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The Department of Cell Biology and Physiology saluted two of its most eminent personages on Thursday and Friday, October 22 and 23, 1992. Carlton Cuyler “Cuy” Hunt, Ph.D., (left) and Albert Roos, Ph.D., were honored with a symposium that featured presentations by Paul DeWeer, Mordecai Blaustein, Denis Baylor and others, and the Erlanger/Gasser Lecture by Nobelist Bert Sakmann. Hunt, who trained at Cornell, is renowned for having built three excellent physiology departments and for having trained many of the nation’s most prominent physiology department chairpersons. He also is known for his research into muscle spindles, the small bodies inside muscles that regulate fine control. Roos recently terminated the National Institutes of Health grant that had funded his lab without interruption since 1948, making it the longest running grant on record. His work investigating intracellular pH and cells of the carotid body that signal the brain to control respiration is internationally recognized. “He has been a leader in his department, a leader in his field, and a mentor to younger faculty,” says department head Philip D. Stahl, Ph.D.
One Giant Step

One mechanism by which critical cells in the pancreas are killed sets a new direction for diabetes research.

The New Cartographers

The human genome is no longer uncharted territory — the initiative to map it is working.

Improving Life’s Quality

Researchers investigate a drug that alleviates the pain of bone cancer.

Good Data

Taking part in a study of the vestibular system, the writer recounts his experiences and his small contribution.

Newsbriefs

Student Stage

Silhouette: C. Barber Mueller, M.D.

Alumni Report
Alumnus Receives Nobel Prize

Edwin G. Krebs, M.D., a 1943 graduate of the School of Medicine, received the Nobel Prize in Medicine on October 12, 1992, for his research into a regulatory mechanism that is known to "concern almost all processes important to life," according to an announcement by the Karolinska Institute in Stockholm, Sweden.

The biochemical process, first discovered in the mid-1950s, involves the class of enzymes — protein kinases — that activate and deactivate cellular activity, regulating cell metabolism. By speeding up the chemical bonding of phosphorus to proteins, kinases act as what has been called the "life switch" that turns off and on many biological functions in a cell. Those functions include inflammatory reactions and the breakdown of glycogen into glucose, among many others.

Krebs' studies — and research based on his work but conducted by other scientists — have had an impact on investigations into subjects as diverse as transplantation, endocrinology, cancer, growth and development and the immune response.

In addition to being a graduate of the medical school, Krebs, now 74, completed a research fellowship in the school's biological chemistry department and served his residency in internal medicine at Barnes Hospital.

While a student, resident and research fellow in St. Louis, Krebs worked under and was influenced by Washington University's Carl and Gerty Cori, noted biochemists who themselves received the Nobel Prize. The Cori lab has now spawned eight Nobelists: Krebs, Earl Sutherland, Christian De Duve, Luis Leloir, Arthur Kornberg, Severo Ochoa and the Coris.

For more than a decade, the Cori lab received recognition for its ground-breaking research that helped launch the golden age of biochemistry. Krebs shares the Nobel Prize with Edmond H. Fischer, M.D. The two have worked together for almost 40 years at the University of Washington in Seattle.

Krebs has maintained his relationship with Washington University School of Medicine through the years. He is a member of the Eliot Society and has received awards including the university's Distinguished Alumni Award in 1972 and the medical school's Alumni Achievement Award in 1988.

Help Where It's Needed

Acting on referrals from building managers, family members, neighbors and clinic physicians, the medical school's Memory and Aging Project Satellite is reaching out into the community to help those with Alzheimer's disease or other forms of dementia who otherwise would receive no help. Since they began in June, the workers have identified and assisted 43 people, none of whom had been diagnosed previously.

According to project director Dorothy Edwards, Ph.D., the team that goes out into the community is funded by a Congressional appropriation designed to extend the effectiveness of 18 of the nation's Alzheimer's Disease Research Centers, including the one here. The funding is not for research, but for delivery of what has been learned and for addressing the needs of minority and medically underserved adults — those isolated or disconnected from the system.

The outreach program is operated through the medical...
school’s Program in Occupational Therapy, in collaboration with St. Louis Regional Medical Center, the city’s Department of Health and the St. Louis Area Agency on Aging.

The team has three core members, two social workers and a nurse trained by Leonard Berg, M.D., and John Morris, M.D., of the Alzheimer’s Disease Research Center (ADRC). After making an appointment with an individual referred to them, team members do an on-site screening, take a social history and check on the client’s status with Medicaid and other healthcare delivery systems. “Eighty percent of the people we’ve seen have been Medicaid eligible but not Medicaid certified,” Edwards says.

The direct approach taken by the satellite effort has shown its advantages. Edwards believes that the intervention of the team already has saved at least two lives, including that of a woman, isolated from the system, who was found in her dwelling, starving.

Alzheimer’s Link Sought

Researchers at the School of Medicine are investigating how driving performance changes with time and age and how Alzheimer’s disease may affect driving ability.

The study’s principal investigator, John Morris, M.D., associate professor of neurology, and coprincipal investigator, Linda Hunt, instructor of occupational therapy, say their research will help determine when patients with Alzheimer’s disease should stop driving. It also will provide useful information for establishing public policy regarding driving competency and license-renewal intervals for the elderly.

“Often, the elderly and their families are uncertain whether driving is impaired and whether driving privileges should be relinquished,” says Hunt. “This study will help families with the decision process.”

The study, funded by the National Institute on Aging, will evaluate healthy elderly drivers as well as drivers with very mild senile dementia of the Alzheimer type (SDAT) and those with mild SDAT.

Each study participant will take a series of tests to evaluate memory and cognitive function and be asked questions about how they perceive their driving ability. In addition, they will complete a one-hour road test and undergo a series of neurological, visual and motor control tests at the School of Medicine’s Alzheimer’s Disease Research Center. Skills such as maintaining vigilance, switching attention and paying attention to multiple activities will be measured.

University Hosts First Debate

With the world watching, the first nationally televised, three-person presidential debate in U.S. history was held on the Washington University campus on Sunday evening, October 11.

In a week-long flurry of activity, university staff members prepared the Athletic Complex’s Field House, transforming it from a basketball court surrounded by bleachers into a debate hall. Four network platforms were constructed at one end of the court, opposite the huge set that had been built in New York, dismantled, then trucked to St. Louis for the event.

Approximately 1,000 members of the media received credentials for the debate that was broadcast to what producers estimated to be the largest non-sports viewing audience ever. Only about 1,200 people — half of them members of the press — were accommodated in the debate hall. Among the total were 250 Washington University students, 140 of them seated on the floor of the hall and the others admitted to the press balcony.

The event’s producer, Ed Fouhy, referred to the first debate as perhaps “the most important 90 minutes of the campaign.” Fouhy later said that all preparations had paid off and that the program had gone off perfectly.

Even at that stage of the campaign, few people outside strictly partisan circles were willing to proclaim a winner of the debate; each of

Short-term memory—the ability to recall a phone number or name for a short period of time as needed—works best when people silently rehearse the information instead of trying to remember what the words or numbers look like, say researchers here.

Recent research into reading disabilities like developmental dyslexia emphasizes the importance of recoding visual information into a speech-based representation. These findings on short-term memory may have practical applications as scientists learn more about how the brain contributes to dyslexia, says Steven E. Petersen, Ph.D.

Petersen used positron emission tomography (PET) to measure changes in the cerebral blood flow of 12 volunteers as they performed either a memory task or a fixation task. For the memory task, volunteers were presented with five words on a computer screen, one at a time, prior to the start of the scan. Each person was instructed to try to remember the five words during the 40-second scan while staring at a small cross on the computer screen. At the end of the 40-second scan, the volunteers were asked to recite all the words they could remember.

To ensure that the PET scanner measured brain activity related solely to the memory task, the scan did not include reading the five words and reciting the words aloud. Subjects also were asked to stare at a small cross in the center of the computer screen during scanning to help control extraneous brain activity. After the memory task, control images were made as volunteers were scanned while staring at a fixation cross. “When the brain activity from the fixation is subtracted away, we see the parts of the brain that change in activity when the subject tries to hold words in memory,” Petersen says.

The memory–fixation task activated a right frontal area and two motor areas, medial supplementary motor cortex (SMA) and left premotor cortex.

Increased activity in the first two motor areas and decreased activity in an area responsible for mouth movements suggest that subjects used a silent, internal articulatory strategy to remember the words, Petersen says.

In a second study, Petersen’s group scanned subjects performing the same memory task as they tried to remember pretend words that followed the spelling rules of English, like “loop.” The task activated the same areas that were activated for memory of real words, but there also was activation of an area responsible for attention, the medial anterior cingulate.

Petersen separated the subjects into two groups based on their performance in the nonword task: good performers and bad performers.

Those who performed poorly showed increased activity in the visual cortex. Good performers showed increased activity in the left premotor area. “These results suggest that poor performers used a visual strategy in addition to an articulatory rehearsal strategy to remember the items,” Petersen says. “We believe that people who use only an articulatory strategy to temporarily remember information will be more successful.”

Medoff, Simchowitz Fill New Positions

Gerald Medoff, M.D., and Louis Simchowitz, M.D., have been chosen to fill two new positions in the Department of Internal Medicine. Medoff, professor of medicine and molecular microbiology, has been named vice chairman for clinical affairs; Simchowitz, professor of medicine and of cell biology and physiology, has been named vice chairman for research affairs.

The appointments were announced by John P. Atkinson, M.D., professor of medicine and molecular microbiology. Atkinson became chairman of the Department of Internal Medicine on October 1. More vice chairs will be named in the coming months, he says.
In his new post, Medoff will manage clinical affairs in the department, fostering a closer working relationship with Barnes Hospital. “Our goal is to improve ambulatory services to patients and to utilize the ambulatory care setting more efficiently in the teaching program in medicine. We also will try to expand clinical research in the department, which will have direct applicability to improving patient care,” Medoff says. An important goal of these new programs will be to train more physicians with an interest in primary care and in clinical research, he says.

As vice chair, Medoff will continue his past involvement in the quality assurance program at Barnes Hospital. He has served as chairman of the hospital’s infection control committee since 1981. In addition, he will conduct research on clinical infectious disease and will remain co-director of the division of infectious disease.

Simechowitz will coordinate research activities within the department. “One of my goals is to foster interactions among the medical subspecialties in the Department of Medicine and with other basic science departments throughout the university,” he says. His responsibilities include initiating and developing new research initiatives in the form of center grants, specialized centers and program projects in areas such as aging, cancer and genetics.

Simechowitz will organize efforts to take better advantage of funding opportunities from private foundations and pharmaceutical companies, with the aim of helping to support research by young faculty members. He intends to play an active role in assessing space and equipment needs of the department and will participate in recruiting activities.

Simechowitz plans to continue his research aimed at understanding the physiologic function of human neutrophils, blood cells that are important in inflammation. His work has focused on the role of intracellular pH and calcium ion movement in neutrophil activation. In addition, Simechowitz has worked with pharmaceutical companies to explore new leads for developing anti-inflammatory drugs.

Frisse Named Library Director

Mark E. Frisse, M.D., has been named associate dean for academic information management and director of the Washington University School of Medicine Library and Biomedical Communications Center.

He replaces Susan Crawford, Ph.D., who stepped down after serving for 11 years as director of the library and biomedical communications center. Frisse’s appointment as associate dean for academic information management is a new position.

“Under Dr. Crawford’s leadership, our library and biomedical communications center has become one of the finest,” says William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine. “It is fitting that we have been able to attract someone with Dr. Frisse’s outstanding credentials to succeed Dr. Crawford. Dr. Frisse has a truly unique combination of talents — a first class clinician, teacher, and computer and informatics scientist. Our medical library will be well positioned to develop and incorporate the most modern information and communication services.”

Frisse’s responsibilities as director and associate dean include coordinating medical center communications networks and information management facilities and overseeing medical computing facilities. He also is involved with information management systems planning throughout the medical center. For the past two years, he has been director of the division of medical informatics in the Department of Internal Medicine.

Frisse and his colleagues develop and evaluate biomedical information systems. During the past four years, he has developed a number of techniques to facilitate the construction and use of large volumes of online technical material. His most recent work in this area includes the development of an electronic library system and a method to classify user information needs.
Gado Honored By Peers

Mokhtar H. Gado, M.D., has been named as a fellow of the American College of Radiology (ACR). The announcement was made during the ACR annual meeting held September 12-16, 1992, in Phoenix, AZ.

Mokhtar H. Gado, M.D.

Selected for his outstanding contributions to the field of radiology, Gado was named as one of 144 new fellows by the college's board of chancellors.

Fellowships in the college are awarded to members for significant scientific or clinical research in the field of radiology or significant contributions to its literature. Criteria for selection also include performance of outstanding service as a teacher of radiology, service to organized medicine and an outstanding reputation among colleagues and the local community as a result of long-term superior service.

ACR is a national organization serving some 28,000 radiologists, radiation oncologists and radiological physicists, with programs focusing on the practice of radiology and the delivery of comprehensive radiological health services.

$1.9 Million Funds Heart Disease Study

The School of Medicine has received a $1.9 million contract from the National Institutes of Health (NIH) to coordinate a multi-center study of heart disease in nearly 15,000 families. The study is designed to help explain how a person's genes and family environment work together to cause heart disease, the nation's number one killer. It will be the first research to examine both factors together comprehensively in such a large group.

The four-year contract, from the NIH's National Heart, Lung and Blood Institute, is part of an $11 million collaboration among five universities. Washington University will coordinate the study and analyze data gathered by investigators at the four field centers located at Boston University, the University of Utah, the University of North Carolina at Chapel Hill and the University of Minnesota. Co-principal investigators Dabeeru C. Rao, Ph.D., professor and director of the division of biostatistics, and Michael A. Province, Ph.D., assistant professor of biostatistics, will lead the St. Louis team.

In the past, most heart disease studies have focused on the roles of genes and lifestyle separately, says Province. But, "If you want to understand why it is that heart disease tends to cluster in families, you need to study genetics and environment together. In reality, heart disease is a very complex combination of both," he says.

The St. Louis team will look at family relationships to determine whether similarities among family members are due to shared genes, shared habits or both, Province says. For example, because identical twins have the same genetic material, any physical differences between them must be due to their environment; on the other hand, adopted family members share an environment, but not genes, he explains.

Researchers will keep blood samples to create a storehouse of genetic information. Geneticists will use the storehouse to evaluate newly identified genes that might be important to heart disease, Province says.

SMA Grants Scholarships

In 1992, for the twenty-second consecutive year, students at Washington University School of Medicine have benefited from scholarships granted by the Southern Medical Association (SMA).

The SMA, a regional organization committed to bringing physicians together by providing for their professional and personal needs, this year provided three scholarships for medical school students, the maximum number allowed for any one school.

First-year students Adam C. Eaton, of Missouri, Dione A. Skeete, of Florida, and Catherine J. Stocklin, of Texas, each received a $500 scholarship to help defray the cost of tuition. Application is made by the assistant dean for student affairs on behalf of students with superior abilities who will benefit from tuition assistance.

Washington University School of Medicine students have been fortunate to receive scholarships from the SMA each year since the program began in 1970, and each year the maximum allowable number of students has been named. According to John F. Walters, assistant dean for student affairs, a total of 36 students has now received SMA scholarships, and the aggregate of the support is now $20,000.
Tongue Replacement Surgery Serves Oral Cancer Patients

The surgical "cure" for cancer of the tongue, called a glossectomy, often costs patients their ability to speak and eat, but a new technique pioneered by surgeons at the medical school is changing that.

In patients studied to date, the surgeon-researchers have replaced cancerous tongues with skin and muscle flaps harvested from the back. Bruce Haughey, M.B., Ch.B., assistant professor of otolaryngology and director of otolaryngology at Jewish Hospital, says the surgical technique holds great promise as a treatment for oral cancer patients.

One case involved a 13-hour operation at Barnes Hospital during which doctors removed the diseased tongue, floor of the mouth, nodules on the neck, and a piece of the patient's lower jaw. They then harvested a flap of skin and muscle from near the left shoulder blade, crafted it into the shape of a tongue, connected the blood vessels and nerves, and sewed it into the mouth.

"We've done a fair number of patients with this technique, and the tissue transfer has worked very well," Haughey says. "We harvest the tissue from a donor muscle called the latissimus dorsi. That's a muscle with skin overlying it as well as associated vessels and motor nerves."

The choice of the latissimus dorsi flap is what makes this procedure unique, says John Fredrickson, M.D., Lindburg Professor and head of the Department of Otolaryngology. "We need sufficient bulk from the tissue. It must fill a large void in the mouth. The flap also must have a muscle to replace the tongue muscle, a nerve that can be joined to the tongue nerve and a good artery and vein so the tissue can be revascularized. This flap meets all of those criteria."

Speech pathologist Dennis Fuller, Ph.D., assistant professor of otolaryngology, rehabilitates patients whose tongues have been replaced. He estimates their intelligibility of speech at better than 85 percent following surgery. Several can talk on the phone, and some have returned to work.

As important as speech and articulation are to survivors of oral cancer, talking is only half of the equation. As Haughey says, "Not long ago the method of treatment was to remove the cancer and just sew up the patient — leave them with nothing there. Anything we can accomplish with this new technique is a vast improvement because without a tongue, not only can people not speak, they can't swallow. That means they have to be fitted with feeding tubes for the rest of their lives."

The success rate for the tongue replacement grafts is more than 80 percent, with the only failures coming very early in the series.

Fredrickson and Haughey look forward to the possibility of tongue transplantation in the future. Nerve and vascular graft techniques could make it possible for tongues transplanted from cadavers to restore not only speech and swallowing but also tactile sensation. First, however, researchers must overcome problems with tissue rejection, since cancer patients often are not good candidates for the immunosuppressive medications given to prevent rejection of transplanted tissue.

Stanley J. Korsmeyer, M.D., has been named chief of the newly formed division of molecular oncology sponsored by the Departments of Internal Medicine and Pathology at the School of Medicine.

Stanley J. Korsmeyer, M.D.

The appointment was announced by John P. Atkinson, M.D., chairman of the Department of Pathology. As chief, Korsmeyer will be responsible for further developing a research program in cancer biology in those departments.

Molecular oncology is one of two divisions created in the Department of Medicine as an expansion of hematology and oncology programs. Atkinson, Korsmeyer and Timothy Ley, M.D., associate professor of medicine and genetics, will head an effort to choose a clinical chief for the second division, medical oncology.

Korsmeyer plans to continue his research aimed at understanding how genetic abnormalities lead to various forms of leukemia and lymphoma. His work focuses on the role genes play in early development of the immune system's T cells and B cells.
It might be viral. Perhaps environmental or dietary factors play a role. The cause is still shrouded in mystery, but somehow, a pathogen finds its way into the pancreas — the hammer-shaped cluster of tissue responsible for many digestive functions. The pathogen locates a particular spot — a knot of fibers and blood vessels marked by small tubes and pit-like indentations. Called the islet of Langerhans, this bundle of granular endocrine cells is the part of the pancreas that produces insulin, the protein that allows the body to digest and process sugar.
The pathogen might bind to cells within the islet, but perhaps it simply waits. It has not invaded unnoticed. The body’s immune system dispatches its forces and attacks. The first combatants in the fight are the activated macrophages, cells that protect the body against infection. Trouble is, they also can initiate a process that kills some of the most important cells in the islet, the beta (β) cells that secrete insulin. The activated macrophages set in motion a process that eventually results in juvenile, or Type I diabetes.

Exactly what causes the process to begin is unknown. Various possibilities have been considered, from infection to cow’s milk, but in the laboratory of Michael McDaniel, Ph.D., investigators are studying what happens after that triggering event has taken place. McDaniel and his colleagues recently identified what they believe may be the cellular mechanism that apparently disables and then kills β cells. They also have some ideas about how to inhibit that mechanism. A compound called aminoguanidine can stop and, in some cases, reverse the process of β cell death once it begins.

McDaniel, professor of pathology, and John Corbett, Ph.D., post-doctoral fellow in pathology, are at the forefront of an effort to identify the substance that targets and selectively kills islet β cells. That effector molecule appears to be nitric oxide.

“That’s nitric oxide, not nitrous oxide,” McDaniel patiently points out. Nitric oxide is a highly reactive molecule comprising a single atom of nitrogen and a single atom of oxygen. Nitrous oxide, on the other hand, has two nitrogen atoms. The latter chemical, commonly called laughing gas, can be breathed for long periods of time with little lasting effect; small amounts of nitric oxide can be lethal.

Nitric oxide is a highly reactive molecule. Nitrogen atoms have seven electrons, oxygen eight. That leaves an unpaired electron. Because electrons tend to form pairs, nitric oxide reacts rapidly. As a result, it usually disappears from the system quickly. The molecule plays a key role in neuronal communications and blood pressure regulation. It also appears to be an agent used by immune cells to destroy pathogens. Until recently there was no way to demonstrate the presence of a highly reactive molecule like nitric oxide in the body.

In 1986, McDaniel heard Danish researcher Jorn Nerup speak at a meeting of the American Diabetes Association. Nerup proposed cytokines — substances such as interleukin-1 (IL-1), interferon and tumor necrosis factor — as major culprits in the course of Type I diabetes. McDaniel’s lab soon focused its research on the role of cytokines and on IL-1 in particular.

“We knew that IL-1 was inducing a new protein in the islet. We just didn’t know what that protein was,” McDaniel says. He also knew that islets treated with IL-1 did not secrete insulin as well as untreated islet cells. Though he could prove the bad effects of IL-1 were mediated by a protein or proteins, finding the protein took another few years.
In 1990, when John Corbett joined the lab as a trainee, the research took its next step. "We didn't have an idea of what protein was involved," McDaniel recalls. "John proposed we look at nitric oxide synthase."

Nitric oxide synthase is a protein, the sole purpose of which is the production of nitric oxide. Research in 1990 had shown nitric oxide could produce effects on target cells similar to those caused by IL-1 on the β cell, so Corbett and McDaniel began there. Because of its high reactivity, nitric oxide is hard to find in its free radical form, so the investigators attempted to locate the protein instead. They also looked for the byproducts of nitric oxide production.

Because they knew IL-1 inhibited insulin secretion and ultimately destroyed β cells and suspected that nitric oxide synthase was the protein involved, McDaniel and Corbett treated their cultures with both IL-1 and with compounds that block the pathway through which nitric oxide is released as a free radical.

The best-known inhibitor of nitric oxide is N-monomethylarginine (NMMA). When they treated rat islet cells with NMMA and IL-1, the cells continued to secrete insulin normally. Without NMMA, insulin secretion slowed, and the cells eventually died.

"I think it's pretty well established that the macrophage is a source of nitric oxide, but if the macrophage continues producing high levels of nitric oxide, and if nitric oxide is freely permeating all cell membranes, it's going to diffuse into every cell in the proximity," Corbett explains.

That would result, he says, in the death of other cells in the islet. Instead, their data show that after a short pulse of nitric oxide from exposure to IL-1, the β cells themselves take over. Says McDaniel, "Nitric oxide is either specific because the β cell is more susceptible (and that's possible), or because the β cell can produce nitric oxide and selectively destroy itself."

Therapies require that the production of nitric oxide be shut off in the pancreas without shutting it off in other parts of the body. It turns out that is possible because nitric oxide synthase comes in two isoforms. They are called the inducible and the constitutive isoforms. The constitutive isoform of the protein manufactures low levels of nitric oxide for blood pressure control. It is the inducible isoform that is produced by macrophages and other immune cells.

The constitutive isoform is always there in certain cells. The inducible isoform, as the name suggests, is not expressed unless a cell is exposed to the appropriate cytokine. "The β cell is capable of expressing the inducible isoform of nitric oxide synthase," McDaniel says. "That means if you can block the inducible isoform and ignore the constitutive, you can stop the mechanism of diabetes without creating problems elsewhere."

That is exactly what McDaniel and Corbett have done. They discovered, working with Joseph R. Williamson, M.D., and Ronald G. Tilton, Ph.D., that...
The top figure shows the process within a cell as nitric oxide interacts with iron sulfur centers of iron containing enzymes. A stable complex that can be observed by e.p.r. is the result. The formation of these complexes is shown in the lower panel. Treatment of islets with IL-1 results in the generation of nitric oxide complexes highlighted here. NMMA prevents the formation of this complex.

The process of β cell destruction goes on for a while,” Corbett says. “You may lose 40 percent of your β cells but see no effects on blood sugar. The key is to provide therapy before the process of Type 1 diabetes has measurable effects, halt it, and perhaps even reverse it.”

In early experiments, McDaniel and Corbett have used aminoguanidine to successfully halt the process of β cell death. They have tested aminoguanidine in a rat model, a mouse model and in human islet cells. It does the same thing in all of those experiments.

Data from trials suggest that aminoguanidine can be given to people safely. But there is no data on whether aminoguanidine works in people the same way it works in McDaniel’s lab, and it could be several years before it is used in clinical trials to test its ability to stop β cell death. McDaniel and Corbett have shown that it works, but it may be years before scientists understand why.

Both McDaniel and Corbett believe that questions requiring answers prior to clinical trials deal more with the timing of therapies. “There are various predictors that people are studying. They’re looking for the presence of insulin antibodies, islet cell antibodies, that are thought to provide some evidence that a person may be developing Type 1 diabetes. We need to clarify what those indicators are, and that will give us a better idea of when to give aminoguanidine to treat people who are developing diabetes,” McDaniel says.

In recent experiments, Corbett and McDaniel have used electron paramagnetic resonance (e.p.r.) spectroscopy to demonstrate the presence of nitric oxide in the cells. Earlier research predicted the presence of nitric oxide by locating the building blocks of the free radical and then finding its after-effects. The e.p.r. images allow the investigators to look at the molecule during the few seconds of its brief life.

“The e.p.r. image is our direct evidence for the presence of nitric oxide,” McDaniel says. With e.p.r., the investigators no longer have to operate on assumptions. A detective who sees shoes and a full ashtray might assume a person has been in the room, but with e.p.r. “we’ve measured not only the presence of the shoes in the room,” Corbett says. “We’ve also measured the person in the shoes.”

Fourteen million Americans have diabetes, but with luck it may end there. Much work must be done on the journey to a cure, but Corbett and McDaniel are now leading that research in a new direction. They have identified not only the molecule that may be involved in the disease but also the compound that stops it. They trust fewer miles are left to travel than they have come so far, but how much research is left remains unknown.

In the mechanism by which β cells are destroyed, macrophages release IL-1, which binds to a receptor on the β cell and triggers a series of events leading to one form of nitric oxide synthase (iNOS). This enzyme catalyzes the production of nitric oxide, which impairs function in the mitochondria of β cells. The researchers believe mitochondrial damage results in β cell death. Activated macrophages also produce high levels of nitric oxide that may contribute to cell death.
Someday, there may be a movie theater you can visit — screens and stereo speakers surrounding you — where, for the price of admission, you can tour the human genome as if you were traveling along its length on a virtual railroad. As your car rolls along the double helical rails that span the genome from chromosomes 1 through 22, landmarks along that vast roller coaster of information tell you where you are.

Imagine rolling over stretches of DNA, speeding on sections of rail that represent genes. As you whiz down the twisting track, places with names like "p53," "APP," and "cystic fibrosis locus," jump out at you. Someday such a tour may be possible, even a routine part of elementary school education. For now, though, the railway is still under construction, and it will be awhile before scientists fill the genome with landmarks.

The Human Genome Project proceeds full steam ahead toward that goal. Like once virgin Antarctica, the human genome is now studded with landmarks — more than 1,400 at last count. And scientists continue to map uncharted territory at a fast pace. This year, researchers affiliated with the genome project have published several milestone papers that offer new maps of the genetic railway that lies within each of our cells. The maps are getting better and more informative, and they will undoubtedly assist in the discovery of disease genes, says professor Helen Donis-Keller, Ph.D., director of the division of human molecular genetics, Department of Surgery.

The genetic linkage map is one type of gene map that has proven useful in tracking disease genes. Donis-Keller's group at the School of Medicine is building linkage maps of six chromosomes, nearly one-third of the genome. A linkage map of a particular chromosome shows the location and order of key markers — actually unique pieces of DNA — that scientists can use as "mileposts" or landmarks in locating the position of various genes.

But the marker isn't the final quarry in this hunt; disease genes are. Donis-Keller explains: A genetic marker (also referred to as a locus) is a DNA sequence on a chromosome that varies from individual to individual. It is this difference that allows the tracing of the chromosome segments from parents to children, from generation to generation. Each difference found at the marker is called an allele.

"What we look for in genetic mapping of disease genes is the co-inheritance of the same alleles and the disease trait in families that are passing the disease along," she says. The rule is that the more commonly the gene and the allele are inherited together, the closer they are on the chromosome. "In this way, we find out which markers are close to the disease gene," Donis-Keller says. "Once we find linkage of a disease gene to a particular marker, we test other markers from our map that are in the general vicinity so we can bracket the disease gene on the chromosome. Then, we begin combing the area of the genome between the markers, looking for the disease gene itself."

This method has proven highly successful. Geneticists using the technique have found many genes, including those responsible for cystic fibrosis, muscular dystrophy, neurofibromatosis, a form of colon...
Putting together a linkage map of the entire genome is not easy. But Helen Donis-Keller and her crew know how; they now have constructed two. The first linkage map of the entire genome was published in 1987 by Donis-Keller and staff when she was at Collaborative Research, Inc., a Massachusetts biotechnology company. That map had about 400 markers and was useful in locating a number of disease genes, including one for an inherited form of heart disease. By today’s standards, though, the 1987 linkage map seems primitive. Still, Donis-Keller believes publishing that map gave the Human Genome Project a much-needed boost.

In 1991, scientists funded by grants from the National Center for Human Genome Research (NCHGR) decided to publish an updated genetic linkage map. The committee advising Nobel laureate James D. Watson, then director of the Human Genome Project, suggested that the map should be published as quickly as possible. Not to be outdone, French scientists at the Centre d’Etude du Polymorphisme Humain (CEPH) in Paris said that they would publish a separate genome map.

Concerned that two linkage maps of the human genome would be confusing, the CEPH scientists and those from the NCHGR agreed to combine their data and produce a single genome map. But which lab would take on the monstrous task of assembling the data into a cohesive, publishable manuscript? The committee turned to Donis-Keller and her battle-tested colleagues in St. Louis.

In early October 1992, the most comprehensive, up-to-date linkage map of the human genome rolled off the presses at the journal Science in Washington, D.C. The manuscript contained mapping information from 129 scientists in 70 labs in the United States, Europe, Japan, Australia and South Africa. It is reported to be the longest research article ever published by Science.

As the deadline for submission of the manuscript drew near, Donis-Keller and her staff transformed their labs and offices into a communications center that would be the envy of CNN. “Seven people in my group worked night and day, including weekends, compiling the data,” Donis-Keller says. “This project would not have happened if we didn’t have their cooperation and willingness to work.”

Throughout much of the summer, primary data poured into Donis-Keller’s lab from as far away as Johannesburg, London and Tokyo, and the group worked to piece together the map in correct order. The data for the maps were sent by electronic mail or on computer diskettes. Edited and rewritten where necessary, they were used to draw graphic maps and formatted into tables.

“After we sent the first draft to the 129 collaborators, we received the first wave of corrections,” Donis-Keller recalls. More phone calls and faxes ensued to clear up ambiguities and request missing data. “We simply could not have completed this project on time without a fax machine,” Donis-Keller says. “My phone bill looks like the national debt,” she jokes. But the

The linkage map of chromosome 1 includes a graphic representation of its characteristic banding, with the bands numbered on the right. To the left are the symbols for the individual markers. The smaller numbers show the distance between the markers in centiMorgans, where one centiMorgan equals approximately 1 million base pairs. Chromosome 1 is huge, equal to 10 percent of the genome.

X Marks The Spot

When geneticists first thought seriously of mapping the entire human genome, the looming question was whether such a huge undertaking was actually possible. Could the technology be developed to analyze every bit of an individual’s genetic information? Could the data be managed? After five years, “there’s no longer any doubt,” says David Schlessinger, Ph.D. “The Genome Initiative is working.”

Schlessinger, professor of molecular microbiology, leads the Genome Center here that is aiming to produce maps of both chromosome 7 and the X chromosome. In the center, Eric Green, M.D., Ph.D., leads the 7 team; Phil Green, Ph.D., has directed the necessary software development, and Schlessinger leads the X team and coordinates the overall effort.

The X team’s work was the subject of an article and a “centerfold” in the October 2 issue of Science. Along with other researchers around the world, the team is building a map of the X chromosome they call a “unified, genetic, physical and functional map.” Schlessinger explains: “This map incorporates linkage information about where disease genes are located based on family studies. But linkage informa-
More is known about the X chromosome than any other, probably because of interest in diseases linked to genes located there and because of the characteristic inheritance pattern of X-linked diseases. Males have only a single X; females have two. The result is that recessive diseases are revealed in males who carry the defective gene as their only copy.

About 40 percent of the X chromosome has been mapped in DNA reconstructed in overlapping, aligned fragments. Schlessinger and his colleagues have brought two technologies to bear on the work. The first was the use of YACs, or yeast artificial chromosomes, that allow the isolation of large, discrete pieces of DNA that can be overlapped to reconstitute the whole chromosome the “map.” The second innovation is the use of sequence tagged sites (STS), each a string of the base pairs that make up DNA long enough to be unique. When two large YACs contain the same tiny STS, the mapper knows that they overlap at that STS sequence and is able to piece them together in order. This simple but powerful concept, originated here by Maynard Olson, Ph.D., and Phil Green, now organizes the work of the international mapping community.

One goal of the Genome Initiative is a map of every chromosome with STS markers at an average placement of one every 100,000 base pairs. For the X chromosome, that works out to a total of 1,500 markers arranged along the 150 million base pairs of the chromosome. (To do all the chromosomes at that level of resolution will require 30,000 markers.)

Mapping of the X chromosome is progressing rapidly, Schlessinger says, and the goal is attainable. Another big step will be taken in May of 1993 when the Fourth X Chromosome Workshop convenes in St. Louis, hosted by the Washington University team. From around the world, laboratories interested in the X chromosome will be represented, and the flow of information will accelerate again. —S.K.
depression and schizophrenia may be mapable," Donis-Keller says enthusiastically.

Access to genome data is improving, which should spur more collaboration and discovery. Usually when scientists submit their mapping data and their maps for publication, they do not make the primary data (on which the conclusions are based) available to the scientific community. Donis-Keller and others believe that access to primary data is important. "People can't replicate the experiments and they can't build on the information with just a summary of the data," she says.

After the paper was submitted, all data were transmitted electronically to the Genome Data Base in Baltimore and the CEPH in Paris. "Scientists can now obtain these data by electronic mail, or they can have them shipped to them on computer diskettes," Donis-Keller says.

Also, the genome map becomes a "living document." "If a scientist finds a new marker, he or she now can determine the placement of that marker within the map," Donis-Keller adds.

"The maps can be added to by anyone." Access to information contained in the human genome is a tremendously important issue for the public as well. As a geneticist working to advance knowledge of the meaning of genes, Donis-Keller is aware of the potential misuse of the information her research might make possible. She believes gene mapping is going to change how we view medicine. It will irreversibly alter the doctor-patient relationship, she thinks. "We now can predict from birth who is going to develop diseases like cystic fibrosis or adult-onset diabetes or heart disease," Donis-Keller says. "Knowing these genetic liabilities ahead of time will change the practice of medicine."

A teacher as well as a researcher, Donis-Keller understands she has a duty to make it clear to first-year medical students in her genetics class that they must understand the fundamentals of genetics, how they can be misused and where errors come from. "Students must understand the power of the information and how quickly it's going to change during their period of clinical practice," she explains. "I think these practical applications are an important part of the mapping business, and maybe more important than the map itself."

That duty to make the next generation understand what her generation has discovered manifests itself in unexpected ways. Amid the seriousness of her genetics lab lies a colorful comic book explaining the principles of genetics. Donis-Keller explains: "We're beginning a project to develop a video game to teach genetics to children." Perhaps that guided tour of the human genome will be at a theater near you sooner rather than later.
When cancer spreads to the bone, the pain and suffering associated with it can be enormous. As the disease affects cells deep in the body’s skeletal structure, it causes excruciating pain and weakened bones susceptible to fracture. Patients with bone cancer metastasis also face a shortened lifespan, though some survive for several years and endure the torment of their disease daily.
But researchers are investigating an injectable treatment that may make the pain of metastatic bone cancer easier to bear. They are involved in a National Cancer Institute-sponsored clinical study of the drug strontium-89 that has been shown to relieve pain in 80 percent of people whose cancer has affected the bone.

Once radiation levels are determined to be appropriate, the patient is free to go.

"The pain of metastatic bone disease can be unbearable," says Bahman Emami, M.D., professor of radiology in the Radiation Oncology Center at Mallinckrodt Institute of Radiology. Emami, who directed the study at the medical school, adds, "Over a period of time, the quality of life is affected and it becomes miserable. That's why it's important we develop drugs to provide comfort to patients."

The multicenter study of strontium-89 is being conducted by the Radiation Therapy Oncology Group (RTOG), a national collaborative research organization. Emami is the RTOG study's principal investigator for Washington University.

At present, Emami says, therapies to curb the pain of metastatic bone disease are few. Radiation therapy or hormonal treatment, the most common forms of therapy, successfully decrease pain in 60 to 70 percent of patients.

"Cancers like prostate and breast are hormonally dependent, which means there is a hormone specific to the cancer and we can manipulate it to relieve symptoms," says Emami. "Patients who are hormonally refractive do not respond to hormone treatments. Between 30 and 40 percent of patients fall into this non-responsive category."

Even with hormonal manipulation, external beam radiation is frequently prescribed. "Hormonal therapy is very easy to do and it's safe, so it is the first line of defense," he says. "But it only provides pain relief for 12 to 18 months, and a patient's average survival is 20 to 30 months, so inevitably there will be pain."

When a patient becomes unresponsive to hormonal treatment, two weeks of radiation treatments usually are administered to ease pain. Emami says about 40 percent of patients then become pain free, another 40 percent get some pain relief and 20 percent receive no benefit. However, Emami says radiation therapy is safe only when it is confined to a localized area, and it's not useful in providing generalized pain relief.

An option for treating bone metastasis has been phosphorus in radioactive form, or P-32. Phosphorus and calcium are two elements that occur naturally in bone metabolism. When phosphorus is marked with a radioactive isotope and injected, it is absorbed by proliferating normal cells, and cancer cells at the site are irradiated. Although P-32 is effective at reducing pain, it bone marrow as well as cancer cells. It also has a short half-life, which means that it remains active only for a short time and provides only temporary pain relief.

Emami says that strontium-89 works on the same principle as P-32, but, by following a different pathway, results in fewer and less severe side effects. Unlike P-32, strontium-89 follows the same biochemical pathways as calcium into the bone where, as a beta-emitter, it irradiates cells only within the immediate area of the bone cancer site. It also benefits from a half-life of 50.6 days, more than three times that of P-32.

"The longer the drug remains in the body, the more effect it has on the tumor," says Emami. "Strontium-89 has many benefits. Compared to external beam radiation, which requires a patient to come in for treatment every day for two weeks, strontium-89 is given in a single injection and should be effective for as long as one year." After a patient in the trial receives an injection, he remains in the clinic for about an hour while the level of radiation he is receiving is carefully monitored. Once radiation levels are determined to be appropriate, the patient is free to go.

The first clinical study of strontium-89 as a treatment for bone metastasis pain took place in 1974 and involved 11 patients. Several smaller studies have been done since that time, but the current study is the first large-scale investigation to evaluate its safety and effectiveness.

"The most important result of this treatment is improved quality of life."

causes serious side effects including anemia, hemorrhage and infection because it is incorporated into the cells of the bone marrow metabolically as phosphorus. As a result, it irradiates

A study in Canada showed no significant improvement in survival for patients receiving strontium-89, but pain relief was improved and new sites of pain were fewer. Participants in that
study also reported an improved quality of life, evaluating items such as their own perceptions of pain and their activity levels.

Emami says the goal of the new work is to determine the maximum safe dose of strontium-89, which until now has not been established, and to examine the drug’s analgesic efficacy. The 84 patients who have taken part in the study had previously received and been unresponsive to hormone therapy. “We evaluated the toxicity and efficacy of four different doses of the drug,” says Emami. “The final data is being analyzed now, and the results are very positive, indicating that strontium-89 is very effective for bone pain.”

Carlos Perez, M.D., director of the Radiation Oncology Center, feels that preliminary results with strontium-89 are “encouraging,” and further evaluation may more precisely establish its usefulness in relieving pain caused by bone metastasis. Once potential complications with the drug have been uncovered and scientists are confident the drug is safe, Emami says researchers will evaluate it as an adjunct to hormonal therapy. A protocol examining localized external radiation therapy versus strontium-89, after failure of hormonal therapy, will also be conducted by the RTOG, with participation by Washington University.

Although information about strontium-89 as it relates to patient survival is not yet available from the latest multicenter study, previous investigations have shown that the drug reduces the level of prostate specific antigen, or PSA, in the blood. PSA is a sensitive index for prostate cancer activity.

Bahman Emami, M.D., explores the potential of strontium-89 as a means for alleviating the intense pain of cancer that has metastasized to the bone.

“At this time, we don’t know how strontium-89 is able to reduce PSA levels,” Emami says. But the implication is that the drug may cause tumor reduction besides its analgesic effect. In addition to alleviating pain associated with bone cancer that metastasized from the prostate, strontium-89 also may have applications with bone pain associated with breast, lung, and thyroid cancers. Emami says the drug has been used in a small number of cases with other types of bone metastasis. He emphasizes that it’s not the origin of the cancer that is important, but whether it has reached the bone. “Any cancer has the potential to get into the bone, but the prevalence is different,” he says.

“I am hoping that strontium-89 will provide complete pain relief in 80 percent of patients and for a longer duration than current therapies. We know radiation is safe when used in localized areas, but if I do a bone scan and see five different areas in the bone that are positive, I can give radiation only to the areas that are most painful. With strontium-89, we can affect the whole spectrum of the skeleton.

“The most important result of this treatment is improved quality of life.” Emami continues. “Part of our work in managing acute cancer patients is survival, but there are situations in which there is no cure. In those situations, it is our responsibility to see that patients live a comfortable and active life for as many days, weeks or months as they have left.”
Experiences As A Study Participant

My urge is to resist research fellow Jason Hanson, M.D., as he leads me through the protocol. One of his hands is on my chin and one is on the back of my neck, smoothly turning my head left, then right, in time to a pace set by a computer-generated tone.

The instructions to relax my neck — "just keep it loose," I'm told — are almost impossible to follow. Allowing someone else to move my head for me is agonizingly passive, like letting another person explain my opinions while I remain silent. The need to exert control is elemental, a reflex.

by Steve Kohler
In fact, what Hanson and I are evaluating in me is one of the more robust human reflexes, a critical component of balance called the vestibulo-ocular reflex, or VOR. I've agreed to participate as a normal volunteer in a research study called the "head-shake project." That's what has put me in this set of unusual circumstances. None of it is unpleasant, but the total effect is foreign; the overwhelming feeling is that anything might happen next.

In his medical school laboratory, Joel A. Goebel, M.D., addresses the issues of balance. He explores abnormalities in the vestibular system that is responsible for an individual's sense of balance. He researches the aging of the system and the subsequent increase in dependence on vision as a means of maintaining balance at a time of life when vision also is failing.

In a third exploration, Goebel, assistant professor of otolaryngology, and post-doctoral fellow Hanson are conducting a study with direct clinical applications. The so-called head-shake project aims to create an effective, portable device for measuring the vestibulo-ocular reflex at the bedside of critically ill patients undergoing chemotherapy or treatment with powerful antibiotics.

There is need for such a device because, Goebel explains, "many of these powerful drugs are ototoxic — toxic to certain cells in the ear." Among the susceptible cells are those dedicated to balance and hearing. As a result, critically ill patients who undergo the most powerful therapy frequently emerge from their treatment with damaged balance and hearing.

"Twice as many ototoxic patients suffer damaged balance as damaged hearing," Goebel says. "A new way of assessing the damage may allow us to stop the treatment from killing so many cells." If Goebel can find the threshold at which damage to cells affects balance and can measure it accurately, he will be able to advise other physicians when irreparable damage is being done to the balance system. The device must be portable because critically ill patients can't come to the vestibular lab that Goebel directs.

To measure potential damage to the ear's sensitive cells, Goebel uses the VOR, a primitive reflex that probably evolved as a survival mechanism to allow the head to move erratically while keeping an image steady on the retina. Such a reflex would be important while chasing a game animal over rough terrain, as our early ancestors must have done.

To witness the VOR at work, extend a finger at arm's length and shake your head back and forth while watching the stationary fingertip. The image should be perfectly maintained without blurring by a healthy VOR. In contrast, holding your head still while wiggling that finger back and forth and trying to follow it with eye movement alone should demonstrate the effectiveness of the reflex.

When the cells in the ear are damaged or killed by ototoxic drugs, their death shows up in reduced performance of the VOR. Quantify the decrease in the VOR and you can measure the effect of ototoxicity on balance, according to Goebel.

To add to the strangeness of my situation, I'm wearing the "helmet of doom," a contraption that mounts on an adjustable headband and drops a black, featureless shield a few inches in front of my eyes. In it, I must resemble Darth Vader minus the voice and the cloak. The idea, I'm told, is to isolate the vestibular input from the visual input. My eye movements are driven by the vestibular organs in my ears.

Mounted on the helmet's headband is a velocity rate sensor that feeds information to the computer concerning the speed at which my head is moving. Stuck to the temples beside each of my eyes are electrodes designed to pick up minute changes in voltage indicating eye movement. "The eye is a
Joel A. Goebel, M.D., (rear) studies the human vestibular system. Assisting him is laboratory supervisor Doug Fishel.

Despite all attempts by Goebel, Hanson and laboratory supervisor Doug Fishel to avoid qualitative words like "good" or "excellent," I try my best to track the imaginary spot accurately, to relax my neck. I'm participating because I want to do well.

I want to know how I compare. How are my reflexes holding up? If I'm better than average — and can get them to tell me so — I can feel good about myself, set back the clock. In the process, I get to learn about my guidance system, a fascinatingly complex operation that gets almost none of my attention.

Unfortunately for me and my mindset, the VOR is a true reflex; I can't increase my performance by trying, Goebel says. In fact, distraction from the task brings what he calls the "gain" — the movement of the eyes over the movement of the head — closer to the optimum.

Several problems confront the researchers in their attempt to perfect their device. In daily life, the speed of head movements is often high. A glance at the curb and then back into the line of travel is a quick motion; the impact of a tackle on the football field is a high-speed jarring. Those high frequencies are impossible to reproduce by hand, and the headgear that records the speed of the movements slews around at even moderately high speeds. That has made the replication of real-world head speeds difficult.

Fortunately, however, lower frequencies are where damage to the vestibular cells of the ear appear first, Goebel says. "We hope to be able to catch the damage at the low end, before it gets into the troublesome range," he says. But there also is difficulty in maintaining constancy of motion when speeds are very slow. To help with the problem, the recording computer also serves as a metronome, and Hanson has practiced his movements.

Because the researchers are looking for the very best performance they can get, they test three ways of imparting movement to the patient's head. Each subject has his head moved by Hanson, has the swivel chair in which he's seated.
moved back and forth by Hanson and finally moves his own head in time to the beat. The resulting numbers — analyzed by computer algorithm to remove artifacts — are compared to insure that all three methods are reliable.

Verification of results from the portable unit is provided by the lab's higher technology equipment. All participants in the study first have their VOR and VVOR assessed in a computer-controlled rotary chair that imparts precise movement. The chair is capable of precisely reproducing frequencies ranging from one direction change every four seconds to four direction changes every second. Tests in the chair are performed with eyes open and a bright target to focus on, in the dark while imagining a focus point, and with the visor in place.

These tests serve as a baseline for assessing the accuracy of the portable measuring system that will soon employ a laptop computer and a portable screen to provide patients with points of light on which to focus. The portable system should also be affordable for institutions that can't manage the $100,000-plus required to install a rotary chair. Then smaller hospitals and clinics will be able to evaluate ototoxic damage to balance, Goebel hopes.

Some of the data for the study I've already provided. Baseline tests involved a ride in a rotary chair. Like a carnival ride gone to graduate school, the chair sits inside a circular screen on which spots of light or contrasting stripes of black and white are projected to capture my visual attention.

The chair moves in carefully controlled arcs at up to 300 degrees per second. With images whirling past my eyes or blackness surrounding me, I quickly lose my orientation and can't tell where I am in relation to the door by which I entered. Still, the sense of being conformed to the chair and presented with visual tasks is not one of helplessness, but of precision. Astronauts and fighter pilots sit in chairs like this, taking measure of their abilities.

While my visual attention is focused on the object — real or imagined — the researchers ask me to list women's names alphabetically. Instead of "Ann," "Betty" and "Chris," I choose "Athena," "Beatrice" and "Calliope." I get stuck on "E" and end up going with "Ethel."

I wish they'd quit distracting me so that I could concentrate on doing a good job of focusing my eyes. But of course, the scientists want to test my reflexes, not my effort.

When my part of the study is over and the data have been analyzed, it turns out that my VVOR is close to what it should be; I overcorrect only a little so that my eyes move slightly more than they must to correct for my head movement at a ratio of about 1.05 to 1.0. Without visual input, my vestibular organs correct at a rate of about .7 to 1.0. Again, well within what is to be expected. And on the portable equipment, I matched the results from the rotary chair.

I've contributed a little something, maybe helped out in the development of a system that will benefit seriously ill patients. And I've still got my reflexes; I'm still as sharp as ever. As I leave the lab, Goebel thanks me for my effort and pays me the compliment: "You gave good data."
Medical students are supposed to be bright, talented and self-motivated. We are also critical, skeptical and overwhelmed by the enormity of our task — to become physicians in four years. This combination of factors makes educating doctors-to-be a daunting challenge, particularly during the first two years of medical school that consist primarily of classroom learning. However, many faculty members at Washington University bring special talents and devotion to the task.

Our great teachers earn our gratitude and respect. More tangibly, we express our appreciation through teaching awards. Annually since 1986, students have chosen a Professor of the Year from among full professors and a Lecturer of the Year from among other faculty for special recognition. What sets the recipients of these awards apart?

Glenn Conroy, Ph.D., coursemaster of gross anatomy, was named Professor of the Year for 1991-92, and his course is consistently named Course of the Year by first-year medical students. Conroy and his wife, Jane Phillips-Conroy, Ph.D., both anthropologists, moved to Washington University from Brown in 1983. They originally visited St. Louis to advise the chairman of the Department of Anatomy and Neurobiology on the feasibility of luring anthropologists to teach gross anatomy. After expressing their confidence that anthropologists would gladly join the Washington University faculty, they couldn't resist the forthcoming job offers and moved to St. Louis. In 1988, Conroy assumed the leadership of gross anatomy from retiring coursemaster Roy Peterson.

The course has "changed with the times," Conroy reports, with a reduction in class hours and more clinical lectures than before. Conroy teaches about eight lectures during the course and spends countless hours in the gross anatomy lab, going from table to table to guide dissection and instruct students. In addition, he attends virtually every lecture given in his course, as do all of the core faculty in gross anatomy. For students, this practice is proof of the faculty's interest and dedication.

Conroy uses the Socratic method, calling on students to answer questions in class. Although students initially may be intimidated by this process, Conroy's ability to make them feel comfortable and think through a problem allows them to relax and enjoy the experience of talking about anatomy.

Morton Smith, M.D., who teaches ophthalmology to sophomore medical students and was voted Professor of the Year for 1991-92, also uses the Socratic method. His enthusiasm for the material is infectious, and students look forward to the liveliness of his lectures. After medical school in his native Maryland, Smith trained at Washington University in ophthalmology and pathology. With one year spent in Washington, D.C., studying ophthalmological pathology and one year as chief resident in ophthalmology, he joined the faculty in 1966 with a joint appointment in pathology and ophthalmology. At that time, he was placed in charge of teaching ophthalmology to medical students.

Twenty-six years later, Smith is still teaching students about the eye. The format of the sophomore lectures, which are part of the preparation for clinical medicine course, has changed over the years as the courses have responded to student feedback. However, the objectives in these lecture series are straightforward: students should learn to recognize ocular manifestations of systemic diseases and common eye pathology as well as the use of the ophthalmoscope. Smith gives every lecture and has for the last 10 years. In this way, he assures that there is no redundancy and maintains his own high standards.

"A system of strictly didactic lectures turns bright people into dull people," says Ed McCleskey, Ph.D., who was named Lecturer of the Year for the second time in a row last year by the freshman class. Although he humbly attributes his popularity to the subject matter he teaches in cell biology, students know that 13 hours of membrane transport and excitability could be a nightmare if McCleskey weren't helping them sort it out for themselves. In his commitment to aiding independent thought and interactive learning, this fall McCleskey radically changed his successful lecture format to a more problem-based approach and added several clinical lectures.

McCleskey received his Ph.D. in physiology and biophysics from the University of Washington in 1983. After post-doctoral work at Yale, he accepted a faculty position at Washington University in January 1987, and was recently promoted to associate professor of physiology. According to McCleskey, one of the ad
Teaching award winners Morton Smith, M.D.; Edwin McCleskey, Ph.D.; Kevin Roth, M.D., Ph.D.; and Glenn Conroy, Ph.D.

The pathology of the nervous system becomes a bright spot in the second year curriculum through the inspired efforts of Kevin Roth, M.D., Ph.D., who was named Lecturer of the Year by last year's class. Roth took over the neuropathology section of the pathology course when he became a faculty member in 1989. He enjoys the challenge of teaching medical students and takes an interactive approach, recognizing that clinical relevance is especially appreciated by the students as they approach their third-year clerkships. Roth emphasizes the importance of learning the material. His obvious enthusiasm for teaching and the subject matter makes the experience enjoyable.

Roth graduated with an M.D. and a Ph.D. in neuroscience from Stanford in 1985 and came to Barnes for his residency in anatomic pathology, followed by a fellowship in neuropathology. He accepted a faculty position at Washington University in 1989. Clinical work takes up one-third of his time, and another third is devoted to research on the regulation of neuropeptide gene expression. The remainder is spent teaching medical students and residents. Roth "like(s) to teach people who want to learn," so he also meets with undergraduate psychology students a couple of times a year to show them gross neuropathological specimens "for as long as they'll stick around."

Besides giving three lectures and leading many laboratory small-group sessions in the pathology course, Roth is familiar to students from autopsy conferences on Thursday mornings, where it is hard to tell him from the residents. Students seeing Roth in tennis shoes and a baseball cap are encouraged to believe him when he says, "I'm just like you, just further along."

Many other special teachers have inspired us with the organization of their thoughts, their enthusiasm for their subject matter and their ability to convey it to us efficiently and meaningfully. For all of them, the time-consuming job they do to pass on what they know seems to be an enjoyable experience that challenges and fulfills them. When we see Ed McCleskey rollerskating to work or Kevin Roth playing air guitar in our class show, when we hear Mort Smith talking about the sports car he'd like to drive or Glenn Conroy reminiscing about his old Harley-Davidson, we recognize people who love life and love what they do.

Ed. Note: Victoria Akins is a third-year medical student, married, with two children.
For his 50th reunion in 1992, C. Barber Mueller, M.D. '42, thought of a unique gift to honor his teachers at the School of Medicine. Now Professor Emeritus of Surgery at McMaster University in Ontario, he had long felt a need to express his gratitude to the school that had given him a full four-year scholarship in 1937.

While he had been a generous contributor over many years, he sought a special way to express his feelings for the professors who had provided him with a first-rate medical education. Thanks to his generosity and imagination, his gift stands in the atrium of the new medical library: a history display recounting the story of this school and people who made major contributions to its development. On nine sides of three triangular kiosks are pictured six of the professors who made such a difference in Mueller's education — as well as others from decades before and since he graduated.

A modest brass plaque contains his tribute to them: "This display is dedicated to those men and women of the faculty who so enriched my life as I passed by...." Visiting alumni will certainly find memorable teachers from their years here, many who achieved national and international prominence — among them Carl and Gerty Cori, Evarts and Helen Graham, George Bishop, James O'Leary, Mildred Trotter and Carl Moore.

"The key person in my medical education was Philip Shaffer, because he opened the door," Mueller says, speaking of the distinguished biochemist and dean who made the fateful decision to give him a full-tuition scholarship. In the fall of 1937, Mueller's mother had read that the medical school was starting the Jackson Johnson Scholarship Program. "This was still the Depression, and with my family's limited resources, it was almost certain that I was going to the University of Illinois Medical School; in fact, I never considered anything else," he remembers.

However, with his mother's encouragement, young Mueller agreed to visit St. Louis. Shaffer interviewed him. "I was a boy strictly out of the cornfields," he recalls. No doubt what impressed Shaffer was the candidate's superior academic record both at Blackburn College and the University of Illinois. Their conversation lasted all of 15 minutes. "I suspect Dr. Shaffer himself constituted the entire admissions committee for the Jackson Johnson Program," Mueller says. Shaffer's ability to discern academic quality was superb; of eight Jackson Johnson Scholars accepted the first year, seven graduated in the top 10 of their class four years later, among them Barber Mueller.

Two weeks after his visit, a letter arrived with the news that he had won admission and a four-year scholarship, along with a National Youth Administration (NYA) job to help with his living expenses. "The National Youth Administration was a New Deal program to put young people into paying positions; Washington University was given a number of these to distribute to students," he explains. For Mueller, the tasks he performed contributed directly to his future career; in addition, the job paid eight dollars a week.
through his four years at the School of Medicine.

The first of his tasks was reading nerve tracings and preparing lantern slides for George Bishop and James O'Leary in the Department of Neurology. The next year, Mueller worked for Nathan Womack, a professor of surgery whom he describes as "a most unusual and imaginative man. He put me to work doing pancreatectomies in dogs to study a proposed diabetogenic hormone. This was my first bit of surgery." That experience led him to choose surgery as his major interest and eventual specialty choice. During Mueller's second and third years, he worked on wound healing studies which led to his first two papers, published with Evarts Graham.

As a senior medical student, he naturally sought Graham's advice about a surgical internship. "I told plural pronoun, I think the decision was strictly his."

In the spring of 1943, Mueller decided to accept a commission in the United States Navy and made an appointment to tell Graham about it. Graham offered to have his commission deferred so that he could finish surgical training. The young intern said he'd return in a few days with his decision. "I knew that if I made up my mind in front of Dr. Graham, I'd make it up his way, and I didn't want to do that. In the end, I decided to leave."

Mueller served as a medical officer with the U.S. Marines in the Pacific Theater, making sure the wounded got back to ships. He was himself wounded at Iwo Jima.

But his old chief had not forgotten him. In 1945, Graham wrote him, asking whether he'd be interested in a Rockefeller Fellowship.

Mueller replied that as soon as the war was over, he'd accept. At his military discharge in 1946, they met in St. Louis; Graham asked him with characteristic directness: "What would you like to do?" Mueller answered that he'd like to study biochemistry at Harvard, and

### "I am, first of all, an educator."

with Graham's help he did so in the laboratory of Baird Hastings. "It was a spectacular year," he recalls. "That time opened up mineral and glucose metabolism, membrane dynamics and turtle hearts." Graham intervened again in 1949, offering him the first position as a Markle Scholar. Under this new five-year program, he could move smoothly from laboratory and clinical training to a faculty position.

In 1956, Mueller left his position as an assistant professor of surgery at Washington University to become the first full-time head of surgery at the State University of New York, Syracuse. Mueller remembers: "Experiences at Washington University and Barnes Hospital certainly colored my approach to my new role. Evarts Graham had structured the program for student education, progressive responsibility and clinical excellence. I introduced many of these ideas into the surgical scene at Syracuse." Though justly proud of his specialty, Mueller says of his career: "I am, first of all, an educator."

Eleven years later, he accepted an invitation to head the new Department of Surgery at McMaster University in Hamilton, Ontario. Here, too, he put his convictions about the best possible surgical training to work. "At McMaster, as at Syracuse, there was no residency program when I arrived." Building excellence from the ground up had become his educational specialty.

An emeritus professor since 1983, Mueller continues to work and travel at a remarkable pace, serving on committees of special interest at McMaster that deal with education and medical ethics. In 1988, students there honored him with the Students' Teaching Excellence Award. Despite his long residence in Canada, Mueller never has given up his midwestern roots; he serves as a trustee of Blackburn College and has endowed fellowships in the humanities at the University of Illinois. Washington University honored him with a Founders Day Award in 1977 and an Alumni Achievement Award in 1987. "All these years later, my dearest friends are in St. Louis," he says simply. "I've been trying to figure out how to show my gratitude to the medical school for the last 50 years."
A gala dinner at the Ritz-Carlton Hotel was the setting on Friday, September 11, when the School of Medicine presented the three Second Century Awards for 1992. Made of the most precious materials — gold, silver and marble — the award celebrates the advent of the second hundred years of excellence in research, teaching and patient care at the medical school. It is presented in recognition of individuals whose long-term commitment, dedication and generous participation have made a great difference, enabling the School of Medicine to enter its second century with unparalleled strength and confidence.

Says William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine, “With this award, we show our appreciation to those people who have provided the means, the inspiration, the intellect and the spirit to drive our important work forward.”

This year, Second Century Awards were presented to Oliver H. Lowry, M.D., Ph.D.; P. Roy Vagelos, M.D., and Spencer T. Olin.

Lowry, Distinguished Professor Emeritus of molecular biology and pharmacology, has for 45 years devoted his outstanding scientific, educational and administrative abilities to the medical school. He came to the school in 1947 as professor and head of the Department of Pharmacology and led the department through a period of tremendous growth. From 1955 through 1958, he served as dean of the School of Medicine. He retired as department head in 1976 and became professor emeritus in 1979, but maintains a highly active research career.

An internationally renowned histochemist whose techniques and approaches have had profound effects on science, Lowry has widely influenced research in the areas of neurobiology, neurochemistry and biochemistry. He was elected to the American Academy of Arts and Sciences in 1957 and to the National Academy of Sciences in 1964. The annual Oliver H. Lowry Lectureship was established in 1978, and the Oliver H. Lowry Prize for Excellence in Pharmacology was created in 1980. He was awarded an honorary Doctor of Science degree from Washington University in 1981.

P. Roy Vagelos, M.D., is a scientist and physician with a gift for innovation and corporate leadership. President and chief executive officer of Merck & Company, Inc., since 1985 and chairman of the board of directors since 1986, Vagelos is widely recognized as the leader who changed the focus of drug development from simply treating symptoms to finding ways to block the processes that actually cause medical problems.

He joined Merck in 1975 as president of its research division after nine years as chairman of the Department of Biological Chemistry at Washington University School of Medicine. At the medical school he put together an outstanding research team and gained renown as a biochemical researcher and as a person who recognized talent, challenging his associates and his staff to reach their full potentials. He also founded the university’s division of biology and biomedical sciences and directed the division from 1973 through 1975. The division continues as one of the major bridges between the medical and hilltop campuses.

Vagelos received the Enzyme Chemistry Award of the American Chemical Society in 1967. He was named 1992 Chief Executive of the Year by Chief Executive Magazine, and he has been profiled in many of the nation’s major business publications. On August 13, 1992, he received the coveted Ellis Island Medal of Honor. He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. He holds an earned Doctor of Medicine degree from Columbia University College of Physicians and Surgeons and has been awarded honorary doctorates from seven universities, including a Doctor of Science degree from Washington University presented in 1980.

Spencer T. Olin, now retired, has been a business and community leader in St. Louis for many years. He has been a major benefactor to Washington University and the School of Medicine.

Since beginning his business career at Western Cartridge Company in 1921, Olin has been dedicated to community improvement. He became a member of the board of trustees of Washington University in 1957 and was awarded an honorary Doctor of Laws degree in 1969. In 1975, he received the Eliot Society’s Search Award.
The award, designed by Heikki Seppa of the School of Fine Arts, signifies the school’s highest purpose: the healing of humanity. It is fashioned from a flat triangular sheet of gold into a strong form suggesting the corners of the world from which knowledge is gathered. That knowledge, refined and expanded by dedicated teachers, researchers and clinicians, is manifested as a pure silver flame in the center.

The first Second Century Awards were presented last year, during the school’s centennial celebration. The two recipients were Robert J. Glaser, M.D., and Harriet Baur Spoehrer.

Glaser received his medical degree from the Harvard Medical School and trained in internal medicine at Barnes Hospital and Peter Bent Brigham Hospital. He joined the Washington University medical school faculty in 1949 and rose to the rank of associate professor of medicine and associate dean. In 1957, he went to the University of Colorado as vice president for medical affairs and dean of medicine and later served in the same capacity at Stanford University.

Since 1970, Glaser has been involved in medical and scientific philanthropy. He was president and chief executive officer of the Kaiser Family Foundation and now is a trustee and director for medical science of the Lucille P. Markey Charitable Trust.

P. Roy Vagelos, M.D., receives his award from William A. Peck, M.D.

Glaser is a member of the American Academy of Arts and Sciences and the Institute of Medicine of the National Academy of Sciences. He has received many honorary degrees, including one from Washington University, and has served on the university’s board of trustees since 1979, where he chairs the educational policy committee. He also is chairman of the medical school’s National Council.

Harriet Baur Spoehrer’s unrivaled involvement in the St. Louis community included her deep commitment to the intellectual growth of students at the medical school and to the education of youth in general. She endowed the Spoehrer Professorship in Pediatrics and was a long-time volunteer at St. Louis Children’s Hospital.

The recipient of the 1973 St. Louis Globe-Democrat Woman of Achievement Award, Harriet Baur Spoehrer was a supporter of civic organizations and programs such as Junior Achievement.

A graduate of Washington University, she was a life member of the Eliot Society. Recently, her generous support of the School of Medicine made it possible for researchers to lay the groundwork for innovative programs, particularly in the fields of pharmacology and the Human Genome Project. Mrs. Spoehrer also was a dedicated supporter of the medical school’s new Medical Library and Biomedical Communications Center.

The presentation of the Second Century Awards has become a major event on the School of Medicine calendar. “This is one small way in which we are able to acknowledge some of the generosity that our supporters show to us, and it is the beginning of what will become a long tradition,” says Peck.
John W. Records, M.D. '36, has had a chair endowed in his name in obstetrics and gynecology at the University of Oklahoma. The endowment was made possible by a gift from his son, George J. Records, and his family and contributions from the faculty, with matching funds provided by the State Board of Regents for Higher Education.

Roger J. C. Meyer, M.D. '55, continues to serve as clinical professor of pediatrics and public health at the University of Washington. He has been newly appointed to direct the Acute Illness Clinic at Madigan Army Medical Center for Health Specialists. In addition, he works overseas occasionally as an Army Medical Corps reservist. In that capacity, he recently helped immunize 57,000 people against N. meningitis as part of a State Department campaign in Cameroon. Meyer calls the experience “the most exciting and productive public health contribution,” of his professional life, because thousands in that area die of the disease each year without immunization.

Verne F. Goerger, M.D. '40, has attained the age of 77 and describes himself as a “computer nut” who cares for a salmon-crested cockatoo and a cockateel at his home in Harlingen, TX. Retired for 10 years, he is father to a son and a daughter, grandfather to a grandson and a granddaughter.

J. Stewart Whitmore, M.D. '49, has been appointed adjunct clinical professor in the department of radiation oncology at East Carolina University School of Medicine in Greenville, NC. He and his wife of 43 years have lived in Washington, NC since his retirement from private practice five years ago.

Gerald W. Cady, M.D. '52, retired from practice in May, 1992. In 1991, he received the Founding Father Award from the San Diego Chapter of the Western Orthopaedic Association.

Edward S. Hume, M.D. '75, serves as chairman of the Department of Psychiatry at Community General Hospital in Syracuse, NY and maintains a small private practice in forensic psychiatry. Married to the former Sue Ferrara in 1986, he is the father of one child, Katie, age three.

Free Advice

When reunion-goers gathered in St. Louis in May 1992, the alumni and development staff again asked (among other things) for any advice the alumni might offer to current students as a result of their long experiences.

Many of the responses followed three basic themes:
1) Impending changes in medicine and its practice will test you.
2) Guard your integrity jealously.
3) In clinical practice, put patients first. Here are a few of the more concise pieces of advice for today’s students, arranged by their class of origin. A complete package of all of the responses was prepared by the Alumni and Development staff and distributed to medical students. The selections here appear minus attribution, for the protection of the advice-givers.

Take advantage of every opportunity to enlarge your knowledge of medicine — all phases.

I view with considerable regret the commercialization of American medicine. During the 50 years since graduation, there has been no significant change in the two-tiered system in which we practice — the best medical care in the world for those who can afford it, and much less for those who can’t. I believe in equal access to equal quality of care for all Americans and that medical care has no business being a business. If anything, medicine has become much less of an idealistic profession than it was 50 years ago.
Gary L. Baker, M.D. '77, F.A.C.S., assistant professor of plastic surgery practicing at Kansas University Medical Center, has been elected to the status of fellow in the American College of Surgeons. Baker is the only Kansas City plastic surgeon currently certified by four separate American Board of Medical Specialties-sanctioned boards.

1942

Strive to become the best physician you possibly can be, but also pay great attention to politics and participate to whatever extent you can, because political trends are shaping our lives.

1947

I have been teaching medical students since I graduated from Washington U. I have found myself repeatedly quoting Dr. Ed Reinhard who summarized medical school education by advising: “Listen to the patient long enough and he will tell you what is wrong with him. Listen 10 minutes longer and he will tell you what to do for it.”

1952

Fight as hard as you can to defend the medical profession's honor, integrity and place in society.

1962

Do your best for the right reason, then roll with the punches.

1967

Hang in there. It is really worth the time and effort to succeed at a school like Washington University.

Jeffrey P. Cichon, M.D. ’79, has “reactivated” as a clinical professor at the University of Nevada Medical School. He is involved in the residency training program in orthopedics, and his wife, Vicki, is active in the American Junior League and with a local medical auxiliary chairing committees for charitable events.

Training received in medical school is more important than often realized. Though medicine changes constantly and much of early education becomes dated, it provides a foundation for later.

1972

Ask, “How can I make a difference?”

Everything is relevant to the practice of medicine.

Don’t put up with sexist behavior.

1977

You are privileged to be going to the finest medical school in the country. Never forget the word “privilege” and remember where you and many of your classmates came from. Never lose the youthful zeal and idealism that brought you to medical school.

Donald A. Opila, M.D. ’79, F.A.C.P., has been named Young Internist of the Year by the American Society of Internal Medicine. The award has been given annually since 1969 to recognize outstanding contributions to the social and economic environment of internal medicine. Opila is a clinical assistant professor of medicine at State University of New York at Buffalo. As the coordinator of the Primary Care Track Residency Training Program, Opila develops and implements the curriculum of internal medicine residents and medical students. He organizes problem-based discussion groups and arranges mentorships with primary care physicians. Students often spend their primary care rotation in a rural or HMO setting rather than the traditional hospital or clinic. In 1991, Opila directed a demonstration project funded by the New York State Department of Social Services. The project helped non-acute Medicaid patients who seek care in emergency rooms to see primary care physicians instead. Currently, Opila is president of the Buffalo Academy of Medicine, a member of the New York State Society of Medicine board of directors, immediate past president of the Western New York Society of Internal Medicine and is a fellow in the American College of Physicians.
Dennis P. DeVito, M.D. '80, has joined Children's Orthopaedics of Atlanta, P.C., a private medical practice devoted to the orthopedic care of infants, children and adolescents and affiliated with Scottish Rite Children's Medical Center. DeVito and his wife, Niki, reside in Alpharetta, GA with their four children.

John S. Pratt, FHS in surgery, was an invited speaker on breast cancer at the 5th Annual Symposium on Medical Malpractice sponsored by the Law Journal Seminars Press at the Waldorf Astoria in New York, June 8 and 9, 1992.

Harper S. Jackson, HA '79, senior vice president at the Methodist Hospital in Houston, was recently advanced to fellowship in the American College of Healthcare Executives. Jackson heads Methodist's Patient Services Division, the hospital's largest division, with more than 3,600 employees and an annual operating budget of more than $200 million.

Jeanette Dansberry, OT '59, is a supervisor in the Division of Vocational Rehabilitation for the Wisconsin Department of Health and Social Services. She has worked for the State of Wisconsin for 26 years.

Sandra H. Phipps, PT '85, and her husband, Edward, announce the arrival of their second child, Martin Edward, who was born on November 27, 1991, weighing eight pounds and two ounces. He was welcomed home by his sister, Helen.

Gina M. Musolino, PT '87, has accepted an appointment as adjunct assistant professor with the University of Central Florida's Program in Physical Therapy. She also will practice with the staff in physical therapy at a sports medicine and industrial rehabilitation center in Orlando.

David Apirion, Ph.D., professor of molecular microbiology, died August 29, 1992, after suffering a heart attack. Apirion was cycling on a tour in west St. Louis County at the time of the heart attack.

A highly regarded researcher in the field of molecular genetics and especially RNA metabolism, Apirion had been a faculty member at the School of Medicine since 1965. He had published more than 175 papers in his field and was the recipient of many awards for his work.

Apirion was active in his synagogue and volunteered in the Big Brothers/Big Sisters organization. At the most recent Senior Olympics, held in St. Louis, he won five medals in swimming and cycling events.

Among his survivors are a daughter, Alison Apirion of Clayton; two sons, Jonathan of Morganton, NC, and Michael of Los Angeles; and several brothers and sisters, all living in Israel. Apirion was born in Petah Tikvah, one of the first Jewish settlements in what later became Israel. He was 57 years old.

A fund in his honor has been established. Contributions may be sent to Washington University School of Medicine, Department of Molecular Microbiology, Box 8230, 660 S. Euclid, St. Louis, MO 63110. The fund will be used for the purchase of new books and journals for the library and the preservation of the rare and historical book collection.
This three-dimensional reconstruction of a bundle of brain capillaries was built up from more than 700 electron micrographs. The reconstruction, prepared by Lyndon S. Hibbard, Ph.D., and his colleagues in the Laboratory of Neuroimaging, was created using computer programs to align the images and to isolate the capillaries from surrounding tissues. The picture is a stereo pair. By holding this page at arm’s length and gazing “through” it at a distant point, the viewer may be able to fuse the two elements and perceive a single 3-D image.
The three major candidates for president in 1992 appeared on Washington University's hilltop campus on Sunday, October 11, to debate the issues in front of what was estimated to be one of the largest television audiences ever. The Athletic Complex's Field House was transformed from a basketball court into a sound stage for the event, said by its producer to be perhaps the most important 90 minutes of the entire campaign.