs and compare their effectiveness. The team will administer standardized interviews to examine a number of factors, including relapse to drug use, needle sharing and high risk sexual behaviors, the programs' retention rates, employment, psychiatric symptoms and rates of HIV infection. ■

Loewy awarded MERIT status

Arthur D. Loewy, Ph.D., professor of anatomy and neurobiology, has received MERIT status from the National Institutes of Health (NIH) for his latest grant.

The five-year grant, totaling \$1,382,685, will enable Loewy to continue his research on the neural mechanisms involved in cardiovascular control. The grant is from the National Heart, Lung, and Blood Institute, part of the NIH. MERIT (Method to Extend Research in Time) status guarantees Loewy uninterrupted financial support without the time-consuming paperwork and other delays traditionally associated with grant renewal applications.

Loewy's work has led to greater understanding of the nerve mechanisms involved in controlling blood pressure and heart function, and may ultimately lead to the development of better drugs for treating high blood pressure and other cardiovascular diseases.

He and his colleagues have developed a method for studying the central nerve pathways that regulate blood pressure and cardiac function. In the laboratory, they make discrete viral infections in the sympathetic nerves that serve the heart or blood vessels; after several days, the infection spreads to the specific sets of central neurons that are instrumental in regulating cardiovascular control. The technique allows viruses to be transported along specific chains of nerve cells in the brain. By applying histochemical methods, researchers can identify the neurotransmitters used by these

nerve cells, and thus decipher the central mechanisms that are involved in blood pressure regulation.

This information may be used in the future to design new therapies affecting the brain pathways that control blood pressure. Loewy plans to use the technique, along with



Arthur D. Loewy, Ph.D.

physiological methods, to evaluate various centers in the brain that have not yet been explored. He predicts that this combination of anatomical and physiological techniques will provide new insights into the organization of central cardiovascular pathways.

Loewy received a doctorate in anatomy from the University of Wisconsin-Madison in 1969. He has been on the School of Medicine faculty since 1975. Before that he held research positions in neuroanatomy at the Mayo Graduate School of Medicine in Rochester, Minn., and the University of Chicago.

Loewy was the recipient of the American Heart Association's Established Investigatorship Award from 1982 to

1987. Currently, he is a member of the Experimental Cardiovascular Study section of the National Institutes of Health and a reviewer for a health research program of the Oklahoma Center for the Advancement of Science and Technology. He also serves on two editorial boards for the

American Journal of Physiology, and is a former editorial board member of the Journal of the Autonomic Nervous System. Loewy is co-editor of a forthcoming book "Central Regulation of Autonomic Functions" to be published in 1990. ■

Kornfeld honored by biochemists

Stuart A. Kornfeld, M.D., professor of biological chemistry and medicine, recently was selected as the 1989 Harden Jubilee lecturer and medalist, one of the highest honors given by the British Biochemical Society.

The lecture, established in 1961 to commemorate the society's 50th anniversary, is given every few years by a biochemist of international distinction. Recipients discuss their research at the society's annual meeting, with each lecture published in the society's journal, *Biochemical Society Transactions*. Lecturers also receive the Harden Medal, named after Sir Arthur Harden, a Nobel Prize-winning British biochemist.

Kornfeld, co-director of the School of Medicine's hematology-oncology division, is recognized for his research on the biochemistry of glycoproteins. His work has helped to explain the structure of the carbohydrate units of these molecules and to define the steps involved in their biosynthesis. These carbohydrate units are important because they serve as specific recognition markers in a variety of biologic reactions.



Stuart A. Kornfeld, M.D.

His current studies look at how carbohydrate units of one family of proteins, the lysosomal hydrolases, function in the targeting of these enzymes to the lysosome, where they act to degrade unwanted materials.

A 1962 graduate of Washington University School of Medicine, Kornfeld served his internship and residency at Barnes Hospital. He has been on the School of Medicine faculty and the staff at Barnes Hospital since 1966.

In 1982 Kornfeld was elected into the National Academy of Sciences and in 1988 he was made a member of the American Academy of Arts and Sciences. ■

Washington University and Monsanto extend fruitful research agreement

Washington University and Monsanto Company have extended their eight-year research agreement for an additional four years. This extension brings total funding commitments to nearly \$100 million.

The Washington University/Monsanto Biomedical Research Agreement is the largest research collaboration between an American company and an American university. The agreement provides a framework for university and corporate researchers to collaborate on extensive investigations of proteins, peptides and other molecules that modulate cellular function.

Such a collaborative program seeks to shorten markedly the time between fundamental discoveries and the

development of novel preventive and therapeutic products for human disease. Key to Monsanto's participation in the program are the research, development and marketing capabilities of Searle, Monsanto's wholly-owned pharmaceutical subsidiary.

First signed in June 1982, the collaboration began with a \$23.5 million commitment for five years. In 1986, after a favorable review by an independent panel of respected scientists, the agreement was extended through 1990 and was increased to approximately \$62 million. This latest extension calls for more than \$9 million per year for each of the years 1991 through 1994.

The program supports 50 research projects involving 120 university scientists. To date,

the research has resulted in over 40 patented or patent-pending discoveries that could eventually lead to commercially useful products.

The agreement was originated by David M. Kipnis, M.D., Adolphus Busch Professor and head of the department of internal medicine at Washington University, and Howard A. Schneiderman, Ph.D., Monsanto's senior vice president for research and development and chief scientist. The extension guarantees continuation of what is generally considered a unique and successful model of university/industry cooperation.

According to the agreement, patent rights on all inventions are owned by Washington University, and Monsanto has the right to an exclusive license under mutually acceptable terms.

Decisions on which university research projects will receive financial research support are made by an advisory

committee consisting of ten representatives, half from each institution. Kipnis serves as program director. Researchers must submit a proposal that the advisory board judges on the basis of merit. The award process involves the same sort of rigorous review that characterizes grant deliberations at the National Science Foundation and the National Institutes of Health. Approximately 30 percent of the funding is expended in support of exploratory projects and the balance is directed toward special or applied research.

"This agreement has enabled both institutions to pursue their strengths with assistance from the other," said Kipnis. "Together we can accomplish more than either is capable of alone. The track record of this association is outstanding and our extended collaboration should continue to speed the development of new and vitally important health care products." ■

Fetter appointed associate vice chancellor and associate dean of administration and finance

Lee F. Fetter, formerly assistant vice chancellor for medical affairs, has been appointed associate vice chancellor and associate dean for administration and finance.

His is the first appointment to be made in an administrative reorganization at the School of Medicine.

Fetter, assistant dean and chief financial and planning officer, will extend his responsi-

bilities from finance and financial planning into operations, including personnel and facilities management.

Fetter joined the School of Medicine in 1983 as assistant vice chancellor for medical affairs. Previously he had served four years as Missouri's first executive director of health and educational facilities, responsible for implementing financial policies and operating systems



Lee F. Fetter

for hospitals and institutions of higher education, and two

years as director of planning for St. Louis University Medical Center.

Fetter serves on the board of directors of Southern Medical Center Insurance Company, the Washington University Medical Center Health Plan/Partners HMO, Locust Street Mutual Fund, Washington University Medical Alliance Corp., Field Inversion Technologies Inc., and Telecommunications Facilities Corp.

Fetter received a bachelor's degree in 1974 from St. Louis University and a master's in 1975 from Harvard University. ■

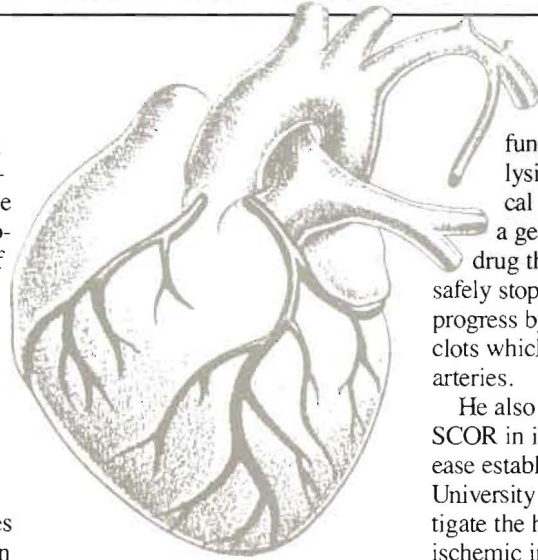
School awarded \$18.6 million for heart and vessel research

The School of Medicine has been designated as a Specialized Center of Research (SCOR) in Coronary and Vascular Diseases and awarded a SCOR grant of \$18.6 million from the National Heart, Lung and Blood Institute.

The five-year grant will support research designed to improve prevention, detection, diagnosis, and treatment of heart and vascular diseases. The SCOR is directed by Burton E. Sobel, M.D., Tobias and Hortense Lewin Professor of Cardiovascular Diseases and director of the cardiovascular division at the School of Medicine.

The SCOR grant enables 49

investigators from the School of Medicine and Hilltop campuses to conduct multidisciplinary projects encompassing both laboratory and clinical research. The 14 projects include several that will explore the potential of molecular variants of clot-dissolving agents such as t-PA (tissue plasminogen activator); two that will focus on the causes, treatment and prevention of heart arrhythmias, irregularities in the heartbeat that can cause death; and several cardiac imaging projects that use noninvasive techniques such as ultrasound and positron emission tomography (PET) to characterize the heart's response to drugs such as t-PA and potentially protective mea-



asures such as calcium channel blocking agents.

Sobel, the principal investigator, is recognized throughout

the world for his innovative research on heart function and thrombolysis and for the clinical introduction of t-PA, a genetically engineered drug that can quickly and safely stop a heart attack in progress by dissolving blood clots which block coronary arteries.

He also has directed a SCOR in ischemic heart disease established at Washington University in 1974 to investigate the heart's response to ischemic injury and to develop new and more effective approaches for the treatment of heart disease. ■

New treatment for hepatitis C

School of Medicine investigators are part of a team that has found an effective treatment for reducing the liver damage caused by chronic hepatitis C, one of several types of hepatitis caused by viruses that attack the liver.

Results of a multicenter study published in the Nov. 30 issue of *The New England Journal of Medicine* indicate that a six-month course of Intron A, a genetically engineered protein that has antiviral and immunogenic properties, resulted in significant improvement in liver function tests in about half of patients with hepatitis C. Hepatitis C accounts for more than 90 percent of all hepatitis cases contracted through blood transfu-

sions—approximately 150,000 cases per year in the United States. Half of those cases will develop chronic hepatitis C, which can lead to cirrhosis of the liver and liver failure.

Robert P. Perillo, M.D., associate professor of medicine, directed the local trial of Intron A. Washington University was one of 12 centers participating in the 166-patient study, the first large, controlled trial to assess the efficacy of alpha interferon therapy in treating hepatitis C.

All participants in the study had contracted hepatitis C by blood transfusion or occupational exposure to blood. One-third of the group received three million units of alpha interferon given three

times weekly for six months, one third received one million units on the same schedule, and the remaining third did not receive any treatment.

Compared with the untreated group, those who received three million units of interferon showed a significant reduction in liver damage. Levels of an enzyme that indicates liver damage promptly fell to normal in 38 percent of patients who received three million units, in 16 percent of those who received one million units, and in 4 percent of untreated patients. Furthermore, patients taking the larger dose showed a significant reduction in liver damage, as measured by liver biopsy.

Of those patients who improved, one-half showed improvement lasting longer than six months after treatment

ended. In addition, many patients experienced a lessening of the debilitating fatigue and malaise that characterizes chronic hepatitis C.

Side effects associated with interferon therapy—flu-like symptoms such as muscle ache, headache and fever—typically improved or ceased as therapy continued.

“We are extremely encouraged by the results of this study, but future studies are needed to determine whether a different dose or longer duration of treatment will increase the frequency and durability of response,” notes Perillo. Such a study is now underway at the School of Medicine, in conjunction with the VA Medical Center. ■



Blind Boy, New York City

Out of the

Oedipus, of course, caused his own in a fit of extreme remorse. Saul's was visited on him as retribution. Classically, blindness was among the harshest punishments available, reserved for the most serious crime or disobedience. And though we have come to understand that our health, including vision, is not meted out as a judgment on behavior, blindness is still among the most frightening vagaries the future can hold. Even the language we use to characterize it is final: an acquaintance *has* cancer or diabetes, but he *went* blind.

Before too long, however, we may again get to change the way we think of and talk about blindness. Seminal investigations being conducted at Washington University Medical Center have resulted in the successful transplantation of light-sensing tissue into blind eyes. From collaborators at the Central Institute for the Deaf (CID) and the Department of Ophthalmology comes hope for a relatively simple surgical procedure to restore lost sight, though it may be years before the promise can be fulfilled.

Most neural blindness is caused by damage to and degeneration of the eye's rods and cones, the photoreceptor cells that begin the conversion of light into nerve impulses. Among older adults, perhaps 15 percent lose some or all of their vision to age-related macular degeneration, a syndrome that affects photoreceptors, particularly those in the fovea, the tiny area at the retina's center that is most responsible for sharpness of vision. Degeneration often becomes apparent as age increases the need for magnifying glasses with which to read

small print. Add to that population the many victims of *retinitis pigmentosa*, a degenerative disease that affects younger adults, and those who damage their eyes by overexposure to sunlight or other bright sources, and the number of people in the United States with impaired photoreceptors exceeds five million.

CID scientists Martin S. Silverman, Ph.D., and Stephen E. Hughes, Ph.D., pioneered techniques to replace missing photoreceptors with transplanted photoreceptors in the hope that the new cells might take over the task of responding to light. In collaboration with Henry Kaplan, M.D., professor and head of the Department of Ophthalmology, their experiments show that it is possible to place the cells in the correct location within the retina and to do so gently enough that the cells' characteristic shapes are generally preserved. The cells even make the essential neural connections with adjacent layers of the retina. It remains to be seen, however, whether sight is restored.

The concept of replacing damaged photoreceptors is revolutionary, but "once we had the idea, it was really just a matter of overcoming the technical problems," Silverman says. His thesis for solving those problems sprang from his work at CID transplanting the sensory "hair cells" of the inner ear. The hair cells are the first-line cells responsible for the sense of hearing, and Silverman knew they were similar to photoreceptors in the eye. A few diseases, such as Usher's syndrome, even attack both.

Leaping Technical Hurdles

Intrigued by complex questions that might ultimately have relatively simple answers, Silverman wasn't deterred by the long-standing belief that restoration of vision is impossible after the loss of photoreceptors. The first hurdle he faced was isolating the microscopic photoreceptor cells from the donor retina. Because their strict organization is as important to sight as the photoreceptors themselves, traditional cell-harvesting techniques that dissociate and purify tissue were inappropriate.

As an alternative, Silverman and Hughes developed a technique to flatten the donor retina from an eight-day-old rat and affix it to a block of gel to stabilize it. By sectioning down through and microscopically examining each of the five layers of the retina, they knew when they had reached the photoreceptor layer. There, they took a thicker section of approximately 200 microns—about as thick as a three-by-five index card—of perfectly organized photoreceptors, along with a gelatin substrate. That section of tissue became the transplant.

In an initial study of 54 rats, reported in the August 1989 edition of *Investigative Ophthalmology and Visual Science*, the researchers first destroyed the outer nuclear layer of the host rodents' retinas by constant exposure to normal fluorescent light. "That eliminates 99 percent of the photoreceptor cells in the albino rat," Silverman says.

Darkness

BY STEVE KOHLER



The illustrations above depict (from top to bottom) a normal retina with blue photoreceptor layer, the isolation of the photoreceptor layer in a donor retina, the undercutting of the photoreceptor layer, the taking up of the photoreceptor layer into the syringe-like transplant device, insertion of the transplant device into the recipient retina, the depositing of the photoreceptors and an overview of the transplanted receptors.

Positioning the Tissue

The researchers then attempted to move the transplant tissue, about the diameter of a match-head, into the appropriate spot in the eye of a host rat via a conventional approach: entering through the choroid and sclera, or back of the eye. That approach made sense—the space occupied by photoreceptors is near the outside of the retina and close to the back of the eye—but often, their efforts were thwarted due to bleeding in the eye. “Extravascular blood is toxic to the retina,” Silverman says, “and bleeding frequently destroyed transplants.”

To solve that second problem, Silverman decided to enter through the cornea, which does not bleed, at the front of the eye. Because the subretinal space he had to reach is removed in distance from the cornea, it was a novel approach. However, the cornea heals quickly and is often entered surgically for other procedures, including cataract extraction.

That technique proved successful. The transplant tissue was moved—still on its stabilizing gel base—into the eye through a small incision in the cornea; the retina was gently detached, and the transplant was inserted into the subretinal space from which the photoreceptors had been eliminated. No sutures were required, and the retina reattached itself as the gel dissolved and the cornea healed. The retina, like the cornea, shows remarkable powers for healing.

A later refinement of the technique, arrived at with Kaplan’s assistance, moved the incision from the cornea to a new location still on the front of the eye. Repositioning the incision reduced any chance of damaging the cornea, yet left the retina easily accessible.

Because new photoreceptors are transplanted intact as the outer nuclear layer, they come into direct contact with the adjacent layer of the retina. Silverman’s hope was that, with no great distance over which to regrow, the axons would re-establish the necessary connections between the two layers. He says, “once transplanted, the photoreceptor cells usually retain their columnar arrangement, forming a new outer nuclear layer with the host’s retina.”

The investigators encountered only a few difficulties. Where minor disruption of the photoreceptor layer was unavoidable, rosettes formed when the cells reorganized themselves. The rosette formation, for which the cells seem to have a propensity, almost certainly reduces visual acuity. But in 68 percent of the cases, rosettes were either small and infrequent or intermediate in both size and frequency.

Testing for Restored Sight

But does the transplant restore sight? Working toward the answer to that question, the investigators first determined that the transplant was identifiable by its appearance in discrete patches. Further, the transplanted cells displayed the round bodies characteristic of photoreceptors. As a control, the team examined the rats’ other eyes—the ones that did not receive transplants—and found that very few photoreceptors remained.

Silverman and Hughes then tested the transplants using a monoclonal antibody specific for the production of the protein opsin. Normal photoreceptors produce opsin, which together with vitamin A makes rhodopsin, the compound that transduces light in the eye by converting it to nerve impulses. The transplanted photoreceptors were producing substantial amounts of the substance, Hughes reports. At one week, three weeks, and on out to three months, 36 of the 54 transplants in one study remained vital, normal looking and opsin-producing.

Later studies employed an initial test for recovery of function. Because light-damaged retinas might still transduce some light, the researchers compared activity in damaged areas of the retina with that in the small portion where transplants had been accomplished. By administering a labeling agent called deoxyglucose, which is taken up in direct relation to neural activity, they produced functional maps of light-damaged retinas, both with and without photoreceptor transplants.

Under conditions of darkness, the retinas showed an increased uptake of the radio-labeled glucose in the region of the transplant. (It is interesting to note that photoreceptors are “on” in the dark and shut down as brightness increases.) When a flickering strobe light was applied as a stimulus, increased uptake was demonstrated in the transplant and extending through the thickness of the retina, but only in the region of the transplant. This suggested that activation of the retina by the transplanted photoreceptors was occurring. In contrast, nearby damaged retina without a transplant recorded little neural activity.

Examination of the cells with electron microscopy has revealed that the photoreceptor transplants also make the necessary synaptic contacts, re-establishing neural connections. However, it is still not clear that those contacts are ordered appropriately. Says Silverman, “There’s a good chance that at least light sensitivity has been restored. But in order to say that sight is restored, we must show that objects are being distinguished visually.”

To take that next step, it will be necessary to train primates to push a button when making a visual distinction. The trained macaque monkeys then will undergo the transplantation protocol and finally be retested to determine if they are again capable of sight. Kaplan, Silverman and Hughes have those studies underway, with results expected in about six months, Kaplan says.

That the necessary axons grow back and the synapse is formed, "is not out of line with other information being developed," according to Raymond Lund, Ph.D., chairman of the Department of Neurobiology, Anatomy and Cell Sciences at the University of Pittsburgh School of Medicine. Nonetheless, Lund says, it would be easy to get "too optimistic" about the work, since its application to the human condition remains theoretical. "We're not there yet. One hopes this work will continue in the same direction. It's a good approach and the right sort of thing to do," he says.

The Right Material

Overall, "photoreceptors turned out to be almost ideal tissue to transplant," Silverman

reports. Because the tissue is avascular, meaning without a direct blood supply, revascularization is not required. Revascularization problems tend to limit the success of other types of neural transplants. Also, the threat of rejection is reduced when direct contact with blood is avoided.

The scientists—funded by grants from the National Eye Institute of the National Institutes of Health, the National Retinitis Pigmentosa Foundation, Retinitis Pigmentosa International, Monsanto Company and a Sloan Foundation Fellowship—first used only the immature cells thought to be most appropriate for transplant. The more extensive studies that followed show that mature cells are no less effective and exhibit no greater proclivity for rejection. The team's recent studies reveal that the transplants are successful not just in damaged eyes but in genetically blind strains of mice and rats as well. Employing immune suppression drugs, Silverman and Hughes have even successfully implanted photoreceptors from human eye-bank eyes into blind rats. The ongoing work with macaque monkeys also uses eye-bank transplant material.

The transplants can be placed in any area of the retina, even near the central part of

the retina at the extreme back of the eye. That placement will be important if sharp vision is to be restored to blind individuals.

In a normal afternoon's work, team members can perform as many as 12 transplants, replacing up to 30 percent of the photoreceptors in each eye. They predict that a similarly sized transplant into a human eye, placed near the fovea, might theoretically restore high acuity vision in a neurally blind human being. A larger transplant could potentially eliminate the tunnel vision probable with such a small transplant.

If the studies with nonhuman primates are successful, the logical progression is next to organize clinical tests for restoring sight to blind humans. The hope is almost too big for Silverman to discuss. He prefers to be cautious and tones down the implications by suggesting what might go wrong: "Even in a worst case scenario, it's not a life-threatening transplant technique. The very worst that might happen, in the event of massive infection, is the loss of a non-functioning eye. And the best, well . . ." He leaves the promise unspoken. ■

Research heats up on the back burner

Though they may eventually be involved, photoreceptors are not at the root of all retinopathies. For example, macular edema, a common symptom of diabetes, has been traced to a failure of retinal pigment epithelial (RPE) cells to perform normally. When they fail, the photoreceptors which rely upon them also fail, and blindness results.

Epithelial cells form the retinal layer just outside the photoreceptors, and one of their functions is to consume excess fluid and the debris that collects when photoreceptors—which grow continually—shed their lengthening ends, Kaplan explains. If the RPE cells fail to clean up that debris, it accumulates and blindness can occur.

So it was big news in 1989 when researchers elsewhere reported that they had successfully transplanted pigment epithelial cells and subsequently saved, or "rescued," photoreceptors that otherwise would have degenerated. The experiments were conducted in a strain of lab animals known as RCS rats, rodents which lose their photoreceptors at the age of about one month. The blindness

is a result of a preserved genetic mutation.

Silverman and Hughes, noting that their own work transplanting photoreceptors into RCS rats also seemed to prevent the death of RPE cells, expanded on the work. They discovered that it was not the injection of new epithelial cells that rescued the photoreceptors, but apparently the re-stimulation of the existing cells.

Performing sham operations in which they transplanted no cells but introduced only saline or inert gel, the Washington University scientists learned "that the rescue of photoreceptors in this animal . . . does not require transplantation of normal RPE cells, but only the surgical manipulation for such transplantation. . . . Temporary retinal detachment alone can induce photoreceptor rescue in the RCS rat."

With that discovery, a second line of inquiry was born. Just how, Silverman wondered, did surgery re-activate the RPE cells. Aware that lasers are employed in the treatment of macular edema, he theorized that the trauma con-

nected with surgical intervention might force the production of heat-shock proteins, also a probable effect of the laser treatment.

Experiments are being conducted to see if raising the temperature of lab animals to 41 degrees centigrade for 15 minutes has the same effect as both the sham operations and the first transplantation of RPE cells.

If disorders of the retina's pigment epithelial layer can indeed be treated with heat—the cells' phagocytic function re-established through the generation of heat-shock proteins—Silverman and his collaborators may have arrived at not just one but a pair of revolutionary treatments for eye disease. Silverman foresees the possibility that irradiation with precisely controlled infrared heat might stimulate the cells and avoid damage to the photoreceptors. Laser therapy, its operant mechanism unknown, unfortunately kills photoreceptors even as it treats RPE cells.

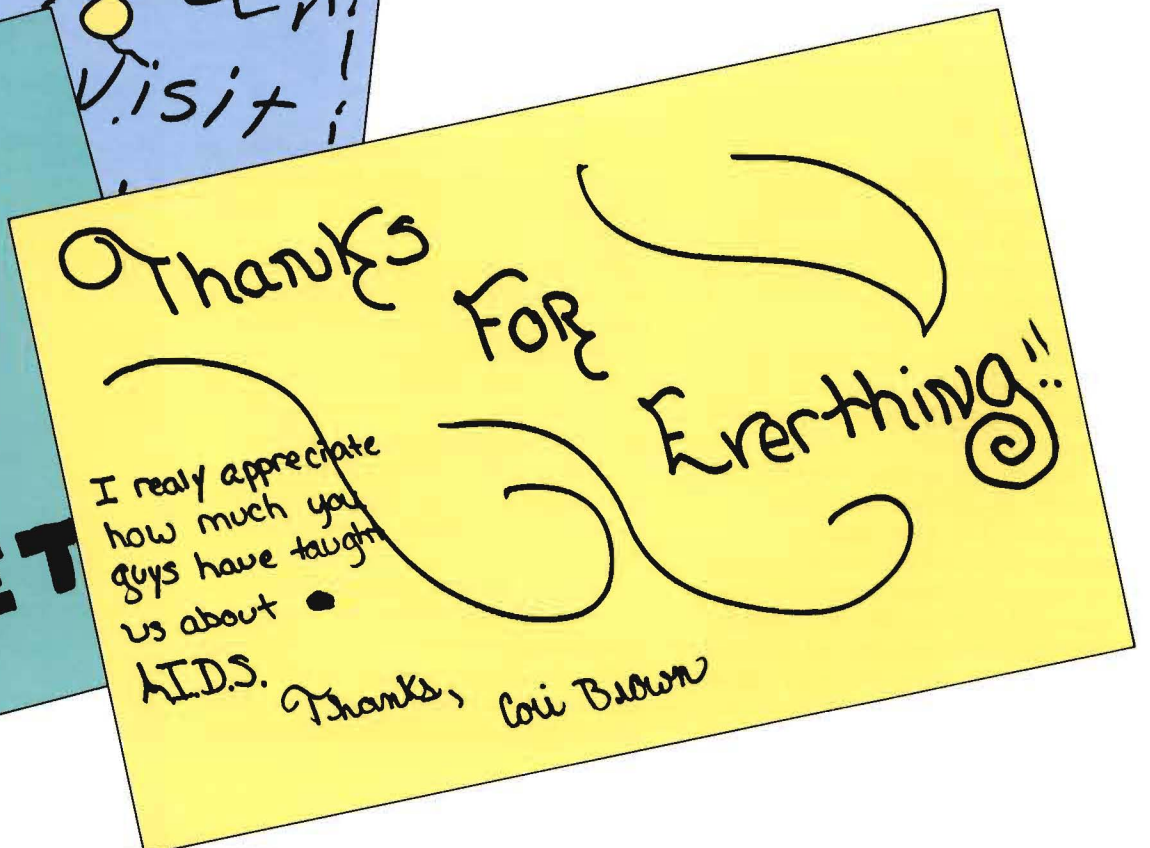
But, Kaplan warns, a therapy for such disorders may be even farther off than the development of clinical procedures for transplanting photoreceptors: "We're not as far along with this line of inquiry," he says. ■

STOPPING AIDS

AIDS

BEFORE IT STARTS

BY DEBRA BERNARDO



"Ill always remember this you can't catch Aids by touching the Aids victim & always, always, always have safe sex." "Don't do drugs. Don't have sex." "We learned a lot about

AIDS and how it can kill you. You made it clear to us how you can get AIDS and how you can't get AIDS."

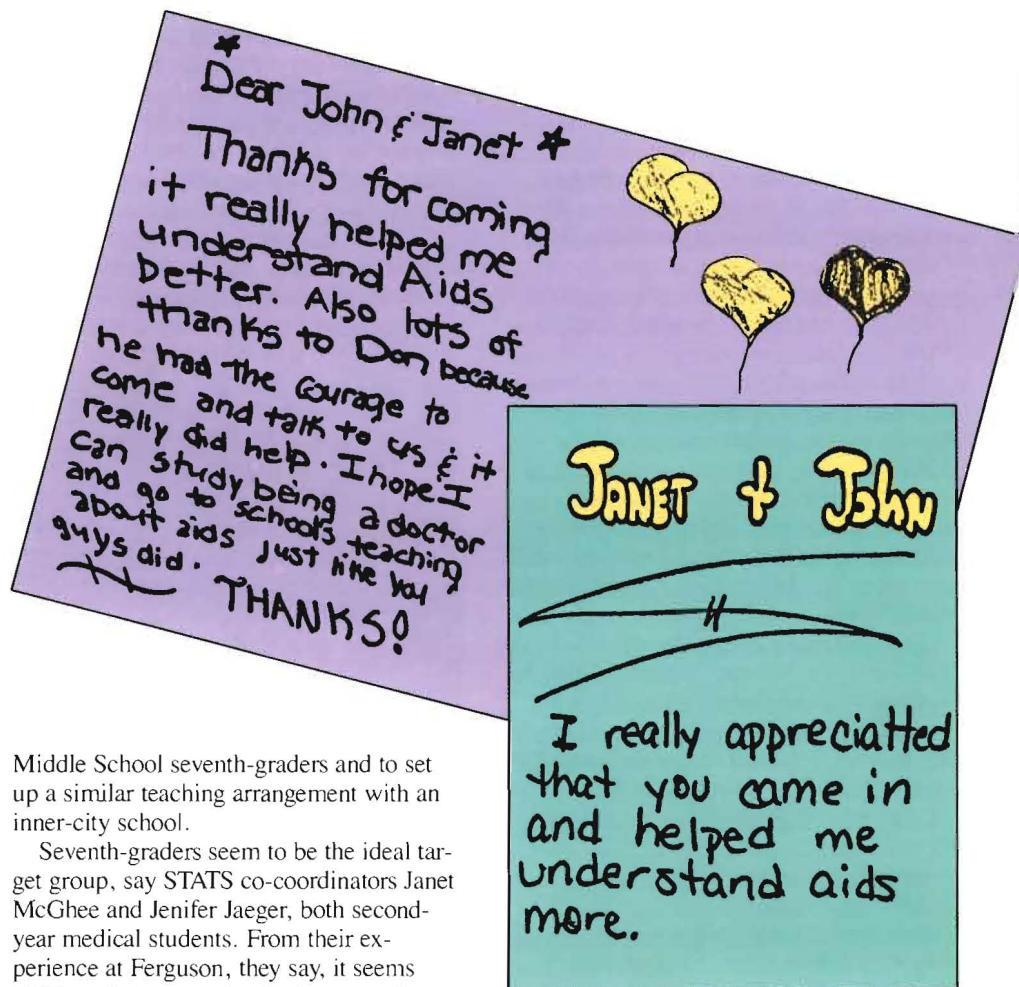
"I've learned alot, and I will be careful."

Those are among the reactions from Ferguson Middle School seventh-graders, who learned about AIDS recently in a novel program taught by Washington University medical students (Ferguson is a St. Louis suburb). Medical students here went to Ferguson Middle School this past fall as part of a pilot project designed to educate young people *before* they begin behaviors that put them at risk of catching AIDS. The students believe that's the best way to prevent the spread of AIDS among teenagers, whom experts predict will be hit hardest by the disease in the next few years.

The program, called Students Teaching AIDS to Students (STATS), is one of several volunteer projects of the American Medical Students Association (AMSA). Washington University AMSA members have altered the program in two ways that they believe dramatically improve its success: they are educating not only the 12-year-olds but also their parents in order to encourage open communication, and they have enlisted AIDS patients to go with them into the classroom to answer questions about their illness. The program was offered twice at Ferguson Middle School in the fall, and went so well that the organizers are suggesting that AMSA incorporate the alterations to make them part of the STATS basic curriculum.

"We've been very pleased with the program's results," comments STATS adviser Sessions Cole, M.D., associate professor of newborn medicine. "Not only did we appear to have some immediate impact on the students' perceptions of what AIDS is and how to protect themselves, but also we have initiated a considerable discussion, a process of peer education within the school, which is equally important in confronting the AIDS problem."

Some 50 medical students, organized into teams, went to Ferguson Middle School in September to test the STATS program with the school's 16 seventh-grade classes; because of the pilot project's success, they returned in November to teach the school's eighth-graders. Plans now are to offer the program each fall to Ferguson



Middle School seventh-graders and to set up a similar teaching arrangement with an inner-city school.

Seventh-graders seem to be the ideal target group, say STATS co-coordinators Janet McGhee and Jenifer Jaeger, both second-year medical students. From their experience at Ferguson, they say, it seems children that age are beginning to explore, but generally have not yet begun, activities like sex and drug use that could put them at risk of catching AIDS.

"We try not to talk just about how you get AIDS, but about attitudes," McGhee says. "We really want the kids to come to their own conclusions and to think about how their behavior will affect their own lives. The facts are available in a lot of places now, but if we can get these kids while they're still young, before most of them start making decisions about sex and drugs, then that's where we can have a really strong impact."

"Seventh graders are at the brink of learning and exploring these things, but they still have that child-like quality and are eager to learn," she continues. Adds Jaeger, "They're just beginning to experiment with their sexuality and with risk-taking, and that's why this grade is targeted. I don't think we would be as effective in trying to instill safe behavior after people have been practicing unsafe behavior for a long time."

Before talking to the seventh-graders, the medical students hold a parents' night at which they present a mini-version of the program. Jaeger explains, "What we're trying to do is not just lecture to the kids, but

rather to create a context in the community, to involve parents, teachers and students. We present this program to the seventh-grade students, and we provide the same information to their parents in hopes of stimulating open communication at home about concerns, fears and family morals." Children whose parents preferred they not take part in the STATS program—there were fewer than 10—spent that time studying in the library.

As Washington University students have designed it, the STATS program supplements classroom lesson plans for units on immunology and transmission of sexual disease. The three-hour program—taught over two days—begins with an 18-minute videotape in which teenagers deliver straightforward information about AIDS. Afterwards, the medical students spend five minutes talking about the disease and defining terms, and then answer "secret questions," which students have submitted anonymously. These questions—which deal with everything from how condoms work to whether French kissing is safe and whether animals can get AIDS—stimulate discus-

sion. To further encourage dialogue, the medical students lead educational games that reinforce key messages, most importantly, safe behavior.

At the second session the medical students are accompanied by AIDS patients, or PLAs (People Living with AIDS). The young people are allowed to ask questions freely, and the entire time is spent discussing attitudes and reactions—the PLA's as well as those of his or her family and friends—to the disease.

The PLAs, all from the speakers' bureau of the St. Louis Effort for AIDS (EFA), may be the most effective aspect of the AIDS program, Cole points out. "Certainly if you look educationally at what early adolescents understand during lecture-type presentations, the availability of a real person with a problem gives that problem some reality," he says.

The PLAs have a powerful impact, Jaegar comments, because "until these kids actually meet and talk with somebody who has AIDS, everything we teach is still abstract. They don't realize that their lives can be changed by this disease. The PLAs' participation brings home the importance of what we're saying, and it does so in a very profound, personal way."

Most important is that they get the young people thinking, McGhee says. "I could tell they were responding to what we taught, but I had no idea if we were really reaching them until I saw their faces when they were talking with Don, the PLA in my room. When he walked in and sat down they sort of looked at him for a few minutes, and then one of them raised a hand and said, 'You don't *look* like you have AIDS.' And Don said, 'You know, you're right, and that's one of the most important things about AIDS, is you can't look at a person and tell that they have it.' So that message was clearly communicated."

The seventh graders were not at all hesitant about asking questions, Jaegar recalls. "They were a lot more forward and a lot more compassionate than the PLAs and we medical students had anticipated. Of course the very first question was 'How did you get AIDS?' But they also asked questions like 'How did it feel when you told your family?', 'Did you have any friends who didn't understand?' and 'How would you like to be treated by other people?'"

PLA Blaine Richmond gives at least one talk a week through EFA, but this is the first time he's spoken to children. They were not only receptive, but asked questions that were in-depth and insightful, he found. Richmond's biggest concern had

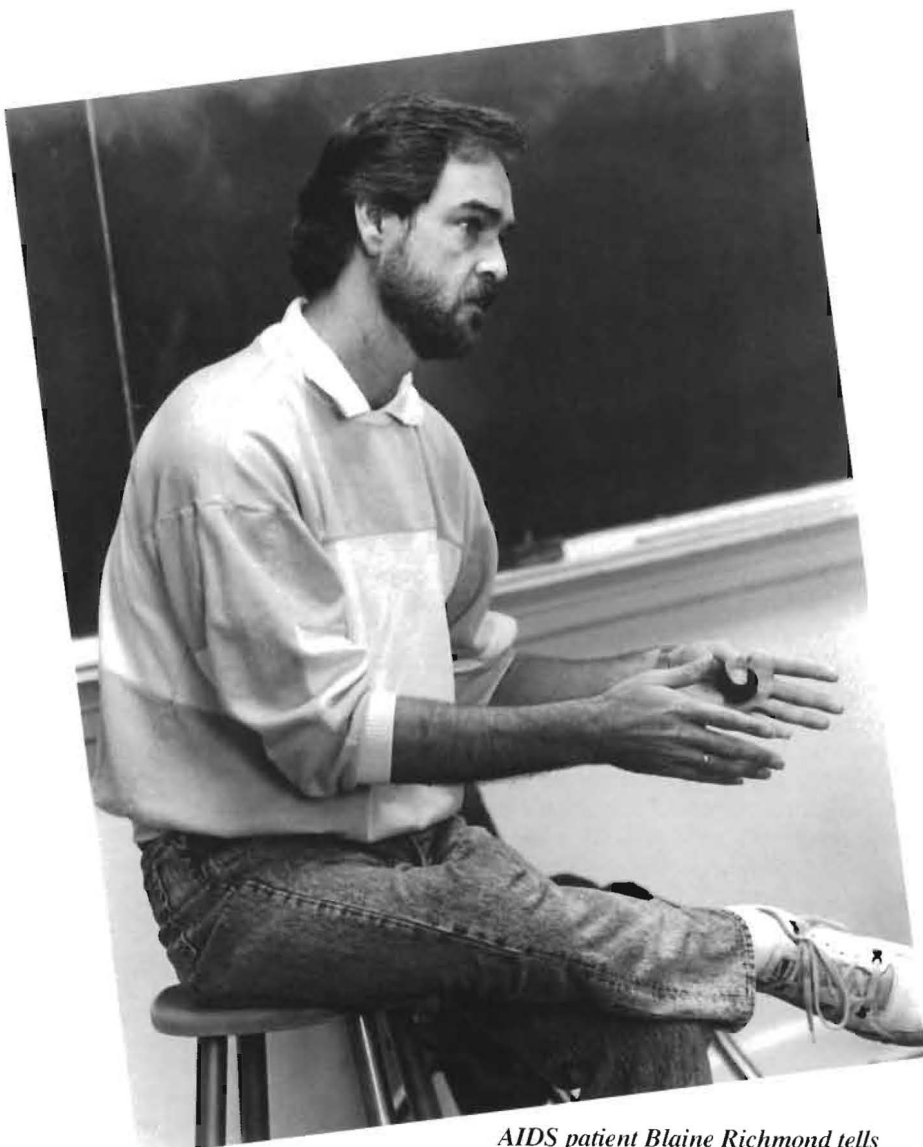
been parents: how explicit did they want him to be in answering their children's questions? However, as he learned at the parents' session, where he also was a speaker, Ferguson parents wanted their children to have full information, regardless of the question.

The children seemed most interested, he reports, in learning the disease's cost, emotional and otherwise. "I had my pills with me, and when I tell them that this little pill costs me \$800 a month, and I've got to take six other pills every day, it really strikes home. Something that also strikes home is when I tell them how limited my activity is because of the manifestations of this disease. Here their day is filled with running and playing and school, maybe basketball

practice or a friend's house afterwards, and I have to limit myself to one activity a day to conserve my energy."

Response to the PLAs was "wonderful," says seventh-grade life sciences teacher Julie Van Pelt, one of the people instrumental in bringing the STATS program to Ferguson. Van Pelt notes that the children, some of whom were tense at the prospect of meeting an AIDS patient, overcame their initial nervousness and demonstrated concern for the PLA.

"Probably the most touching thing was that, as the program ended and we were leaving the classroom, all the students went up to make sure they shook the PLA's hand. There was this big long line," she recalls. "I couldn't believe it, because they will not



AIDS patient Blaine Richmond tells seventh-grade students what it's like to live with this debilitating disease.

stand in line sometimes to hand in their homework, but they stood in this long line at the end of the day, time to go home. And the PLA looked at me and he said, 'You know, I don't have adults come up and shake my hand, and every kid in here made sure that he thanked me.' All the work that we'd put in and all the effort was paid off, right at that moment.'

Most of the credit for the STATS program's success, however, must go to the



Seventh-graders from Ferguson Middle School get some straightforward answers to the many questions they have about AIDS and how it is spread.

medical students themselves. Ferguson Middle School principal Daryl Hall comments, "The medical students were not so much older than our students that they couldn't relate to them as people. Reaction from the kids has been very, very positive. The teachers felt good about it too, because there were some issues that the kids brought up, sexual issues, that they never would have discussed with the teachers. With the Washington University students, they felt free to ask their questions and be open and honest."

The seventh-graders respected the medical students, but still identified with them as students, McGhee says. "Being a medical student opens doors for us. In the seventh-graders' minds we're authorities, and we try to be prepared, to live up to that

expectation. The fact that we're still students also really helps. We tell them we're skipping classes and we'll make up the time later, or that we have tests to take, and they relate to that."

One of the true measures of the program will come this spring, Hall says, when Ferguson seventh- and eighth-graders will take a post-test to check their retention of the information they learned about AIDS. No grades will be assigned, but scores on the

post-test will be compared with those of a pre-test that each student took before participating in the STATS program.

AMSA's STATS program began two years ago. National president Grant Haven, a 1984 Washington University graduate who went on to medical school at the University of Missouri-Columbia, designed the program and won a U.S. Department of Health and Human Services Secretary's Award for Innovations in Health Promotion and Disease Prevention. According to AMSA, some 75 medical schools now offer or are trying to establish some version of the STATS program.

The turnout of volunteers at Washington University has been "amazing," Jaeger notes, considering the demands on their time and the hours of training required for

this program. STATS participants attended three one-hour training sessions on immunological aspects of AIDS, sociological/psychological issues, and techniques for communicating with a seventh-grade audience. A final three-hour workshop taught by University of Missouri AMSA members included techniques and practice sessions for presenting the program.

Because of the rigors of their medical school schedules, students here are unable to offer STATS widely to area schools, though they plan to teach at an inner-city school in the spring. They hope to encourage AMSA chapters elsewhere to adopt the program with the elements they've added, and to explore ways that the Washington University chapter can serve as a training resource. Funding for the local program has come primarily from the Alumni Association, with additional support from the Department of Infectious Diseases, Upjohn Corp. and AMSA.

"This has been without any comparison the most exciting part of medical school for me," McGhee says. "It's probably the most rewarding, fulfilling project I've ever undertaken. One incredible benefit that I didn't foresee is that I have a deep respect now for my classmates and their ability to handle situations that might be sticky with such grace and maturity. It's a very committed group of people."

Jaeger concludes, "Out of this we get the opportunity to do what it is that we're in medical school to do, which is to serve the community. With regard to AIDS, prevention must be the most immediate concern of the medical profession. It's imperative that we step into the community and do what we can."

Perhaps the most telling assessments come from the seventh-graders themselves:

"Thanks for teaching me about aids. I think my brain needed it."

"You gave us answers to the questions we wanted to know and I thank you for understanding us."

"Thank you for your time and effort you put into making this class for us. One of the better parts about it was you got me out of 3 classes. Thanks."

"Hopefully somebody some day will make a cure for AIDS so not everyone will have to die from such an awful disease." ■



Survival Secrets for Atomic Attacks

Rock n' Roll
NEVER LOSE YOUR HEAD

Reds

1955

1959

DIRECTION
HEAT FLA

RADIATION

ONE TELEPHONE

AFTER THE FALLOUT

THE LOWDOWN ON LOW-LEVEL RADIATION

BY KATHY HEINE

Those were the happy days of Elvis and bobby socks, drive-ins and jitterbug, souped-up Chevies and malted milks, blue jeans and 45s. And teenagers were still naive—at least about radiation.

In 1953, when Betty Lou was getting ready for the sock hop, she would go to the local shoe store for a new pair of saddles and stick her newly clad feet under a fluoroscope to make sure the shoes fit just right.

Then she would stop at the dermatologist's for a regular dose of X-rays to clear her acne.

Today in the 90s, people wouldn't dream of needlessly irradiating their feet, much less their pimples. Betty Lou is worried about the radon level in her basement, and avoids unnecessary medical X-rays. She knows better now. Or does she?

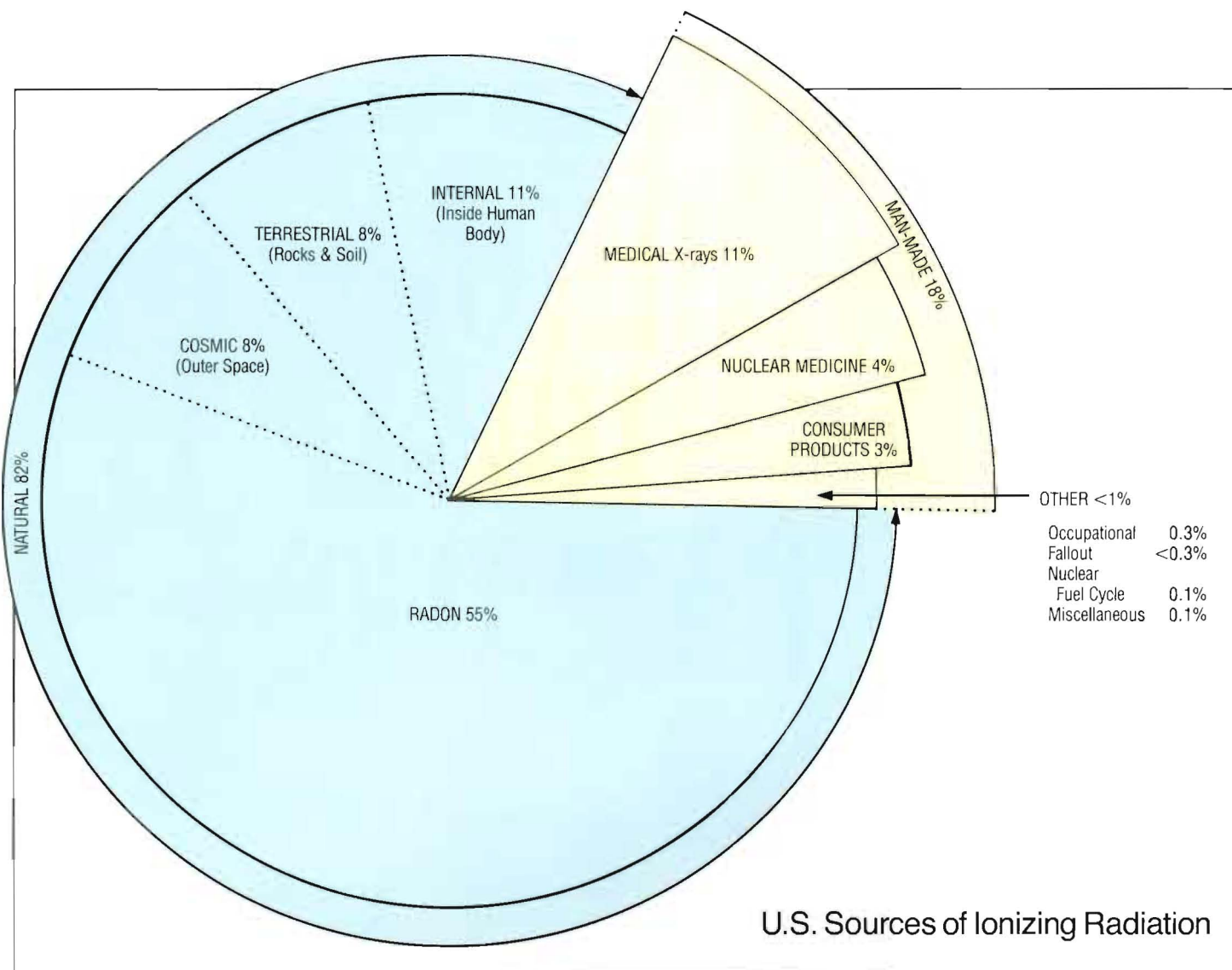
A new report by the National Academy of Sciences indicates that low levels of radiation may be even more dangerous than we thought. In fact, the risk of developing cancer from low-level radiation may be as

much as three- to four-times what was previously believed.

Released this past December, the report by the NAS Committee on the Biological Effects of Ionizing Radiations (BEIR V) also observes that young people—especially those under the age of 25—are at the greatest risk for cancer from low-level radiation exposure. And fetuses exposed to low levels of radiation run a higher risk of mental retardation than was previously recognized.

Perhaps the only silver lining in the report is that the BEIR V committee found the genetic risks, or risks to future generations, to be actually less than expected. "The main risk of radiation to you is cancer in any part of your body," says Daniel S. Hartl, Ph.D., James S. McDonnell Professor and Head of Genetics at the School of Medicine, and vice chairman of the BEIR V committee.

Low-level radiation is not likely to affect future children or grandchildren, Hartl ex-



(Source: National Council on Radiation Protection and Measurements)

plains, unless they themselves are exposed to radiation, or their mothers are pregnant when exposed. The radioactive mutants depicted in many science fiction novels, according to Hartl, are simply that—science fiction. “Human reproductive cells are surprisingly resistant to radiation,” he says.

Although the BEIR V study formally began in 1986, the roots of the study and all previous BEIR studies date as far back as that fateful day 45 years ago when Yoshihiro Kimura and his fellow citizens of Hiroshima, Japan, became the first human guinea pigs of the nuclear age:

“Pretty soon we heard a hum and saw a little aeroplane in the sky to the south-east. And this gradually grew larger and came over our heads. I was watching the aeroplane the whole time. I can’t tell whether it is a foreign plane or a Japanese plane. Then suddenly a thing like a white parachute came falling. Five or six seconds later everything turned yellow in

one instant. It felt the way it does when you get the sunlight straight in your eye. A second or two later, CRASH! there was a tremendous noise. Everything became dark and stones and roof tiles came pouring down on our heads.”

(Yoshihiro Kimura, *Children of the A-Bomb*)

In that one blinding moment when the bomb was dropped, Kimura and his neighbors in Hiroshima were exposed to more ionizing radiation than any other humans in history. Three days later, a second bomb irradiated the residents of Nagasaki.

Within six weeks of the blasts, 100,000 inhabitants of Hiroshima (15 percent) and 40,000 Nagasaki residents (20 percent) were dead. Yet the story did not end with the fallout.

Soon physicians began to notice effects that had never before been detected in populations exposed to much lower levels of ra-

diation. Cancer, leukemia, mental retardation—these were the later, more insidious effects.

American scientists and government officials began to wonder whether the low levels of radiation to which they were exposing Americans—medical and dental X-rays, among others—could be causing some of these same effects on a smaller scale. Hence the people of Hiroshima and Nagasaki became the largest single group of people ever studied for evidence of the consequences of radiation exposure.

With the help of Japanese scientists, American researchers interviewed approximately 76,000 survivors, asking them to describe where they were at the time the bomb dropped, the position of their bodies, the rooms they were in and the types of buildings that were nearby.

The researchers used these descriptions to estimate the dose of radiation each survivor received, and then tracked their medi-

cal histories. As the effects of radiation became increasingly clear, Americans took steps to protect themselves. Fluoroscopes were removed from shoe stores, radiation treatments for acne and ringworm were discontinued, and the government began to set exposure limits for radiation workers.

Yet recent findings by the BEIR V committee suggest that these steps—especially the exposure limits for workers—may not be enough.

BEIR V reports that for every 100,000 workers exposed to one rem (see footnote) of radiation per year from age 18 to 65, there will be 3,000 extra cancer deaths. That is, exposure at this level increases workers' chances of dying from cancer by almost 20 percent.

The Nuclear Regulatory Commission's current recommendations allow workers to receive five times this amount, or five rems per year, an occupational exposure that nearly doubles their cancer risk. And loopholes in these recommendations allow some transient workers to receive as much as 12 rems per year.

"Obviously, the NRC may need to re-think these upper exposure limits to protect those individuals who actually work at these high levels," says John O. Eichling, Ph.D., associate professor of radiology at the School of Medicine's Mallinckrodt Institute of Radiology. He adds that Great Britain has already voluntarily lowered its occupational limit, from five rems a year to 1.5 rems a year, while its regulatory agencies decide whether this limit should be lowered even more. But the BEIR V report is not likely to affect the vast majority of radiation workers who, Eichling says, work at levels that do not greatly exceed background levels.

Worker distribution data shows that the percentage of radiation workers who work at exposures of five rems a year or more is only about .1 percent, and that only about 2 percent of all radiation workers are exposed to one or more rems a year. In fact, the majority of radiation workers in this country work at levels too low to measure.

New standards, if they are developed, are not likely to affect the use of radiation in

*A rem is a unit that expresses radiation dose in terms of its biological damage potential. It not only takes into account the amount of radiation absorbed per gram of body tissue (rads), but also how damaging that particular form or forms of radiation are to human tissue. Neutrons and alpha particles, for example, are more damaging to tissues than X-rays. So one rad of neutron particle radiation equals more rems than one rad of X-rays. There are also some proponents of a dose rate reduction factor that figures low doses sustained over long periods of time to be less damaging than equivalent doses received all at once.

medicine, Eichling explains, because the doses to which workers are exposed are already low. If anything, they will affect the nuclear industry, where the doses tend to be higher.

The new risk estimates cited in BEIR V are the result of both the accumulation of another entire decade of data and an improved understanding of the types of radiation emitted by the atomic bombs.

Because the types of radiation released are now thought to be less biologically damaging than before, the dose estimates for each bomb survivor had to be lowered, according to Hartl. Lower dose estimates mean that the excess rates of cancer observed in these populations were actually due to lower doses, he says. "In other words, the risk at any given dose is higher than we thought."

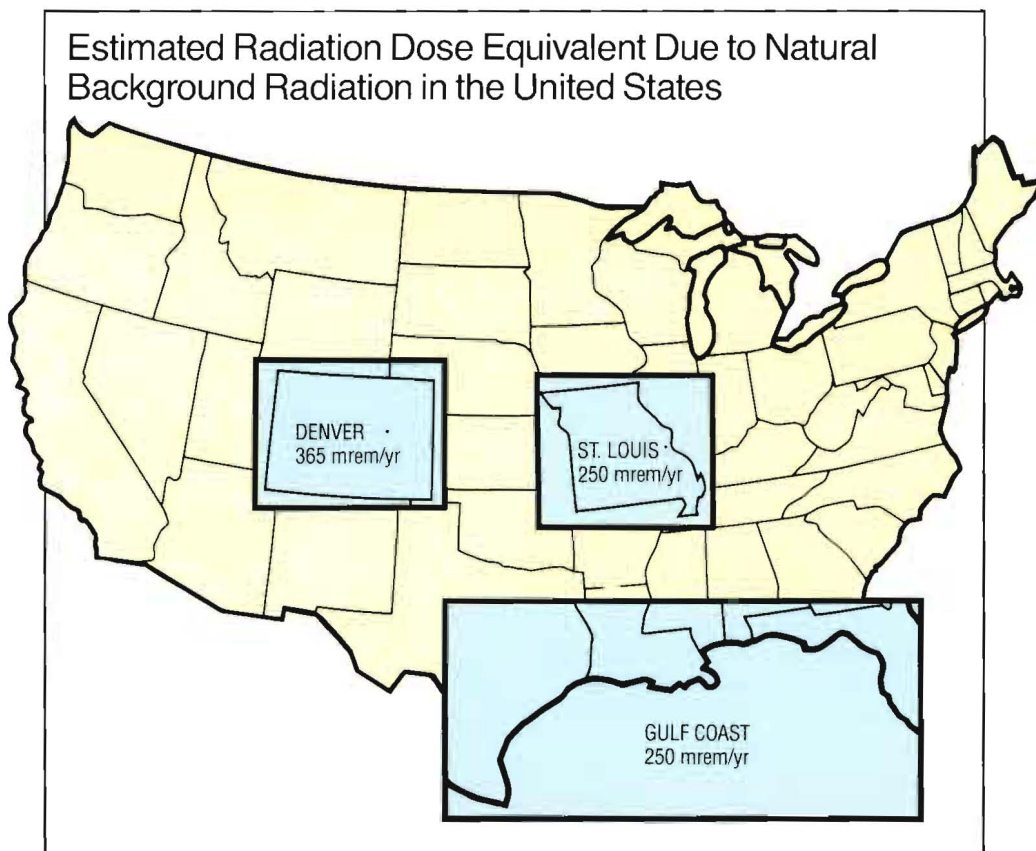
The BEIR V report also marks a change in the way scientists extrapolate the cancer risks of low-level radiation from the high-level effects observed at Hiroshima and Nagasaki.

Although it was hotly debated at the time, the previous BEIR committee that dealt with this issue selected a linear qua-

dratic equation to extrapolate cancer risks. This approach assumed that the effects of radiation are negligible at low doses and climb steeply at higher doses.

The recent re-evaluation of bomb survivor data, on the other hand, led the BEIR V committee to conclude that the cancer risks better fit a strictly linear model in which risks at low doses are proportionally just as great as risks at high doses. Unlike the linear quadratic model, this straight-line model implies that there is a proportionally equal effect—even at infinitesimal doses.

So what does BEIR V mean to Betty Lou and those of us who don't work with radiation? It definitely does not mean that people should avoid medical or dental X-rays, if they need them, or otherwise become alarmed, according to BEIR V committee chairman Arthur C. Upton, M.D., from the department of environmental medicine at New York University Medical Center. This is particularly true for mammograms, as the radiation risk associated with breast exposure—in contrast with the risk to other tissues—was not shown to be higher in the BEIR V study.











People living in Denver are exposed to more background radiation than people living in St. Louis or the Gulf Coast, yet surprisingly, researchers have been unable to find any significant difference in cancer rates for these populations.

(Taken from "Low-Level Radiation Effects: A Fact Book," published by the Society of Nuclear Medicine, Inc.)

How Low Can We Go?

The following actions are thought to result in a one-in-a-million chance of death:

Action	Nature
10 mrems of effective dose equivalent radiation	Radiogenic cancer
 5 years in Miami	Carcinogens in drinking water
50 days working in typical factory	Accident
 10 days in New York	Air pollution
 5,000 miles by airline	Accident
 10 months in Denver	Elevated cosmic radiation
150 cans of saccharin-sweetened soda	Carcinogen
 1,500 miles by car	Accident
 5 hrs. in a coal mine	Black lung disease
30 months in stone building	Natural radioactivity
 50 miles by bicycle	Accident
30 miles by canoe	Accident
 7 cigarettes	Cardiovascular disease, cancer

Taken from: "Low-Level Radiation Effects: A Fact Book", Society of Nuclear Medicine, Inc. N.Y., N.Y., 1985 p. 6-12.

Although the risks to most other body tissues may be three- to four-times greater than we thought, the risks are still relatively low, according to Henry D. Royal, M.D., associate professor of radiology at the School of Medicine, who points out that it took such a catastrophic event (the atomic bombings) to be able to even detect any risks. "To me, the amazing part of the story is how long it's taken to get any certainty at all about the effects," Royal says. BEIR V itself estimates that only 500 to 1,000 bomb survivors have since died of radiation-induced cancers, he explains. "The fact that so few people have died from a radiation-induced cancer, despite surviving an atomic blast, is one of the best-kept secrets in radiation biology."

The other part of the story is that no matter what we do, we cannot completely eliminate the risks. "We all have to live with a certain amount of background radiation," says Michael J. Welch, Ph.D., professor of radiology, also at Mallinckrodt. We get it from solar and cosmic radiation, rocks and soil, groundwater, radon and potassium decaying in our own muscles. These natural sources, according to Welch, account for 82 percent of the radiation most of us receive. "So the vast majority of radiation we get, we can do next to nothing about," he says.

Then there are the radiation sources we can control. Medical and dental X-rays, for example, constitute another 11 percent of the radiation we receive. Nuclear medicine yields another 4 percent and consumer products about 3 percent. How do the risks we face from these sources of radiation compare with other risks we take in our everyday lives?

According to data adapted from Report 94 of the National Council on Radiation Protection and Measurements, the radiation from about two chest X-rays (about .01 rems) exposes us to a three- to four-in-a-million chance of dying from cancer. But smoking seven cigarettes exposes us to the same risk of dying from either cancer or cardiovascular disease. Riding 1,500 miles in a car, 5,000 miles in an airplane, 50 miles on a bike or 30 miles in a canoe exposes us to an equal risk of dying in an accident, and living only 10 days in New York City places us at the same risk of dying from air pollution.

"There are risks to nearly everything we do," says Royal. In deciding whether or not to take a risk, Royal explains, people must weigh the benefits against the risks. Bicyclists, for example, believe that the enjoyment and fitness they derive from cycling is worth the risk of being run over by a car,

and people who like to travel still take airplanes.

The same may be said for radiation. Women over 40 should have regular mammograms, because they stand a better chance of surviving breast cancer if it's detected early, according to Judy M. Destouet, M.D., associate professor of radiology at the School of Medicine. "At that age," she says, "the benefits far outweigh the risks." People sleep more soundly at night with the minute level of radiation in their smoke detector sensors because they know they will be awakened if their houses catch fire. And some people believe that nuclear power is a viable alternative to coal burning, which produces harmful pollutants and may contribute to acid rain and global warming. None of this means that people should ignore the risks of radiation, Royal says. It simply means that they have choices to make.

One good choice people can make is to go to a large, modern center for radiological exams and procedures, Eichling advises. "Not all equipment is optimal. You can still find equipment that dates back to the days before World War II," he says. As a result, the radiation dose of a dental X-ray at one facility may be as much as 100 times the dose of that same X-ray at another facility, according to data cited by John W. Gofman, M.D., Ph.D., in his book, "X-rays: Health Effects of Common Exams." And the radiation doses for many common medical exams may vary by as much as a factor of 40. (Gofman is a co-discoverer of uranium 233 and was one of two scientists to isolate the world's first workable quantity of plutonium.)

People also might want to check the radon levels in their homes, according to Royal, who is surprised that there has not been more public furor over this greatest source of radiation.

"The point is," Hartl says, "that low-level radiation is dangerous. People should avoid needless X-rays and radiation whenever possible, especially women who are pregnant." Some critics claim that the risks of low-level radiation cannot be extrapolated from high levels because the body is able to repair damage at low levels. But what is a low level? Hartl explains that it is important to keep in mind that BEIR V is by no means the end of the story. "There's much we still don't know about radiation," he says. "Half of the people who were exposed at Hiroshima and Nagasaki are still alive, still experiencing the effects of radiation. So as the years go by, these risk estimates may change again," he says. "So it's best to err on the safe side." ■

A Two-edged Sword

Low-level ionizing radiation is dangerous to humans because it damages their genetic material, or DNA, according to Joseph L. Roti Roti, Ph.D., professor of radiology in the School of Medicine's division of radiation oncology.

DNA damage occurs when high energy waves or particles of ionizing radiation interact with cells and excite, ionize or chemically alter DNA molecules, he explains. This causes temporary breaks in the strands of DNA, which the cells then try to repair.

The extent of permanent damage depends on how quickly and how well the cells are able to repair these breaks, according to Roti Roti, who studies how cells repair themselves after exposure to ionizing radiation.

This has to do both with dose, or the amount of energy deposited per gram of tissue, and time of exposure, he says. Higher doses tend to be more damaging, yet cells are equipped to repair damage—even from high doses—if the dose is delivered over long periods of time rather than short ones.

Extremely high doses of 200 or more rads cause so much damage to the DNA of dividing cells that the DNA can no longer be separated and copied during cell division, and the cells die. Bone marrow cells, for example, die in this way at exposures of 200 to 500 rads. Non-dividing cells, on the other hand, live on to die of other things at even higher exposures. Brain and spinal cord cells, for instance, die at exposures of 5,000 to 15,000 rads. Cells of the cardiovascular system can survive up to 10,000 rads.

DNA damage from low-level radiation can be repaired, Roti Roti says. "But repair is a two-edged sword." The more broken up DNA becomes, the harder it is for the cells to put it back together again without making a mistake. Pieces get misplaced and are pieced together improperly, and some of these mistakes can change a normal cell into a cancer cell. "Just because a cell repairs itself doesn't mean that it hasn't changed somehow," Roti Roti says. "A dead cell won't give you cancer, but a misrepaired cell might." ■

Against the Odds:

Helen Nash's 40 Years in Pediatrics

by Marion Hunt

“Sell a house and send her to medical school,” said Antoine Graves on his deathbed—thereby assuring the first year of Helen Nash’s medical education. Though her father, Homer Nash, M.D., was a physician, he

was skeptical of her commitment to a medical career. Fortunately, her grandfather was willing to support her immediately, even if it meant selling family property.

The investment proved a wise one; in June of 1989, Helen E. Nash, M.D., celebrated forty years as an attending physician at St. Louis Children’s Hospital. In private practice since 1949, she was—with the support and counsel of senior Park J. White, M.D.—the first black physician to join the hospital’s attending staff.

Four years later, she passed the qualifying exam administered by the American Board of Pediatrics. Some were so astonished at her success on the first attempt (the examination was given in Baltimore) that the news of her success preceded her return to St. Louis.

Succeeding against the odds has been the hallmark of Nash’s medical career. A young black woman starting out as a physician in the 1940s had to face the dual obstacles of bias against both her race and her gender. Just one of these biases could be a formidable enemy; the combination might have been devastating. But Nash’s determination has always been equal to the challenges in her life. Providing quality care to patients and gaining equality of opportunity for herself and others have been her twin passions.

Educated at Spelman College in her hometown of Atlanta and at Meharry Medical College in Nashville, Tenn., Nash remembers little difficulty with preclinical courses. The undergraduate science courses at Spelman, a college founded to educate black women after the Civil War, were excellent; indeed, her professors were graduates of Vassar and Smith. And despite obstacles to blacks and women in medicine at this time, it never occurred to her that she could not become a physician. In forty-five years of work, Nash has built both a thriving private practice in pediatrics and a unique reputation as a public advocate for child welfare.

Most important in her eyes is the fact that she has helped raise three generations of St. Louis children. She inspires such



loyalty that former patients who have moved to the suburbs bring their children and grandchildren to see Nash in her midtown office. Her advocacy of child health has reached far beyond the confines of her practice; over the years, she has established a reputation as an outspoken advocate for youth.

A patient suggested to Harvey Colten, M.D., Harriett B. Spoehrer Professor and Head of the Department of Pediatrics, that her four decades in practice deserved a celebration. So on June 16th, 1989, he declared a "Helen Nash Day." The festivities honoring her included a lecture by Morris Green, M.D., professor of pediatrics at the

Her entire medical career speaks eloquently of a single-minded devotion to children's health in the broadest possible sense of that term. As a 1976 honor citation from the St. Louis Medical Society stated: "She has given of her time and herself unstintingly throughout her career in improving the health of all children regardless of socioeconomic or ethnic status." And her concern has always been broad in scope. In 1974 she spent six weeks in the Phillipines training nurses to care for children in four clinics because, as she remembers, "I had always been envious of Peace Corps volunteers and wanted to see if I could do something like that myself."

In her case, the usual pattern has been reversed; though much of her practice is from the surrounding neighborhood, patients also come from outlying areas in Missouri and Illinois. As she recalls her father telling her: "Your office is in the right place. You are needed there." Nash says, "That sense of being needed every day is one of the constant rewards my practice brings."

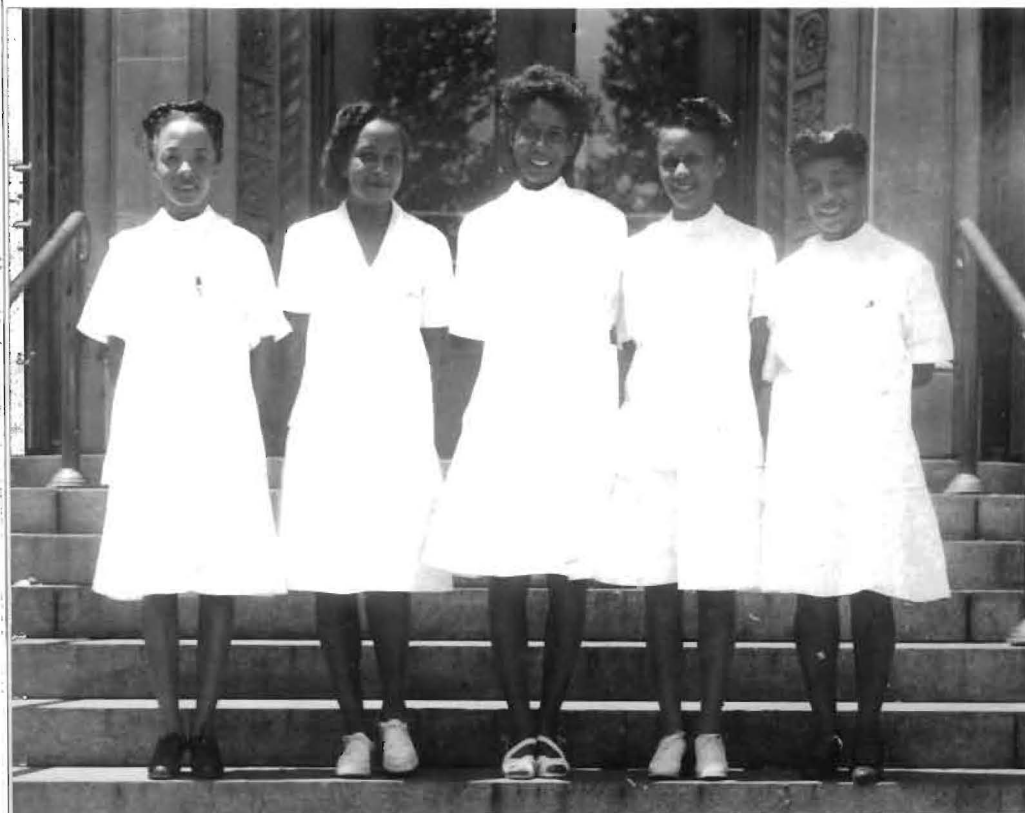
In a single morning office hour she sees a drug-abusing teenager, a baby whom she has helped remove from his incompetent mother's custody (the grateful grandmother brings him in to show his weight gain) and a bright nine-year-old with a father in prison and a firm ambition to be a pediatrician.

Though she sees troubled youngsters and their families often enough, hope is endemic to her work because Nash is prepared to help youngsters in any way possible. She does not take a passive or limited view of the doctor/patient relationship; she treats the whole child in the family context. The population she serves struggles to raise youngsters against tremendous economic and environmental odds. She gives these children and their families information, support and, when needed, firm guidance and discipline.

Nash treats each patient for far more than the presenting symptoms—always asking about home conditions, school problems, the family situation. Her all-embracing style of care brings warm responses from children and parents. Adolescents are a particular concern; she has an examining room especially decorated with bright colors and moviestars' photos to put them at ease. When asked about the upper age limit of her patients, Nash replies, "Oh, twenty-four or twenty-five." Her commitment to patients is not something she cuts off automatically at a certain age.

The busy waiting room and color-coded examining rooms are hung with photographs Nash took in Africa and reproductions by Picasso, Modigliani, and Kollwitz—she takes pride in both the efficiency and aesthetics of the office she and her husband designed and built in 1965.

Yet despite her considerable personal success, and the improvements she has seen in medical care, she is deeply troubled by the rising infant mortality rate (the United States has fallen behind 21 other countries in lowering this toll). And she is equally troubled by evidence that black infant mortality remains double that of white children—just as it was when mentor White surveyed the problem in St. Louis 65 years ago. Not enough work is done in the field of prevention, she believes; "By the time a



Helen Nash, M.D. (on left) with four other house officers at Homer G. Phillips Hospital.

Indiana University School of Medicine, and a gala luncheon for Nash's family, friends, colleagues and patients.

On the previous evening, there had been an elegant harpsichord concert at Colten's home to honor her pleasure in music. In music, as in medicine, Nash believes in commitment; she has expressed this in musical terms by endowing a chair for piano soloists to play with the St. Louis Symphony, on whose board she serves. And she encourages busy young house officers to go to symphony concerts, reminding them that "there is life outside of medicine."

Well-known for her longtime commitment to a full range of family planning services for women, Nash sees no contradiction between this belief and her role as a pediatrician. Indeed, she believes it is her special responsibility to see that children can be born to parents ready to nurture them well.

And while her practice reaches families of all backgrounds, Nash has rendered particular service to inner-city children by maintaining her office in downtown St. Louis during the past four decades—a time when many physicians followed their patients to the suburbs.



Nash cares for babies at the first well baby clinic in Homer G. Phillips Hospital.

teenager gets pregnant, it's already too late."

Still deeply involved in improving the quality of children's lives, she spends no time resting on her laurels. In her private office hang diplomas and awards, beginning with her kindergarten certificate and including her father's 1910 medical degree. There is the strong sense that for Nash, life and work are one.

The elegance and grace of her 40th anniversary celebration belied the harsh struggles Nash had to face in the early years of her career. As one of her friends recalled, "She had to walk into rooms where she wasn't wanted; she has demanded respect for women and for Afro-Americans."

As a young medical school graduate, her most important goal was obtaining the best possible clinical experience. On arriving here to take a rotating internship at Homer G. Phillips Hospital in 1945, she knew this was an institution where there would be plenty to learn. Opened in 1937 as a segregated hospital to serve the black community, this was the only place in St. Louis where non-white doctors could get internships and residencies.

Like other black physicians of her generation, she had to choose the hospital where she would train very carefully. With segregation in force at some institutions, and rac-

ism accepted practice in many others, it was difficult for a black medical school graduate to find a place where fair treatment and professional opportunity were available. Though Homer G. Phillips was a segregated institution, it offered a wealth of learning experiences. There she worked on twelve services during her rotating internship year and then finished three years of residency training in pediatrics.

She remembers delivering 50 babies that first year; neonatal care would always remain one of her primary professional interests. It was watching Nash handle newborns at Homer G. Phillips that made White, then supervisor for pediatric care, decide to support her career in any way he could.

In those days black physicians were not allowed to attend or train at St. Louis Children's Hospital, and few white physicians made any effort to visit Homer G. Phillips. White was an exception to that rule. A senior attending physician at St. Louis Children's Hospital with a flourishing private practice and a deep commitment to social justice, he gave generously of his time to improve medical treatment in the black community. St. Louis Children's Hospital had opened a segregated building in 1927; no black physicians were allowed on the staff.

Homer G. Phillips treated only black children and had no white physicians on its full-time staff. White and Nash were determined to break down some of these rigid racial barriers at both hospitals, and, in time, they succeeded in doing so. Despite their difference in age, race and gender, an extraordinary collaboration developed between these two physicians.

As White's 96-year-old widow, Maria, remembers, "It was not just a professional relationship; there was deep personal friendship between them." The young black woman house officer and the senior white pediatrician made a formidable team as they helped to bring racial integration to one hospital and improved patient care at the other. Separate wards for black children were abolished at St. Louis Children's Hospital in 1947; Nash's appointment to the attending staff came two years later.

She remembers with some irony that integration came during a polio epidemic when the separate wing built in 1927 for "Negro patients" turned out to be the only place children could be effectively isolated. Isolation to prevent an epidemic's spread proved to be a higher priority than racial segregation—a small sign of progress.

The integration of the medical staff was accomplished with a similar lack of fanfare,

as a matter of common sense. Lawrence Kahn, M.D., (now a professor of pediatrics) who served on the hospital housestaff with Nash, remembers no negative reaction to her joining the group as the first black member in 1949. As he pointed out, "What mattered to us was that she was a good pediatrician."

Dorothy Jones, M.D., associate professor emeritus, worked with Nash at Homer G. Phillips Hospital. Their friendship was forged in an atmosphere of continual crisis—as they tried to give young patients the best possible care under far less than ideal conditions. She respected Nash both on the hospital wards and in her later role as a private physician: "I admire her practice; she is a really good pediatrician."

The respect of professional colleagues Nash gained over the years resulted in her election as president of the St. Louis Children's Hospital attending staff in 1977; she now holds the rank of clinical professor. But her strong sense of history never lets her forget the struggle preceding this success.

Improving conditions at Homer G. Phillips, a hospital with a tradition of training only non-white staff and serving only black children, was not an easy task in the conservative racial climate of the 1940s and 50s. Yet over the years Nash and White worked together, they saw to it that the premature newborn death rate dropped from 80 percent to 16 percent—in large part due to relatively simple improvements in hygiene and equipment such as acquiring individual isolettes to replace large beds with partitioned spaces for up to ten babies.

It took an outbreak of diarrhea in the nursery (with 30 deaths) before these large beds were finally replaced. The upgrading of nurses' training and the requirement that there be nurses on the infant ward between midnight and 7 a.m. substantially improved patient care.

Along with White, Nash also took an active interest in housestaff training. As one of her former interns, Otis Smith, M.D., of Atlanta remembers, "No matter how many hours it took you at night to get it done, the next morning when she did rounds, your patients better have gotten everything they were supposed to get . . . She taught me always to put the patient first . . ."

One of her former patients, prominent film producer Henry Hampton recalled how she approached him when he was a teenager stricken with polio: "She taught me that life remained to be lived. There was no time for self-pity. Our chief want in life is to find someone who can help us do what we can—Helen is certainly that for many."



Nash and Park J. White, M.D., a month before he died.

Nash has always been a powerful role model for her young patients and takes justifiable pride in the fact that at least 50 have become pediatricians—no small tribute to her influence in their lives.

Though her father had initially been skeptical of her commitment to medicine, she well remembers his influence on the path she chose to take. Nash Sr. graduated from Meharry Medical College in 1910 and worked as a general practitioner in Atlanta until his death at the age of 94.

Her younger brother, Homer E. Nash Jr., M.D., shares her professional commitment to pediatrics and has a thriving private practice in North St. Louis. His daughter, Alison Nash, M.D., has also earned a medical degree, so there will certainly be members of the family practicing medicine here in the 21st century.

Nash herself may well be among them; watching her at work with patients in her busy office, there is no sign of any intention to retire or even slow down—despite the gala celebration of her 40 years in practice.

Indeed, this occasion was as much a joy to other people as it was for Nash—a shared happiness was clear in the faces of the many guests: patients, former patients, colleagues, family, friends. As Hampton said, "Helen's life is a broad, rich quilt. She is a pioneer for both her race and gender. This day exudes a potent word—pride."

Such pride is both mutual and well-earned; Nash has given much to the medical school and hospital that gave her a special day of celebration last June. In recognizing her achievements, pediatrics brought honor to itself. Colten alluded to the progress she helped others make through her insistence on equality of opportunity

and quality health care:

"When Helen was a house officer, black house officers were permitted to attend grand rounds but not to touch patients . . . Park White was instrumental in overcoming this disgrace. It must have been difficult for Helen to tolerate . . . she refers to those days now just as 'that black stuff' and 'that woman stuff.' She overcame it and brought us to the point at which the only stuff that matters is 'the quality stuff.'"

Perhaps the highest tribute to Nash came from one of her young patients who said:

"Sitting before us today is a woman who exemplifies the teenage word 'cool.' Parent, counselor, and best friend all rolled into one, she not only listens and understands me, but plays an active role in helping me solve problems."

That rare ability to be absolutely there for her patients, ranging in age from infancy to adolescence and beyond, has made Nash a precious resource to them and to the larger community; as former patient Hampton declared:

"She is a long distance runner, who connects the now to then to what will be."

Eloquent evidence of her commitment to continuity is the fact that Nash is now busy raising funds to endow a chair in the Department of Pediatrics named for White—whose friendship and support were so important to her career and to the black community. By honoring him, she hopes to remind future pediatricians of the specialty's roots in a compassionate commitment to youth—a quality embodied in White's practice and in her own. ■

Vintage Karl

By Robert Lowes

For more than half a century, Michael M. Karl, M.D., has practiced—and some say perfected—this kind of medicine:

The phone would ring after 11 p.m. Karl would stop reading his medical journals in preparation for teaching rounds the next morning, answer the phone and talk to the last patient of the day. Quite often, the worried voice on the line belonged to another physician, or a physician's spouse or child. Karl would dispatch the caller to a hospital emergency room.

Then Karl would drive to the emergency room to personally assess and reassure his patient, who would feel as if he had been Karl's only patient that day. Before he returned home (it was now close to midnight), Karl would take an extra 20 minutes to discuss the case with the house staff.

Karl ended his private practice in 1987 to become director of clinical affairs in the Department of Medicine at the School of Medicine. But to the medical community of St. Louis, Karl is better known by unofficial titles. Doctor's doctor. Patient advocate. The epitome of the teaching clinician.

Karl's lifetime of humane medicine was aptly honored April 26 when he received the Ralph O. Claypoole Sr. Memorial Award from the American College of Physicians. The award is given to an outstanding practitioner of internal medicine who has devoted himself to patient care, earned the respect of peers for his

clinical skills and served as a role model on a medical school faculty.

"This is an exact depiction of Dr. Karl," wrote Kenneth M. Ludmerer, M.D., an associate professor at the School of Medicine, in a nominating letter to the American College of Physicians. "The award has been established to recognize

as people as well as a medical problem.

"One thing that it led to—physicians referred their own families to Dr. Karl. He's taken care of a lot of my family. Mike's practice was more doctors' families than any other doctor I know."

To Karl, patient empathy is the norm, not the exception to



Michael Karl, M.D., and resident examine patient.

precisely those qualities his work and career have always exemplified."

A nimble-looking man whose thick wavy hair is now white, Karl has led the kind of life in which personal and professional qualities blend together. "He is not only a superb physician, but he is marvelous with patients," says William H. Danforth, M.D., chancellor of Washington University and a former pupil of Karl. "He understood them

the medical rule.

"They're not inanimate objects," he says with a tone of gentle reproof. "Most of my patients I have regarded as friends."

Such a relationship exacts a price—watching a friend suffer ill health, and having to deliver bad news. But even the latter is a friend's duty, says Karl.

"You do a friend an injustice if you don't lay it on the line."

Karl, raised in Milwaukee, is the son of Russian immi-

grants. His father, Louis, was a shopkeeper. A casual observer might suspect that personal tragedy during his youth motivated him to enter the healing profession. His mother Bertha died when he was three. When he was 14, his older brother Harry died of a mysterious malady which made the front pages of the Milwaukee papers. Karl doesn't attribute his medical calling to these distant griefs, but his older sister Minnie remembers that when brother Harry was dying, Karl asked, "Why can't they find out what's wrong?"

After flirting with a degree in English literature, Karl embarked upon medicine, a career which Karl says made good use of his scientific bent. He earned his M.D. at the University of Louisville in 1938, completed a fellowship in cardiology at the School of Medicine in 1940 and completed a residency in internal medicine at St. Louis City Hospital in 1942.

Joining him in his medical pursuits was a new wife, Irene Elsie Stark, Ph.D., a biochemist. Their relationship began during college as a typically Karl-ish mixture of business and pleasure. A part-time shoe salesman, he sold her a pair of navy blue pumps one day and then asked her for a date.

World War II sent Karl to Burma and India; for a time, he labored in a crude, steamy Army general hospital where everything was in short supply except casualties. At war's end, he returned to St. Louis to resume his private practice and raise a family (daughter Bonnie was born in 1944, daughter

Terry in 1947). And if that wasn't enough to consume his waking hours, he served as an assistant clinical instructor at the School of Medicine, a post he first assumed in 1940.

"He made a lifestyle decision to do that," says David Kipnis, M.D., chairman of the school's Department of Medicine and a past patient of Karl's. "Physicians who practice (at the Washington University Medical Center) must make a sacrifice—coming to conferences, going on rounds with students. That takes them away from their private practices. In exchange, they practice where the cutting edge of medicine is. So they have to read and study. It takes an unusually talented group of doctors to do that.

"He epitomizes that group."

Karl, now a professor of clinical medicine, says he takes pleasure in teaching, but also considers it a professional necessity.

"It's the best way to prolong your career in internal medicine. You're dealing with information that's kinetic, that changes from day to day. Unless you're in a milieu to keep up, most of us don't have the discipline to do it on our own.

"At 10:30 at night, it's nice to plop down to watch television, but if you're going to meet with students (the next morning), you get out your journals and organize your thoughts. You can't bluff people. You really have to put out."

Karl has not only studied his journals; he's found time to contribute to them—in all, 18 solo or co-authored articles and some two dozen clinicopathologic conferences delving into hepatology (Karl's said to have performed more liver biopsies

than any other physician in the country).

His commitment to both learning and teaching has impressed hundreds of fledgling physicians over the years. House officers at the medical center have consistently ranked him as one of the top attending physicians, says Kipnis. Danforth recalls Karl's influ-

your own or go into a nursing home," says Karl.

Working under the auspices of the Jewish Federation of St. Louis, Karl helped provide the hard-pressed elderly with other options—subsidized housing, Meals on Wheels and recreational programs, to name a few. His pioneering work in this field prompted President

"The physician should be the patient's advocate. He should be protecting him from machines, if you will."

ence when he came to Barnes Hospital as an intern in 1951.

"One of the great privileges I had while I was on the house staff was having coffee with Mike Karl in the morning and talking over patients and medicine," says Danforth. "I learned a tremendous amount."

Karl's generous spirit has extended to the entire St. Louis community. In the activist era of the 1960s, Karl tackled societal ills on all fronts. He and other physicians organized and operated a now-defunct medical clinic for the poor in an inner-city ghetto. Under his leadership as president of the Barnes Hospital Society, Barnes integrated its white and black wards.

The elderly also began to preoccupy Karl during the 1960s. He observed that in an increasingly mobile society, older people no longer could count on a son or daughter down the street to cook a meal or drive them to the hospital. "The options were to wing it on

Jimmy Carter to name Karl to a White House Conference on Families in 1978.

While many of Karl's causes are weighty, one activity uncorks his *joie de vivre*. Karl is a wine connoisseur and a long-standing member of a local tasters' club called In Vino Veritas, which translates, "In Wine There is Truth." He has combined this pastime with extensive world travels, accompanying French wine merchants on buying trips. He says he marvels at their ability to taste green wine and predict how it will taste five or 10 years later—an ironic comment for a physician who has loved sizing up the potential of green residents.

In the autumn of his career, Karl has reaped a bountiful harvest of acclaim. In 1983, anonymous donors endowed a professorship in endocrinology and medicine at the School of Medicine in honor of both Karl and his wife Irene, an authority on carbohydrate and muscle

metabolism. The local chapter of the National Conference of Christians and Jews gave him its Brotherhood/Sisterhood Award in 1985, the same year he was named teacher of the year at the School of Medicine. Last year he received a distinguished service award from the Washington University Medical Center Alumni Association.

The Claypoole award from the American College of Physicians is the latest of tributes, but Karl hasn't stopped in his tracks to count them. As director of clinical affairs in the Department of Medicine, he oils the relationship between the School of Medicine and Barnes Hospital—coordinating where residents work and sleep, finding beds for acutely ill patients and managing hospital-employed physicians who have finished their residencies at the medical center. At the same time, he continues to see patients in a consultative role, makes occasional house calls and, according to Irene, "gets telephone calls every single day from former patients who need help."

For those who listen, Karl also offers a seasoned and much-needed perspective on medicine in the age of laser surgery and multi-million-dollar diagnostic equipment.

"There's so much new technology that it's squeezing out the bedside approach to medicine and the personal relationship with patients. Instead of talking to patients, we're letting machines find out information.

"The physician should be the patient's advocate. He should be protecting him from machines, if you will."

The advice is vintage Karl. No wonder his phone is still ringing. ■

Dickinson to head alumni/development

Ruth C. Dickinson, formerly director of major and special gifts at the University of Chicago, has been appointed assistant vice chancellor and director of alumni and development programs for Washington University School of Medicine.

Dickinson replaces Mark W. Bates, who is now vice president for university relations at the University of Portland in Portland, Ore.

Dickinson directed the successful \$150 million Campaign for the Arts and Sciences at the University of Chicago, which surpassed its goal with \$151.7 million. During her 10 years there, she was also associated with campaigns for the Law School and the Business School and raised funds for the support of many other academic units.

Before she joined the University of Chicago in 1979, she was a senior policy analyst for the Office of the Governor in Topeka, Kansas; director of



Ruth C. Dickinson

public information from 1971 to 1976 at the Topeka State Psychiatric Hospital; and assistant project director from 1969 to 1971 at the Menninger Foundation.

A native of Kentucky, she received a bachelor's degree from the University of Chicago, where she was awarded the Student Achievement medal by the Alumni Association, and a master's of public administration from the University of Kansas, where she was chairman of the Student Faculty Advisory Board. ■

AOA initiates new members

Twelve medical students, three graduate trainees, one faculty member and one alum were inducted into the Washington University School of Medicine's chapter of the national medical honor society, Alpha Omega Alpha.

The new AOA members include Bruce Downton, M.D., assistant professor of pediatrics

and genetics; Garrett M. Brodeur, M.D. '75, associate professor of pediatrics; Adam J. Gerber; Robin S. Gossum; Anita J. Holtz; Robert M. Jasmer; Hamid R. Latifi; Peter A. Looby; Lyree N. Mikhail; Benjamin Movsas; William N. Peugh; Michael N. Polinsky; Thomas R. Vendegna; and Rebecca S. Wolfer. ■

Student scholarships established

The School of Medicine recently established a scholarship fund in memory of George H. Zografakis, M.D., assistant professor of clinical surgery, who died this past June.

As a young man of 19, Zografakis immigrated to the United States, where he worked hard to pay his own way through college and medical school. He greatly appreciated that same motivation in others and befriended many young people.

The George H. Zografakis Memorial Scholarship Fund is intended to provide tuition assistance to many motivated and deserving medical students in the years to come. It will require at least \$50,000 to establish this fund in perpetuity. People wishing to contribute should contact the Office of Medical Alumni and Development Programs, Campus Box 8049, 660 S. Euclid, St. Louis, Mo., 63110, or call (314) 362-8278. ■

Teachers of the year use prizes to enhance student learning

Last year the class of 1989 selected three faculty members to receive teacher of the year awards.

Steven Dresler, M.D., Ph.D., assistant professor of pathology, was chosen preclinical teacher of the year for his extraordinary devotion to students. Dresler was chosen after his tragic death of a heart attack.

As pathology coursemaster, he worked long hours revising the pathology course so that it would be more palatable to students. Money from Dresler's award is being used by the pathology department to buy books and provide travel for pathology student fellows.

Penelope Shackleford, M.D., associate professor of pediatrics in the division of infectious diseases, received the clinical teacher of the year award for 1989. In addition to teaching clinical pediatrics, Shackleford is president of the

School of Medicine's chapter of the national medical honor society, Alpha Omega Alpha, and invites at least one student to work in her lab each summer. Money from Shackleford's award has been placed into a special student teaching fund in the Department of Pediatrics.

Lawrence M. Kotner Jr., M.D., instructor in clinical radiology, received the Sydney S. Pearl, M.D. '32 Award for Inspirational Teaching. The award recognizes excellent teaching by voluntary, or part-time, faculty members. Kotner is the radiology coursemaster in charge of senior medical rotations. He says he enjoys being able to introduce different aspects of medicine to people while they are still learning and their minds are still open. The radiology department is using money from Kotner's award to purchase books for students. ■

Noted cardiologist and professor emeritus dies

Edward Massie, M.D., a noted cardiologist and emeritus professor of clinical medicine at the School of Medicine, died Feb. 5 at the age of 79.

"Dr. Massie was devoted to the Washington University Medical Center for more than 50 years," said Burton E. Sobel, M.D., the Tobias and Hortense Lewin Professor of Cardiovascular Diseases. "He is an internationally appreciated figure who by acclamation was an acknowledged member of an elite group of America's finest cardiologists, along with Paul W. White and Samuel A. Levine. His compassion for patients, dedication to teaching, commitment to scholarship and myriad contributions to cardiology and to our medical center are unrivaled."

Massie was a pioneer in using computers to interpret electrocardiograms. He also was instrumental in establishing the medical center's first coronary care unit and Jewish



Edward Massie, M.D.

Hospital's Heart Station, serving as its director as well as director of the one at Barnes.

Massie received his bachelor's and medical degrees from Washington University and joined the faculty at the School of Medicine in 1938.

He was well known for his fund-raising activities at the School of Medicine and in 1985 received an Alumni/Faculty Achievement Award from Washington University

Medical Center Alumni Association. An award for top cardiology students and a research endowment fund are established in his name, as well as an annual cardiology lecture.

A book Massie co-authored in 1951, "Clinical Scalar Electrocardiography," recently appeared in its eighth edition and has been translated into several languages.

Massie was a founding member of the Scientific Council of the American Heart Association, a former treasurer of the board of directors of the American College of Cardiology, and a fellow of the American College of Physicians.

He taught at the School of Medicine until 1980 and retired from medical practice in 1988.

He is survived by his wife, Felice Massie of Clayton; two sons, Henry Massie, M.D., and Barry Massie, M.D., both of San Francisco; a brother, Joel Massie of St. Louis; and three grandchildren. ■

William Seidler Jr., M.D. '43M, and his wife just completed a visit to Prague and East Germany with the Friendship Force. They were there just a few weeks before the "wall came tumbling down."

Bruce W. Armstrong, M.D. '44, had a coronary bypass in 1982. He is semi-retired, but has been practicing part time since 1984. He still writes about pulmonary and exercise physiology.

Marvin T. Pursell, M.D. '44, had a triple bypass operation during the summer of 1987 and retired postoperatively. He has seven children and six grandchildren, the last of whom was born in September. He writes that Newport Beach, Calif., is a great place to live.

James C. Folsom, M.D. '46, received the St. Louis Geriatrics Research Education Clinical Center Commendation for 1989. Folsom pioneered the use of reality and attitude therapy, which has led to high quality care for large numbers of older veterans. Most recently he developed an outstanding extended care program at the Colmery-O'Neal VA Medical Center, which included an exemplary unit for patients with Alzheimer's Disease.

Frank B. Norbury, M.D. '48, retired from his practice of internal medicine in July of last year. He continues to do part-time work for State of Illinois agencies.

Leonard Berg, M.D. '49, professor of neurology and director of the Alzheimer's Disease Research Center at the School of Medicine, was recently elected to the board of directors of the Alzheimer's Association and vice-chairman of its medical scientific advisory board. He also parti-

CLASS NOTES

'20s

Thomas M. Boulware, M.D. '26, now clinical emeritus professor of obstetrics and gynecology at the University of Alabama, delivered 23,000 babies over the course of his career.

'30s and '40s

Paul Kunkel, M.D. '34, retired from patient care this past October.

John L. Horner, M.D. '36, moved into a Villa Estates Retirement condo last September. He stays active by running two piano programs with his brother, Frederic. Horner also needlepoints and participates in Bible study groups.

David Feldman, M.D. '43M, was one of nine physi-

cians to receive a Physician's Recognition Award from the Missouri State Medical Association and the American Medical Association. The award recognizes the completion of 150 credit hours of continuing medical education within a three year period.

Edward H. Kowert, M.D. '43D, has been looking in on Mildred Trotter, M.D., at the Bethesda Dilworth Nursing Home. He encourages classmates to drop her a note. The address is 9645 Big Bend Blvd., St. Louis, Mo., 63122.

icipated in a meeting at the National Institute on Aging, which covered therapeutic strategies in treating Alzheimer's Disease.

'50s and '60s

Robert Allbaugh, M.D. '52, provides overseas consulting for Bechtel Group, Kennecott Corp. and other multinational companies. He also lectures and is on the clinical faculty at the UCSF School of Medicine.

Brent M. Parker, M.D. '52, became professor emeritus of medicine at the University of Missouri this past September. The school established a professorship of medicine in his honor.

George Oliver, M.D. '52, from Farmington, Mo., was elected first vice president of the Western Surgical Association last November.

Cooper D. Ray, M.D. '54, retired June 30 and moved to "the farm" in Martha, Okla.

Laurence Crocker, M.D. '55, is a specialist in internal medicine at Physicians Plus Madison Internal Medicine Associates. He is also a self-taught banjo player and a rose gardener. He and his wife, Pat, have three sons.

Charles W. Markham, M.D. '55, continues to specialize in cytopathology with emphasis on prostate fine-needle biopsies. Part of his work was published last December in a supplemental issue of Urology.

Michael B. Gass, M.D. '58, works at the University of California-Davis' student health center as a dermatologist. He and his wife, Carol, have six daughters in their

combined family. Gass is also an assistant clinical professor in dermatology at University of California at Davis. "I keep hoping to see Ollie Biederman," he writes.

Jerome F. Levy, M.D. '58, is publishing his first book this April. It's a complete guide titled, "Your Breasts."

William H. Gondring, M.D. '62, was recently elected president of the Buchanan County Medical Society. He was also re-elected chief of surgery at Heartland Hospital Systems, East and West, in St. Joseph, Mo. He has been practicing orthopedics there for 14 years.

Bruce I. White, M.D. '64, was one of nine physicians to receive a Physician Recognition Award from the Missouri State Medical Association and the American Medical Association. The award is given upon completion of 150 credit hours of continuing medical education within a period of three years.

Harold Kanagawa, M.D. '65, a Jefferson City cardiologist, has been named a fellow of the American College of Cardiology. Kanagawa has assisted St. Mary's Health Center in expanding nonsurgical and surgical cardiac technology, and has been instrumental in developing that hospital's cardiac catheterization lab.

Morris Pulliam, M.D. '66, was appointed chairman of neurosurgery at the National Naval Medical Center in Bethesda, Md.

Kevin B. Schaberg, M.D. '66, has returned to Barnes and St. Luke's hospitals in St. Louis after practicing obstetrics and gynecology in Seattle for 14 years.

Gary Rachelefsky, M.D. '67, and his wife, Gail, have



Dixie J. Anderson, M.D. '71, shows freshman medical student Michele Francoeur a CT scanner. Anderson and Francoeur are participants in this year's alumni-freshman visitation program in which all first-year students have the opportunity to spend a day with a local alum.

been married for 23 years and have three daughters. Rachelefsky practices allergy and immunology with a heavy emphasis on clinical research and teaching at UCLA.

Ira J. Kodner, M.D. '67, was one of nine physicians to receive the Missouri State Medical Association and American Medical Association's Physician Recognition Award for completing 150 credit hours of continuing medical education in three years.

Wallace B. Mendelson, M.D. '69, has received the Lady Davis Visiting Professorship Award to teach at the Technion Institute in Haifa, Israel for the spring semester.

'70s and '80s

John Gollhofer, M.D. '72, moved to Spokane, Wash., to start a department of obstetrics and gynecology at the Rockwood Clinic.

Roslyn Yomtovian, M.D. '74, gave birth to her fourth daughter on Sept. 28, 1989.

James M. Hudson, M.D. '75, has been inducted as a fellow into the American College of Surgeons.

John S. Cantier, M.D. '76, was elected president of the Wisconsin Dermatological Society for 1990. Six years after adopting infant twins from Korea, his wife, Katy, was expecting a child in December.

Wendy Eider, M.D. '76, and her husband, **Barry Bernfeld, M.D. '77**, settled into their respective practices of rheumatology and general surgery. They now have three children, Jessica, 7; Sean, 3; and Lynsey, 1.

Stephen G. Jolley, M.D. '76, was appointed co-surgeon and chief at the newly formed Humana Children's Hospital in Las Vegas. He is also the chairman of the division of general and thoracic pediatric surgery for the Children's Hospital. Jolley has been practicing pediatric surgery in Las Vegas

for the past four years, and currently holds an appointment to the clinical faculty of the University of Nevada School of Medicine.

Clifford B. Saper, M.D. '77, is the William D. Mabie Professor of Neurology and Neuroscience at the University of Chicago. His wife was expecting their third child this past winter.

Nicholas Couper, M.D. '78, writes that since the ten year reunion, he, his wife and daughter moved from Columbia, Mo., to Greenville, N.C., then back again to Columbia. He is now with a private group at Boone Hospital Center.

Myron Tanenbaum, M.D. '81, has an oculoplastic surgery practice in Miami, Fla. His wife, Monica, works as a neonatologist at the University of Miami School of Medicine. In their spare time, they keep busy with children, Geoffrey and Laura.

Linda O. Douglas, M.D. '82, completed her fellowship in adolescent medicine. Now she is in family practice in Oak Forest, Ill. She is also a part-time faculty member at Rush-Presbyterian-St. Lukes and a resident at Christ Hospital. She has one child, Karen.

Brian Scanlan, M.D. '83, and his wife, Laura, had their second child, Ryan Edward, on June 1, 1989. Mom, dad, Ryan and sister, Kathryn, live in Tinley Park, Ill.

Robert M. Jarka, M.D. '85, finished his residency at the University of California at Davis last July. He now works as an anesthesiologist in Placerville Calif., about an hour west of Lake Tahoe. He retains his clinical staff privileges at U.C. Davis, where he works on his days off from private practice.

Regina A. Kreisle, M.D. '85, was appointed assistant professor of experimental medicine in the department of pathobiology at Purdue University. She is also a member of the Purdue Cancer Center, working in the area of tumor biology and aging.

Karen Mathews, M.D. '85, is a board-certified family physician serving active duty in the U.S. Air Force at Clark Air Base in the Philippines.

Pejman Salimpour, M.D. '87, was voted intern of the year in the department of pediatrics at UCLA. Next year he will join his father's private practice in Encino, Calif.

FORMER HOUSE STAFF NOTES

Last December **Thomas Flynn, M.D., FHS in hematology**, performed the first autologous bone marrow transplant ever done at Abbot Northwestern Hospital in Hibbing, Minn.

Robert J. Sokol, M.D., FHS in obstetrics and gynecology, formerly professor, chairman and chief of obstetrics and gynecology at Wayne State University School of Medicine, is currently dean of that school and chairman of the medical board at the Detroit Medical Center.

Leo Whiteside, M.D., FHS in surgery, recently traveled to Tokyo, Kyoto and Kobe, Japan, to teach orthopedic surgeons and medical faculty about his technique for total knee replacements. Last January, he introduced his knee replacement to the Soviet Union.

Alumni Reunion 1990

May 3, 4, 5

Class of 35, 40, 45, 50, 55, 60, 65,
70, 75, 80

O T H E R

Barry D. Herzog, HA '76, has been administrator of Fayetteville Diagnostic Clinic, Ltd. since 1984. Last year he was chairman of Fayetteville's chamber of commerce, and he is a candidate for fellowship in the American College of Group Practice Administrators.

Harper S. Jackson, HA '79, was appointed senior vice president for patient services at the Methodist Hospital in Houston, Texas. Prior to his new appointment, Jackson served as senior vice president for support services at the same institution.

Mark Boles, HA '83, has been named vice president of administration at Mobile Infirmary Medical Center. Boles was formerly vice president of Rotary Rehabilitation Hospital.

Margaret Winters, NU '53, spent six weeks in Alaska with her husband, Paul, last summer. They drove the Alaska Highway both ways in their motor home, and flew to Point Barrow, Pudhoe Bay, Kotzebue and Nome. She writes that retirement is great for both of them.

Laura J. Bell, NU '62, retired from VAMC. She is active in her church and nursing associations MONA and MLN. She is a district representative for AFS Intercultural Programs and on the board of

Overland Historical Society. Bell has been listed in the new edition of "Who's Who in the Midwest" and will appear in the second edition of "2000 Notable American Women."

Geneva Newman, NU '69, was widowed in 1976. She earned her master's degree in nursing in 1978 from the University of Evansville in Indiana, and retired in 1986. Her hobbies include travel and collecting antique novels. She has two children, two grandchildren and one great granddaughter.

Laura A. Vann, OT '50, is working in the hospice program for the VNA and is chairman of the Oregon Occupational Therapy Licensing Board.

Joyce K. Porter, OT '50, received a bachelor's degree in fine arts at Boston University in 1983. She is now exhibiting sculpture and enjoying four grandchildren.

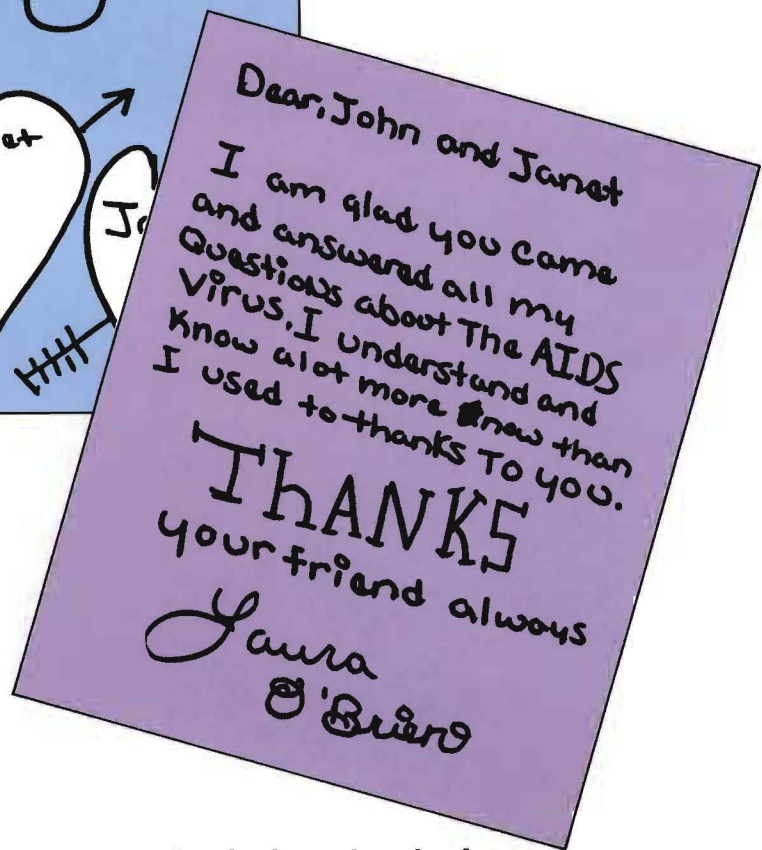
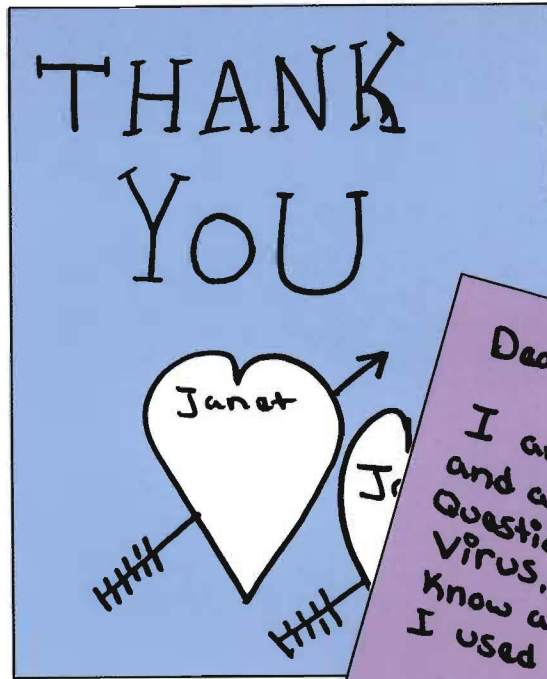
IN MEMORIAM

Louis K. Beasley, M.D. '39, died Aug. 21, 1989.

Merril C. Davenport, M.D. '36, died Oct. 27, 1989.

Frank Hereford Kidd Jr., M.D., FHS in surgery, died Feb. 8, 1988

Paul E. Siebert, M.D. '52, died Nov. 22, 1989.



Medical students get a big thank-you from local seventh-graders for teaching them more about AIDS.

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Magnolias blossom in Hudlin Park across from Barnes Hospital.