In support of the diabetes research of Paul E. Lacy, M.D., Ph.D., and David W. Scharp, M.D., the Barnes Hospital Islet Processing Lab was prepared for a March opening. The process, developed at the medical school, produces purified, vital islet cells from pancreata acquired from organ donors. The lab’s technical supervisor, Dan Fraga, is shown at one of five isolators in which the organs are washed, dissected, broken down into cell aggregates, purified and cryofrozen for banking. The preparations are then pooled for transplantation to diabetic patients who have had kidney transplants or are taking immunosuppressive drugs.
On The Cover:

In pursuit of effective gene therapy, medical school researchers install genes in many types of cells. In the experiments recorded on the cover, David Leib, Ph.D., and Jay Pepose, M.D., Ph.D., tested a particular gene promoter (the DNA sequence that instructs a gene to express the protein for which it encodes) to demonstrate its effectiveness in neurons. They were especially interested in results shown in the third examples from the left in the bottom two rows. The cells in those samples are retinal cells that clearly contain the active gene promoter, as shown by the blue stain. Story on page 12.
Clinicians Get Tenure Track

The votes have been cast and certified by the university’s Board of Trustees, and the School of Medicine will offer a clinician track for doctors who spend more time teaching and caring for patients than doing research.

In a vote open to the entire faculty on November 6, amendments to the tenure policy to make a clinician track possible were approved by a four-to-one margin, according to John N. Drobak, J.D., professor of law and chairman of the Senate Council, an elected body that represents faculty interests in university policy decisions.

“This is a major change in tenure policy resulting from a year-and-a-half of dialogue between the medical school administration and faculty,” Drobak says. “There was full and open discussion, and the end result is that a new career path for physicians is being established that will better serve the needs of the School of Medicine.”

In awarding tenure, the university always has stressed the importance of research, explains James P. Crane, M.D., associate vice chancellor and associate dean for clinical affairs at the School of Medicine. While excellence in research will remain a critical part of the academic mission, he points out that the demands and complexity of medicine make it essential that some individuals devote a major portion of their time to patient care and teaching.

The clinician track, Crane says, rewards physicians for excellence in patient care and teaching. It also should assure a stable patient load to provide adequate learning opportunities for medical students and house staff. In addition, according to Crane, increased clinician activity will benefit research by bringing in more patients to participate in studies. And clinical revenues, he adds, will help support teaching and research activities in both the clinical and pre-clinical departments.

Professorial titles will be the same for faculty on either the investigator or clinician track.

“In the past, we have lost some excellent clinicians and teachers because we could not promote them,” Crane says. “I believe the complementary nature of the clinician and investigator pathways should enhance the ability of our faculty to excel in all aspects of our academic mission.”

The School of Medicine will join good company by offering the clinician track. Of the nation’s 126 medical schools, 112 offer tenure and, of those, 80 also have a clinician track.

Crane and Drobak both applaud Samuel A. Wells, Jr., M.D., professor and head of surgery, who chaired the clinical pathway steering committee, and William A. Peck, M.D., executive vice chancellor for medical affairs and dean of the School of Medicine, for their initiative to secure the future for clinical faculty.

States Directs Biomedical Computing

David J. States, M.D., Ph.D., has been named director of the Institute for Biomedical Computing at the School of Medicine.

Formerly a senior staff fellow at the National Library of Medicine’s National Center for Biotechnology Information (NCBI), States was responsible for the construction and analysis of molecular sequence databases.

In conjunction with his position at the medical school, States also directs the program in biomedical engineering in the School of Engineering and Applied Science on the Hilltop campus. States will oversee expansion of the network communication systems that will enable more researchers to have access to electronic data information. “My goal
is that network communications use will become more widespread and routine at Washington University, an institution which already has expertise in the area of electronic communications,” says States. “Electronic communications are an important aspect of the research environment, and we need to see that all of the university has access.”

In addition, States will be principal investigator on the analysis component of the C. elegans Genome Sequencing Center. His primary research interest is large-scale molecular sequencing and the analysis of genome sequence data.

Sobel Honored Twice

Burton Sobel, M.D., professor of medicine and director of the cardiology division, recently received two career honors: He was named president-elect of the American Professors of Cardiology (APC), a national organization devoted to excellence in fulfillment of the clinical, educational and investigative responsibilities of academic cardiology programs, and he was presented with the 1992 Herrick Award from the American Heart Association’s Council on Clinical Cardiology.

Sobel was named president-elect of the APC by the group’s 118 members, all of whom are directors of academic cardiology programs around the country. He will hold the post for one year from January 1, 1993, then will serve as president for one year, succeeding Yale University’s Barry Zaret.

The prestigious Herrick Award is given annually to recognize a physician whose scientific achievements have contributed to the advancement and practice of clinical cardiology. Sobel accepted the award on November 17 at the American Heart Association’s annual scientific meeting.
Two Share Wakeman Award

Two scientists here have been presented with the Wakeman Award for Research in the Neurosciences. John W. Olney, M.D., professor of psychiatry and neuropathology, and Dennis W. Choi, M.D., Ph.D., Andrew B. and Gretchen P. Jones Professor of Neurology and head of neurology, share this year’s award with Jeffrey Watkins, M.D., professor of pharmacology at the University of Bristol in Bristol, England.

The three were recognized for their work in the area of excitotoxicity. The word, coined by Olney, describes the process by which brain and nerve cells are literally stimulated to death by the brain’s neurotransmitters. Excitatory amino acids, particularly glutamate and aspartate, can have toxic effects on cells in the brain and spinal cord. Injury from trauma or stroke and diseases such as Alzheimer’s cause the release of large quantities of excitatory amino acids and destroy irreplaceable brain and nerve cells.

The Wakeman Award is considered one of the most prestigious in the neurosciences. "It is a special honor, for which I am very grateful," Choi says. "I hope to join Drs. Watkins, Olney and others in continuing to contribute to the excitotoxicity field."

For Olney, the award represents official recognition for the first three generations of contributors to the field of excitotoxicity. Watkins, he says, provided the foundation by identifying how amino acids alter the activity of neurons. Olney later discovered the toxic effects of the excitatory amino acids and demonstrated their potential role in brain disorders. Choi followed by producing glutamate excitotoxicity in cultured brain neurons and clarifying mechanisms by which glutamate excitotoxicity can contribute to neurological disorders.

"The contributions are not in competition with one another, but are rather separate aspects of the same theme that complement one another," Olney says.

The Wakeman Award is presented every two years. It was established in 1972 by Nancy D.W. Gardiner in the memory of her husband, William T. Wakeman.

Ultrasound Spots Kidney Obstructions More Safely

Researchers here have applied the latest ultrasound techniques to develop a safer method for diagnosing kidney stones and other forms of urinary tract obstruction.

Using color Doppler ultrasound and conventional X-rays, the investigators at Mallinckrodt Institute of Radiology produced images of blood flow in the kidneys and of urine entering the bladder to assess whether urine made the journey from kidneys to bladder successfully. The approach may help avoid the adverse drug reactions that occasionally result from the current diagnostic test of choice, says Lane Deyoe, M.D., a radiology fellow.

 Currently, physicians diagnose possible urinary tract obstructions by using a plain abdominal X-ray to look for kidney stones and an intravenous urogram (IVU) to assess urine flow. For an IVU, patients are injected with a contrast material and abdominal X-rays are made. The contrast material produces an image of the path urine takes as it leaves each kidney and travels through ureters to the bladder. If an obstruction exists, an IVU may show the contrast agent pooling up behind the blockage, says Deyoe.

The IVU is generally quite accurate and safe, Deyoe says. But in some patients, the contrast material causes adverse reactions such as nausea, vomiting, irregular heart beat and, in extremely rare cases, death. Mild to moderate reactions affect two to eight percent of patients; severe, life-threatening reactions occur in 0.01 percent to 0.1 percent of patients, Deyoe says. In addition, the test is not ideal for pregnant women because it exposes their fetuses to radiation and to the contrast drug, he adds.

Deyoe and colleagues evaluated 32 patients suspected of having a urinary tract obstruction using a plain abdominal X-ray and three ultrasound techniques. They used IVU exams as the standard for comparison. With a traditional ultrasound exam of the kidney, they looked for urine pooling in
the kidney. They also applied a technique called pulsed Doppler to look for decreases in blood flow to the kidney, which can indicate a urinary tract obstruction. Third, the researchers used color Doppler ultrasound to look for "ureteral jets," the regular spurts that normally send urine into the bladder. Color Doppler, based on a principle similar to police radar, uses sound waves to measure the speed of moving materials.

The ultrasound approach correctly diagnosed all completely obstructed patients and all patients who were completely unobstructed. Of 14 patients with partial obstructions, 11 (79 percent) were correctly diagnosed. There was one false-positive result in one completely obstructed patient. Overall, the tests were accurate in 28 of the 32 patients (88 percent).

"We found that the ultrasound was very good at diagnosing these obstructions. The IVU is a good test, but for patients who should not receive the contrast material, this gives us an option," Deyoe says.

Ultrasound, unlike the traditional X-ray exams, also gives physicians the capability of looking for other causes of abdominal pain, such as appendicitis or gallbladder disease, he adds. The ultrasound approach may be especially valuable for pregnant women, the elderly, people who are allergic to the contrast material and people who have unhealthy kidneys, he says.

Cullen Is Associate Vice Chancellor For Research; Lazarus Named Assistant Dean

Susan E. Cullen, Ph.D., has been appointed the university's associate vice chancellor for research, and Cathy J. Lazarus, M.D., has been named assistant dean for student affairs at the School of Medicine.

As the chief administrator, Cullen coordinates all activities of the research office with other university offices.

"Sue Cullen brings her faculty and research experience, as well as her knowledge of the research office, to this important part of the university's teaching, learning and research endeavors. She has outstanding credentials," says Edward S.

Cathy J. Lazarus, M.D.

Macias, university provost. Cullen is an immunologist who joined the faculty in 1976. In 1985, she was made a full professor in both the Department of Molecular Microbiology and the Department of Genetics.

Lazarus, who in 1990 was named director of the Washington University Medical Campus Student and Employee Health Services, will continue in that position in addition to her responsibilities with the newly created position of assistant dean. She assumed her new role December 1.

"Dr. Lazarus is a fine mentor and clinician, intensely interested in student activities," says William A. Peck, M.D., executive vice chancellor for medical affairs and dean of the School of Medicine. "Her many talents will enhance our very important and already fine student affairs program."

In her new position, Lazarus will assist Patricia L. Cole, M.D., associate dean for student affairs, who will take on the added role of director of the Cardiac Catheterization Laboratory at Jewish Hospital, part of Washington University Medical Center. Lazarus and Cole will be responsible for arranging all student affairs activities at the medical school such as graduation, orientation and other events.

Lazarus, who is an assistant professor of clinical medicine, will continue as director of student and employee health service, overseeing administration of the service and providing direct patient care to medical campus students, including those in the medical school, graduate school of biological sciences, occupational therapy, physical therapy and other programs based at the School of Medicine.
John P. Atkinson, M.D., and Jeffrey I. Gordon, M.D., have been elected to the rank of fellow by the American Association for the Advancement of Science (AAAS). The association bestows this honor on members "whose efforts on behalf of the advancement of science or its applications are scientifically or socially distinguished."

Atkinson, professor and chairman of the Department of Internal Medicine and professor of molecular microbiology, was named for his pioneering research in immunology, for exemplary professional leadership in the field of rheumatology and for inspiring contributions as a medical teacher.

Gordon's laboratory has used a family of genes encoding fatty acid binding proteins as models to study the atomic details of fatty acyl-protein interactions and, through the use of transgenic mouse technology, to examine the differentiation and proliferation programs of intestinal epithelial cells.

William A. Peck, M.D., has been named executive vice chancellor for medical affairs, according to Chancellor William H. Danforth. Peck will continue to carry the title of dean of the Washington University School of Medicine as well.

Peck was named vice chancellor for medical affairs and dean of the School of Medicine in 1989 and is the first person to serve in the dual position. As dean, Peck administers the academic, research and patient care activities within the School of Medicine. As executive vice chancellor, he guides and coordinates the relationships between the school and other organizations and constituencies, such as the affiliated hospitals, the National Institutes of Health and corporations and foundations. Peck also serves as president of the Washington University Medical Center, which includes Barnes, Jewish, Children's and Barnard hospitals and the Central Institute for the Deaf.

"When the decision was made to combine the dean'ship and the vice chancellor's responsibilities into a single position, we knew we would need a leader with exceptional talents in the areas of administration, education and biomedical research," says Danforth. "Bill Peck has certainly proven to have that mix of talents and has guided the school extremely well during a period of growing expectations and challenges."

Researchers at the School of Medicine have received a $400,000 grant from the National Institute of Mental Health to study the heritability of schizophrenia.

Steven O. Moldin, Ph.D., assistant professor of psychiatry, will evaluate 50 schizophrenic patients and three family members to study biological traits common in patients and their relatives who are not suffering from the disease. All will be tested for attention disorders.

"People with schizophrenia tend to have trouble with attention. If you ask them to follow a moving object or perform a task that requires attention, they do poorly," Moldin says. "Their relatives, who might not have schizophrenia, also tend to have impaired attention. With this study we are trying to see how schizophrenia and attention together are inherited through the family."

Moldin will gather data for the five-year grant from inpatients at Malcolm Bliss Mental Health Center and Barnes and Jewish Hospitals at the Washington University Medical Center, where he is an attending staff psychologist.
Perez, Avioli And Civitelli Honored For Contributions

Carlos A. Perez, M.D., director of the Radiation Oncology Center at Washington University's Mallinckrodt Institute of Radiology, has been awarded the 1992 Gold Medal Award from the American Society for Therapeutic Radiologists (ASTRO), the largest society of radiation oncologists, has given the award since 1977 to recognize outstanding contributions to the field of radiation oncology. Perez is among the youngest ever to receive it.

Louis V. Avioli, M.D., and Roberto Civitelli, M.D., have received the Kappa Delta Award from the American Academy of Orthopedic Surgeons for their outstanding contributions to the fundamental understanding of those factors that control bone cell activity and biological function.

High levels of insulin and insulin precursors may contribute to atherosclerosis in non-insulin-dependent diabetics by disrupting their body's built-in mechanism for dissolving blood clots, according to investigators here. A better understanding of these clotting disruptions may generate new approaches to treating atherosclerosis among diabetics.

The findings provide the best evidence to date linking insulin to the high rate of cardiovascular disease in people with non-insulin-dependent diabetes (NIDDM) — a disease that affects 14 million Americans, the researchers say.

Clinical studies have hinted that overabundance of insulin and its precursors — the substances from which insulin is formed — might accelerate atherosclerosis in people with NIDDM, hypertension or obesity, says David Schneider, M.D. He and Janet McGill, M.D., instructor of medicine, are lead authors of the study.

In the first of two studies, Schneider and his colleagues looked at insulin's effect on endothelial cells, the cells that line blood vessels. They confirmed reports that insulin stimulates production of a substance called plasminogen activator inhibitor type 1 (PAI-1). PAI-1 interferes with blood chemicals that prevent clot formation.

In the second study, the investigators measured PAI-1 in 69 people: 34 with NIDDM, 19 non-diabetic obese and 16 non-diabetic lean volunteers. They found that obese and diabetic people had abnormally high levels of PAI-1, findings that confirmed past studies. The researchers then went a step further to see whether such PAI-1 levels altered the ability to respond to blood clots.

They simulated a blood vessel blockage by applying pressure to decrease circulation in an arm for 10 minutes, then measured levels of the natural clot dissolver called tissue-type plasminogen activator, or t-PA. Lean people responded appropriately, by producing the higher levels of t-PA required to break up the clot, had it been real. Diabetics, however, had no such response. The finding marks the first time researchers have shown a direct link between PAI-1 levels and an impaired response to physiologic stress in the same group of people.

The studies suggest that diabetics may not respond properly to microscopic blood clots that may form on a regular basis, Schneider says. "In each of us, a dynamic equilibrium exists between making clots and dissolving them. If there is too much PAI-1 present, dissolution of clots may be impaired. The effect of that may be persistence or recurrence of clotting, which can exacerbate atherosclerosis," he says.

Correction

In the legend accompanying the photograph on the inside front cover of the last issue of Outlook (Winter, 1992), Carlton C. Hunt, M.D., and Albert Roos, M.D., were misidentified as Ph.D.s.
Max Arens, Ph.D., got an unexpected phone call last year as he sat in his office. "Max," the unfamiliar voice said, "this is Michael Whyte at Jewish Hospital. Would you like to go fishing?"

Arens had never met Whyte, but a virologist in an academic medical center with approximately 2,000 researchers becomes accustomed to calls from scientists needing help in tracking viruses.

by Jim Keeley

He accepted the invitation.
Michael Whyte, M.D., hoped that Arens might help solve his puzzle. Whyte’s problem was that two patients with an unusual skeletal disease had been referred to him. Whyte proposed the fishing expedition to pursue the disease’s origin.

In June 1990, Dennis Villareal, M.D., a fellow in the division of bone and mineral diseases, had learned of a 27-year-old woman who later appeared in Whyte’s office complaining of severe pain in her legs. Her referring physician had taken X-rays that showed dense bones. Her medical history was not informative; almost everything appeared normal, leaving Whyte few clues on which to base a diagnosis.

Eight months later, a second patient was referred to Whyte with remarkably similar symptoms. The man also had dense bones and complained of diffuse skeletal pain that had plagued him for two years.

Whyte was perplexed. In the span of a year, two patients with dense bones had come to his office complaining of severe pain. Lab tests seemed nearly normal; they did not fit the standard profile of any known bone malady, and previous doctors had been unable to diagnose the exact source of their pain. The patients had come to Whyte, a professor of medicine, hoping that he and other bone experts at the School of Medicine could find the cause of their mysterious ailments.

At first, there was no hint that the two cases were even related. But after persistent work, Whyte uncovered a few tantalizing clues that these two patients share a single, rare disease. Past X-ray studies showed that years earlier, both patients had normal skeletons. Studies by musculoskeletal radiologist, William A. Murphy, Jr., M.D., professor of radiology, and bone pathologist, Steven L. Teitelbaum, M.D., Wilma and Roswell Messing Professor of Pathology, showed that not only were the patients’ bones growing denser, but they were being built up and broken down at twice the normal rate.

The studies didn’t explain the cause of the abnormal bone growth, but they did provide the reason for the patients’ severe pain. Whyte surmised that as the bones thickened and expanded, pain fibers anchored at the bone surface stretched and fired a pain signal. The
Michael Whyte, M.D., and William Murphy, M.D., are among collaborators tracking down the origin and cure for a newly identified disorder that accelerates bone growth.

Dramatic bone production probably caused the pain fibers to fire often.

With the pain partially explained, Whyte began to consider the nature of the prodigious bone formation. The patients’ histories offered a clue: Both patients had been intravenous drug abusers who had shared needles with others. Whyte saw that their lifestyles could have put them at risk of infection from viruses that may have been passed via contaminated needles. He decided to call Max Arens to see if Arens would test his patients’ blood for suspicious viruses.

Whyte also recalled reports suggesting that viruses may infect bone cells and cause dramatic bone thickening in other conditions. It occurred to him that perhaps the tremendous bone growth in his two patients also was caused by a virus.

In fact, the laboratory tests showed evidence of Epstein-Barr virus and hepatitis C virus in both patients. But the fishing trip that Whyte proposed to Arens snagged no evidence of Whyte’s prime suspect, a retrovirus that can incorporate its genetic information into a host’s DNA. As Arens had feared, they had reeled in more questions than answers. But, like a good fish story, the tale was getting more interesting all the time.

Based on negative virology tests, Whyte proposed a radical notion: Suppose hepatitis C virus or some unknown virus accidentally tripped the bone growth switch in these patients. This rate of new bone growth and generalized skeletal thickening appeared to be a new syndrome associated with intravenous drug use. Uncovering the cause of the disorder, Whyte says, could conceivably help people with osteoporosis who would benefit from reactivating the “on switch” for bone growth.

Before leaping to the concept of viral transmission, Whyte had carefully ruled out the possibility that these patients had a known bone disease. His review of the medical literature turned up several diseases that can increase bone mass, but none was similar to his patients’ condition.

Osteopetrosis — the name means “petrified bones” — is a rare disorder that often has a genetic origin. Researchers understand that this disorder is caused by defective bone-removing cells. Bone is constructed in layers, each layer radiating from the center outward like the rings of a tree. Construction is well regulated by at least two different cell types: osteoblasts and osteoclasts. Osteoblasts add layers to bone. They are in constant communication with osteoclasts, cells that chew away bone and recycle some of its building blocks for future use. Osteopetrosis is caused by a cessation in the orderly breakdown of bone. The layers of bone continue to be stacked one on top of another with no dismantling or recycling. The result is bones that increase in size and density. Bone biopsies of the two patients excluded this disorder.
Paget's disease, another ailment that spurs dramatic bone thickening, is more common than osteopetrosis, afflicting nearly 15 percent of the over-65 population. It is a "patchy" disorder, Whyte says, affecting different bones in different people. Some people with the disease may have an enlarging hat size, because the bones in their skull become thicker. Others may notice bowing of their legs, since the affected skeleton is actually soft. Neither of the patients showed classic signs of Paget's disease.

These patients' bones were gaining mass fast. The average human receives a new skeleton once every eight years. His patients, Whyte says, could probably accomplish the same feat in half that time.

Osteopetrosis and Paget's disease seemed to be excluded as the cause but were not a dead end. The two disorders share more than their ability to increase the density of the skeleton. Reports in medical journals provided evidence that Paget's disease and osteopetrosis may be caused by viruses. The evidence for these disorders is preliminary, Whyte cautions, but there is speculation that canine distemper virus could cause the dense bones of Paget's disease.

Osteopetrosis can be induced in chickens by certain strains of avian leukemia virus. Whyte had these findings in mind when he asked Arens to be his fishing partner.

Arens' virology report didn't support the notion that a known virus was causing the problem, unless hepatitis C is the culprit. Hepatitis C is capable of causing many symptoms, but no one has shown that the virus can switch on bone production, says Arens.

Arens admits that after Whyte's initial phone call he thought he would do the virology work and that would be the end of it. Now, a little more than a year later, he and Whyte are still fishing for the cause of this mysterious disease. "Dr. Whyte is very persistent," notes Arens.

Their discussion of the disorder is qualified by "ifs" and "maybes." The two scientists do not say the bone growth is the work of a virus — they have no proof. But suspicions are that a virus of some type is a prime candidate.

If the cause is viral, Arens suspects it will be a long time before that virus is isolated and identified. "I think it's absolutely reasonable at this point to suspect an unknown virus," he explains, "but identifying the virus is not without its problems." Arens speaks from experience. Several years ago, while on the faculty at St. Louis University School of Medicine, he was asked by a local company to help identify a virus that had run loose in its laboratories, contaminating hundreds of liters of cell cultures. "We isolated the virus, extracted the DNA, and discovered it was an adenovirus the likes of which no one had ever seen before. But finding and identifying the virus took a lot of work."

In August 1991, Whyte took his speculations on the road. He presented his findings concerning the two patients at the 13th Annual Meeting of the American Society for Bone and Mineral Research in San Diego. "Those who came by to see the poster were astounded by the density of the bones," he says. Despite the interest of researchers at the meeting, it didn't elicit the response Whyte had wanted. He'd hoped to hear that there were more cases like the two in St. Louis. "I would have thought that with the frequency of intravenous drug abuse, this disorder would be more common than just two patients who came to St. Louis. But I think the publication describing these patients will take time to percolate in the medical community," he says.

While writing on the subject, Whyte found what he thinks is a third case of this syndrome. The published report details a young woman with a history of intravenous drug abuse who developed the same type of painful diffuse bone thickening with increased skeletal turnover. Whyte writes: "It seems unlikely, but remains possible, that the intravenous drug abuse of our two patients and the similar previously reported patient is merely coincidental."

Whyte and Arens acknowledge that pinning down the cause of this enigmatic syndrome is going to take time. Whyte believes it is a new syndrome and speculates that it is associated with intravenous drug use. Arens remains less convinced, preferring to let the science speak for itself.

Whatever the cause, the two patients with this painful bone condition have benefited from their visits to the School of Medicine. Whyte and his colleagues were able to apply lessons learned from their research on bone metabolism and Paget's disease to stop the accelerated bone growth and the attendant pain. "We recognized that their dense bones were caused by rapid bone formation and rapid breakdown, much like Paget's disease," Whyte explains.

The researchers knew from basic research done at the School of Medicine that Paget's disease is probably caused by faulty communication between osteoclasts and osteoblasts. Experimental work showed that quieting the osteoclasts, or bone-breaking cells, with the hormone calcitonin would also quiet the osteoblasts, the bone-forming cells. "We were hoping the same thing would happen in our two patients," Whyte says.

There was danger involved in the therapy. Whyte explains: "Say you're rapidly breaking bone and rapidly forming bone but the net effect is that more bone is accumulating. If you shut off the bone breakers and the bone formers keep going, these people could get worse." Fortunately that hasn't happened, and now "both patients are feeling much, much better," Whyte says.
en years ago, medical scientists could identify some of the thousands of disorders that have their origins in imperfect genes, but they had no way of knowing where the responsible genes were, and they possessed little grasp of the protein products that genes are responsible for making.

Three Examples of Potential Gene Therapy

by Steve Kohler

Today, medical science is at ground zero in an explosion of knowledge about human genes, their products and the maddeningly complex ways in which they can go wrong.

The leap into tomorrow requires bringing our deepening ken of genetics to patients whose genes malfunction. Gene therapy, as such science is called, proves to be even more daunting than unraveling DNA. In addition to locating and cloning the genes involved, researchers must gain control over the DNA sequences that signal genes to express their messages and other regulators of gene behavior that may be spread out along the chromosome. Then they must devise delivery systems to get enough “good” genes into place so they can do the work that “bad” genes fail to do.

Recombinant theory is already being used to create medicines that can restore health when faulty genes don’t produce a necessary protein. And investigations are rapidly advancing gene therapy’s most ambitious vision, in which clinicians will replace genes inside specific
cells, complete with precise control.
Three examples of gene therapy research being conducted at the School of Medicine show the possibilities:

**Organ system:** Eye
**Application:** Retinitis pigmentosa
**Researchers:** David Leib, Ph.D., and Jay Pepose, M.D., Ph.D.

People who inherit the genetically transmitted disease retinitis pigmentosa (RP) frequently learn of their condition when they notice their ability to see the stars is dwindling. The disease — a slow degeneration of the eye’s retinal cells — begins at the periphery of the retina and most often affects the organ’s more sensitive light receptors, the rods, more than it does the cones, says ophthalmologist Jay Pepose, M.D., Ph.D.

Those affected usually lose their peripheral vision first and learn just how dependent they are on the edges of their sight for navigating. The disease progresses to take all but the 10 per cent of vision in the center — true tunnel vision — at which point a sufferer is legally blind. Central vision also may be affected in some forms or stages of the disease.

Not an uncommon problem, most is known about the autosomal dominant form, in which the degeneration has been identified as being a function of a deficiency in the gene that carries the code for a protein named peripherin.

For research purposes, a strain of mice called rds (for retinal degeneration, slow), has been bred, and both the defective rds gene and its correct counterpart have been cloned and sequenced. Researchers at Southwestern University have created transgenic rds mice that possess the correct form of the rds gene. “The condition is reversed completely in those mice; the degeneration is rescued,” Pepose says.

But transgenic humans are not possible, “so we need a delivery system for the correct genes,” Pepose explains. In their search for a way to deliver therapeutic genes into the cells of the eye, Pepose and his colleague, David Leib, Ph.D., have hit upon the herpes simplex virus, a vehicle well suited to the job.

“Herpes simplex will infect almost any cell type,” Leib says, “but it only persists in a neuron,” or nerve cell. The reason is most likely that nerve cells are post-mitotic; that is, they are no longer dividing. The lack of neuronal cell division allows the virus to persist in those cells for the life of the host.

When herpes virus invades a neuron, such as a retinal cell, it circularizes and enters a latent state. "But that's not a passive state," Leib points out. "It still generates a lot of RNA."

"The herpes simplex virus makes a great Trojan horse," says Leib. "We incorporate our therapeutic gene into the virus' chromosome, then infect the neural cells of the eye." Once the altered virus infects a retinal cell, it may remain latent over time, expressing the therapeutic protein that its added gene encodes.

The researchers use a crippled herpes virus that is made safe by deleting a viral gene necessary for replication. The viral particles remain infectious, but they cannot make more like themselves, because the recipe is missing. Pepose and Leib go farther still in manipulating the virus to do their work. They add a promoter from yet another gene — that for rhodopsin, the protein that allows light to be converted into electrical impulses in the eye. Common to retinal tissue and powerful, the rhodopsin promoter charges the therapeutic gene with added activity.
And they delete the virus' vhs (for virion host shutoff) gene. Normally, that gene slows a host cell's production of protein so that the virus can subvert the cellular machinery for its own use. "It shuts off the cell and kills it," Leib explains. "By knocking out the vhs gene, we reduce damage to the very cells we're wanting to fix."

How is the cocktail of altered herpes virus with its added therapeutic gene delivered? Via direct application to the target cells. A tiny injector is inserted through the clear cornea of experimental animals and inserted into the subretinal space. The "electric thumb," a device engineered for the purpose, gently delivers a microliter of virus in solution each time a foot pedal is depressed. Pepose says the delivery system can treat 90 percent of the retina in an application.

Will the genes delivered via the herpes virus produce the missing protein and rescue sensory cells in the eye? Experiments are in progress to answer that question.
A section of liver from a laboratory animal demonstrates the ability of researchers to deliver genetic payloads. The liver was treated in vivo with a retrovirus carrying an inserted gene. The gene expresses a protein that enables a cell hosting the gene to be stained; here, blue cells have been genetically modified.

cellular DNA. But Ponder is working to find the smallest amount of viral information necessary so that the genetic payload she wants to deliver can be as large as possible.

Using the retrovirus delivery system, Ponder first explored an ex vivo method of gene therapy in which cells were removed and treated in tissue culture before being reintroduced. Several difficulties plague the approach. Cells must be manipulated to get them to replicate, necessary before a retrovirus can infect them. Ponder says only about two percent of the total liver mass can be re-injected once it has been treated, "or you clog up the works." And the technique is time consuming.

A second approach, done in vivo, addresses these limitations. Ponder explains that the liver is unusual because the structure of the blood vessels there allows contact between large particles in the blood and liver cells. Thus, virus particles can be infused directly.

Ponder and her colleagues remove a large portion of the liver in lab animals to stimulate cell growth and replication in what remains. When that replication peaks, about 24 hours after surgery, she injects the genetically altered retrovirus into the portal vein. The researchers then have only five minutes in which to work, after which time oxygen deprivation causes liver cells to die.

"About one percent of the cells are infected by the virus," Ponder says. She would like to achieve better penetration, and work proceeds to produce higher levels of infection. But with the in vivo method, investigators can treat 12 animals in two days instead of just the one per week they could do using the ex vivo approach.

Ponder explores the possibility of getting each infected cell to overexpress the desired protein. Expression level is largely a function of the gene promoter installed with the desired gene. That promoter also affects the length of time for which the protein will be produced. "We now have used a gene promoter normally expressed in all cells, installed it upstream of our gene for alpha-1 antitrypsin and achieved long-term expression of the therapeutic protein," Ponder adds.

"We get reliable levels of protein production for six months," Ponder says. "While we haven’t reached therapeutic levels for alpha-1 antitrypsin deficiency, we’ve been using that serum protein primarily because we can check our results with a simple assay. The same level of expression in other genetic disorders, such as hemophilia, would be therapeutic. We're now working on protein C deficiency, and we're getting close to the genetic disease ballpark," Ponder says.
Timothy J. Ley, M.D., (seated) directs research into the reactivation of genes that normally are switched off at birth. Working with him are graduate students Bruce Hug and Mike Ulrich (right).

Organ system: Blood
Application: Hemoglobinopathies
Researcher: Timothy J. Ley, M.D.

The expression of genes is not constant; mechanisms exist to switch genes on and off. Timothy Ley, M.D., is working to understand one such mechanism. His aim is to be able to open a particular switch.

At about the time of birth, humans normally change from producing one form of hemoglobin, the fetal form, to producing another, the adult form, Ley explains. At the changeover, the gene for fetal hemoglobin is switched off and the gene for the adult version is switched on. All too often, however, the adult version of the oxygen-carrying globin protein is flawed — either misshapen or so reduced in amount as to cause serious health problems, depending on the gene flaw.

When the adult hemoglobin is malformed, one result can be sickle cell anemia. A defect that causes too little adult globin is called beta thalassemia. "An obvious strategy for treating these hemoglobinopathies," Ley says, "is to reactivate the fetal globin genes." The approach is especially attractive because a number of adults continue to express fetal hemoglobin, and they suffer no ill effects from what is called their Hereditary Persistence of Fetal Hemoglobin (HPFH).

"There is good reason to push forward," Ley says. Sickle cell patients in some parts of the U.S. experience annual health care costs that can average as much as $50,000 each. Patients suffer intermittent painful crises when misshapen hemoglobin molecules literally get stuck in blood vessels and rob tissues of oxygen. The lives of sickle cell patients are shortened.

Thalassemia is widespread, particularly in Mediterranean and Asian countries. Its standard treatment involves regular blood transfusions beginning shortly after birth. Iron removal therapy is the only way to lift the burden those transfusions bring, and patients can expect to live only into their 30s or perhaps 40s. Bone marrow transplants have been used with success, but must be done at an early age, and Ley raises the ethical question of whether a preschooeler can give truly informed consent to a procedure that carries a five to 10 percent risk of causing his or her death.

So gene therapy holds promise. But re-activating one pair of genes among the body's 100,000 is easier to explain than to do. Ley has been involved in work to find a pharmacologic agent that will safely re-activate fetal hemoglobin genes. Several have been tried, beginning with 5-azacytidine about 10 years ago and continuing to recent, widely reported work with butyrate compounds. Some of these drugs insult the bone marrow so that it begins to make more fetal hemoglobin when it recovers. Others, originally cancer drugs, block the methylation of DNA on the theory that unmethylated fetal globin genes are more active.

"But none of these agents will be the cure," Ley says candidly. "You can't get comfortable using them in children when you don't know the effects 30 or 40 years down the road. What assurance do we have that we're not also activating an oncogene that causes cancer? If you blindly manipulate blood cell 'programs' and you're wrong, you're going to get another problem, perhaps worse than the one you started with," he says.

A complicated alternative, Ley says, is first to remove some of the patient's bone marrow and purify the stem cells (from which all blood cells are derived). Stem cells account for perhaps one in every 10,000 cells in the bone marrow. Into those cells, researchers would then somehow deliver normally regulated globin genes before destroying the diseased marrow and installing the corrected version.

Several major problems must be confronted before that approach can work. Ley says that it is not yet possible to fully identify stem cells, and the genetic therapy would have to treat every one to be effective. "Perhaps most difficult," he says, "is that the gene you transfer has to be perfectly regulated. If it doesn't make enough globin, you haven't solved the problem. If it makes too much, you've created what's called alpha thalassemia, another destructive disease. So the regulation has to be precise. And that's a tall order right now."

"Still," Ley says, "that would be the very best method." And so researchers continue to pursue means to overcome the hurdles that stand in the way of replacing bad genes with good ones.
Computed tomography, or CT, has earned its place as a clinically valuable exam, but sometimes the bread-slice images it provides are not enough. Small abnormalities may lie between slices and remain undetected. Others may be obscured by the plane of view. And if the original slices do not meet diagnostic needs, the only option is to scan the patient again.

Now a new twist on conventional CT, called spiral CT, is giving radiologists and their colleagues a clearer window into the human body. Hailed as a major advance in imaging, spiral CT reduces the hit-or-miss problems of conventional CT, helps radiologists generate more diagnostically powerful images, and opens up new applications as well.

For a conventional CT exam, a donut-shaped structure called the gantry rotates an X-ray beam once around the patient for each slice. For the next slice, the gantry must be rotated back to its original position and the table moved forward in a carefully controlled increment. A computer assembles a cross-sectional image after each scan.

Conventional CT has several drawbacks, explains Jay Heiken, M.D., associate professor of radiology and co-director of the body CT section at Washington University’s Mallinckrodt Institute of Radiology. One of the biggest problems comes from respiratory motion. Patients must hold their breath during each scan to minimize motion; if breathing is inconsistent from one slice to the next, a small lung or liver lesion, for example, might be missed, he says. And, because the exams take several minutes to complete, it is sometimes impossible to collect all of the data during the limited time when contrast material provides the best enhancement. Also, the computer only holds data for each slice; “If there is something in between that needs to be imaged, we have to rescan the patient,” Heiken says.
Stuart Sagel, M.D., and Jay Heiken, M.D.

Spiral CT eliminates many of these problems, Heiken says. Mallinckrodt is one of the first sites in the country to evaluate it. Investigators Michael Vannier, M.D., professor of radiology and chief of the clinical research division; Stuart Sagel, M.D., professor of radiology, chief of the chest radiology section and co-director of the body CT section; James Brink, M.D., assistant professor of radiology, and others have studied the technology for the past 18 months.

The secret to its power is continuous scanning. An innovation called slip ring technology allows the X-ray tube and detectors within the gantry to spin around the patient continuously as the table glides forward. Because the table travels during the scanning process, the recorded X-rays plot a spiral course through the body instead of a circle. A computer stores raw X-ray data as one volume, a three-dimensional memory of the entire scanned area. The machine speeds through a complete exam — of the chest, for example — in about 30 seconds.

Because spiral CT is so fast, scans are accomplished in a single breath-hold, eliminating respiratory motion problems. The speed also means radiologists get better diagnostic information, because they can do the entire scan when contrast enhancement is at its peak, Heiken says. In addition, they can often reduce the dose of expensive contrast material by approximately 50 percent in chest scans and 25 percent in abdominal scans without reducing image quality.

After a scan, the computer can construct a set of slice images at any interval the radiologist chooses, typically from 2 to 10 mm. If necessary, the radiologist can go back to the computer’s data set and generate thinner slices even after the patient has gone home. It also is possible to compose three-dimensional images and images in any plane; when a transaxial cross section is difficult to interpret, an image reconstructed in a longitudinal plane often provides more information, Heiken says. Multiplanar and 3-D images were possible with conventional CT, but inconsistencies from slice to slice limited their quality, he adds.

Although spiral CT is still considered investigational, clinical studies are uncovering its practical benefits. Studies show spiral CT finds more small lesions in the liver than conventional techniques, Heiken says. At Mallinckrodt, spiral CT is used routinely for exams of the pancreas and for many exams of the neck, chest and abdomen. “We are generating diagnostic images with spiral CT that were not possible before.

On the left, a conventional, invasive arteriogram. On the right, a 3-dimensional, color-enhanced reconstruction produced via spiral CT. The spine is in green; the left carotid artery is in yellow, showing the blockage of the internal carotid that should supply oxygen to the brain. The right carotid artery, in red and not blocked, shows both branches.
ing bile duct obstruction. Similar benefits are possible for imaging blood vessels that supply the kidneys, Heiken says. Preliminary work shows spiral CT may be valuable for imaging blockage and narrowing in the carotid arteries, the vessels that lead from the aorta to the head, says Christopher Moran, M.D., assistant professor of radiology. He uses scan data to generate 3-D color images. “The information they provide is similar to angiograms,” he says. Spiral CT also shows promise for imaging aneurysms in the head, he adds.

Kevin McEnery, M.D., instructor of radiology, is applying spiral CT to bone fractures. He and Anthony Wilson, M.D., Ch.B., associate professor of radiology, and William Murphy, M.D., professor of radiology, are among the few researchers anywhere studying this application. “Conventional CT is used when complex fractures are difficult to accurately assess on plain X-ray or when clinicians need more detailed information regarding the fracture,” McEnery says. “For musculoskeletal CT imaging, when we want to create high quality, 3-D images or multiplanar reconstructions, many thin sections are necessary.” With standard CT, the exam could take 20 minutes or longer. “A patient who is in pain usually can’t be expected to hold still that long,” he says. Even subtle movements cause misalignment of the slices and degrade the images.

“We are excited about spiral CT. We can shorten examination times, reduce the radiation dose to the patient and obtain better data because there is much less chance of a patient moving during an examination that lasts only 30 seconds,” he says.

Another likely application will be helping surgeons zero in on targets with 3-D and multiplanar images. It also may benefit children, trauma patients and others who have difficulty following breathing instructions, Heiken says. And short scan times are a plus for unstable patients, McEnery adds. “As soon as the scan is done, the patient can go right back to intensive care, even though we still are working on the exam at the computer,” he says.

Washington University is one of five schools advising spiral CT’s developer, Siemens Medical Systems, about future refinements. Studies by Brink and others are helping define the technical parameters that generate the best results. And Vannier is developing better computer algorithms to turn raw scan data into meaningful pictures.

According to Vannier, in the future it is likely that spiral CT will replace the conventional method, and Mallinckrodt is embarked on a long-term, cooperative development plan to refine and improve CT imaging. “Eventually, this will be the way routine chest and abdominal CT is done. I would estimate that within five to 10 years, all major medical institutions will be using spiral CT routinely for body imaging,” Heiken predicts.
In October of 1992, Edwin Krebs, M.D. '43, shared the Nobel Prize in Physiology or Medicine for research on reversible protein phosphorylation, a crucial process that regulates many enzymes and greatly affects cell growth and differentiation. This most recent laureate began his distinguished career 47 years ago in the laboratory of Carl and Gerty Cori, who themselves shared the 1947 Nobel Prize. The connecting link is a rare intellectual phenomenon: a generation of Cori-inspired research excellence that has flourished for nearly 50 years.

Krebs belonged to a group of brilliant young scientists who launched their careers under the Coris’ auspices. Among them, Krebs and the late Earl Sutherland, M.D. '42, started research as medical students. While Sutherland assisted the Coris, Krebs worked in Philip Shaffer’s laboratory and later held a postdoctoral fellowship with the Coris from 1946 to 1948. Like Sutherland, who won the 1971 Nobel Prize for discovering cyclic AMP, Krebs followed a line of inquiry clearly opened by the Coris’ research. Another alumnus of what might be called “the Cori School,” Arthur Kornberg, a 1969 Nobel laureate for research on DNA replication, described their laboratory as, “a haven for ambitious, gifted people from all over....right after the war it was the liveliest enzymology lab in the world.” Yet, he notes regretfully, “My students are now totally unaware of the work and spirit of Carl and Gerty Cori and of their guiding influence on my generation of biochemists.”
Krebs’ 1992 prize is the most recent sign of the Coris’ guiding influence. They generated future research excellence by nurturing young scientists in an extraordinary laboratory environment. Though Gerty Cori died in 1957 and Carl Cori in 1984, their scientific legacy remains vibrant. They are among those few scientists to achieve two kinds of intellectual immortality — not only through their own discoveries but through those of their students. By both measures, the Coris’ record is remarkable.

Their collaboration began when they were medical students in Vienna, where they received medical degrees in 1920. In what Carl Cori later called “the doctors’ dilemma,” they realized that post-war prospects for finding two good positions in the same place were poor. The years 1920-21 were a time of near starvation in Vienna; while working as a pediatric intern, Gerty Cori developed symptoms of vitamin A deficiency. Although Carl Cori managed to get a job in Graz, he later described the atmo-
Edwin Krebs received the Nobel Prize last year. He was a research fellow in the Department of Biochemistry from 1946 to 1948 after receiving his medical degree from the school in 1943.

Nonetheless, they persisted in working together.

In 1931, their most fruitful years began in the Department of Pharmacology at the School of Medicine. Despite nepotism rules then in force, Dean Philip Shaffer was wise enough to welcome them as a team. As head of pharmacology, Carl Cori carried major administrative and teaching responsibilities. Nonetheless, he continued research with Gerty Cori (who received an appointment as research fellow). He was well aware that, as he later put it, “a most exciting period in biochemistry had begun to unfold...all previous expectations about the rate of development of biochemistry were surpassed.”

The Coris played a leading role in that accelerated development. Between 1930 and 1935, they published a series of papers analyzing what became known as “the Cori cycle” — elucidating the mechanism of blood glucose regulation. While their work opened up several other areas of research, a decision to focus on glycogenolysis proved wise, for it was the most fruitful field of study.

Arthur Kornberg has provided a penetrating description of their approach: “Carl and Gerty had the experimental gifts and wisdom to extend physiological studies of whole animals and organs to crude cell extracts and, finally, to purified enzymes...while teaching themselves and their students how to examine the molecular shapes and operations of enzymes, they never relinquished their devotion to understanding the function and hormonal control of enzymes in the intact animal.”

In 1947, the Coris shared the Nobel Prize with Bernardo Houssay for research on the catalytic conversion of glycogen. At the Nobel dinner, Carl Cori referred to collaborating with his wife: “Our efforts have been largely complementary, and one without the other would not have gone so far as in

Luis F. LeLoir, Nobelist in Chemistry in 1970, received the prize for his discovery of sugar nucleotides and their role in the biosynthesis of carbohydrates. He was a research assistant to the Coris in 1943.

Arthur Kornberg (left) and Severo Ochoa, Nobel Prize winners in 1959, discovered the mechanisms in the biosynthesis of ribonucleic acid and deoxyribonucleic acid. Ochoa worked in the Coris’ lab in 1941 and 1942; Kornberg was a visiting investigator there in 1947.
In describing their laboratory work, a biographer noted, "The manual labor and tedium of these experiments were considerable. Collaborators were few in number by present-day standards, and automation was nonexistent."

Despite these difficulties, the Coris always attracted young scientists to their laboratory. In his 1971 Nobel lecture, Earl Sutherland recalled: "When I returned to St. Louis after medical service in World War II, I was undecided as to whether I should enter medical practice or go into research. Cori convinced me, not so much by anything he said so much as by his example, that research was the right direction to take." In fact, Sutherland had co-authored a 1941 article (his first) with Carl Cori while still a medical student. His retrospective view is telling, for it reveals how the Cori-created laboratory environment shaped his future: "I believe that kind of stimulating environment, with the necessary critical mass of young and talented investigators, with the opportunity for the free exchange of ideas, is an important ingredient in the making of scientific progress." This acknowledgment meant enough for Cori to quote it in a posthumous National Academy biography of his former student.

Washington University Chancellor William H. Danforth, M.D., also was among those who worked in the Cori lab and had the course of his life affected by the association. At Carl Cori’s memorial service, on November 16, 1984, Danforth said, "The Cori department was no research factory with people following detailed protocol laid out by others; it was a collection of extremely talented individuals doing their own work with their own hands. In that environment, sinking was unthinkable. I felt privileged to be present...."

What was the magic of the Coris’ lab? Sutherland identified two crucial ingredients: a critical mass of talented young scientists and the free exchange of ideas. By today’s standards, their laboratory was small and modest, but the level of intellectual activity and scientific discourse was extraordinary. Severo Ochoa, a 1959 Nobel laureate who worked there in the early 1940s, noted that “everyone was invited to comment on papers before publication.”

As Krebs recently recalled: “The training I received in the Coris’ laboratory as a postdoctoral fellow provided me with the actual tools that I needed to get started.... By ‘tools’ I’m referring not just to techniques but also to a host of other things that go into research — inquisitiveness, thoroughness, breadth of interests and hard work. Gerty Cori’s highest praise for someone was to refer to him or her as a ‘good worker.’...The actual scientific contributions of the Coris served as the basis for what was to become my major life’s work.... My own research was built on the foundation that they laid.”

After the Coris’ 1947 move to the Department of Biochemistry, their research group grew considerably. Even so, the atmosphere of mutual collaboration and collegial support remained. Enriched by the experience, former laboratory members would make independent contributions to knowledge in universities across the country and around the world.

In 1953, Gerty Cori wrote: “For a research worker, the unforgettable moments of his life are those rare ones which come after years of plodding work, when the veil over nature’s secret seems suddenly to lift and what was dark and chaotic appears in a clear and beautiful light and pattern....” Thanks to formative years in the Coris’ research enterprise, many other scientists have experienced those moments.
The worldwide AIDS epidemic was the first epidemic to arise during the modern era of human rights. As a result, it is not surprising that the dialogue between public health and human rights perspectives has been complex and sometimes difficult. Yet, through this experience, a clearer understanding of the inextricable linkage between health and human rights has led to the creation of a new field of academic research, teaching and practice — and to the world’s first center focusing on this critical relationship at the Harvard School of Public Health.

The modern era of human rights started after World War II, with the approval by the United Nations General Assembly of the Universal Declaration of Human Rights. Briefly yet powerfully, the universal declaration responded to the atrocities of Nazi Germany with a clear statement that all people are born with rights that adhere to them simply because they are human and that governments cannot take away. Since the adoption of the declaration in 1948, an important foundation of documents and institutions and a network of nongovernmental organizations have been created to explore the meaning and to work to ensure respect for the entire range of human rights.

I think my own experience is somewhat typical. I never encountered the idea of human rights in any formal sense during either my medical or public health training. Indeed, most physicians are unfamiliar with the basic concepts, the documents, the institutions and the practices of modern human rights. Yet, as I hope to demonstrate, there are practical and powerful reasons — beyond simply being an educated person — for physicians and other health workers to become literate in human rights.

Back for a moment to the AIDS pandemic. During the early years, as policies and guidelines for preventing HIV transmission were developed and as tools such as the HIV serologic test became available, direct conflicts arose between public health experts and human rights advocates. Health officials often acted as if health objectives (preventing HIV spread) and human rights objectives (protecting the rights and dignity of the individual) were at loggerheads.

For example, some public health officials promoted mandatory screening for HIV infection, while rights advocates resisted practices which threatened individual freedoms. In the end, the human rights viewpoint generally prevailed, as health officials came to the pragmatic conclusion that if the people they wanted to reach with education about HIV were punished or threatened, they would go underground and not participate in prevention programs.

However, as the pandemic intensified and spread to countries worldwide, another dimension in the relationship between health and human rights emerged. Let me explain using an example: In parts of Eastern Africa today, monogamous, married women are becoming infected with HIV. Their risk factor is their powerlessness to influence their husband’s sexual behavior. The inferior role and low status accorded to women results in their inability to say “no” to unwanted or unprotected sexual intercourse. Thus, despite their knowledge about HIV/AIDS and even despite the availability of condoms, these women face a choice between refusing sex, with the likelihood of physical violence and divorce (leading basically to civil and economic death), and risking HIV infection.

In response to this situation, women’s organizations are working to reform the laws and customs governing property distribution after divorce. If civil and economic survival following divorce can be assured, HIV prevention will be helped much more than it would be by the distribution of additional condoms or brochures on AIDS. The general message from this specific example is clear: The fact of being marginalized, stigmatized or discriminated against in society is at the basis of an increased risk of being exposed to HIV.

Once it is clear that discrimination increases vulnerability to HIV — through having less access to information, services and support, or by being less able to put into practice the practical implications of prevention messages — the way for-
even these impacts are often declared conflicts? It is understood. Still another example involves rape during warfare or undeclared conflict. The tragedy in Bosnia is particularly abhorrent because rape has apparently been a systematic and deliberate policy. But how much is known about the frequency and incidence and consequences of rape during other conflict situations, including insurgencies and various undeclared conflicts? It is important to document the health consequences of human rights abuses, systematically and carefully, in order to understand better how to prevent their occurrence and to ameliorate their impact.

A second dimension of the health-human rights relationship involves the ways in which health policies, programs and practices can have adverse effects on human rights. For example, the practices of quarantine and isolation are part of the lexicon of public health responses to epidemic disease. But these practices violate individual rights. How effective is isolation, and what are its direct and hidden costs? Is the evidence strong enough to justify burdening human rights? Before jumping of human rights as legitimate concerns require that health workers become human-rights literate.

The third dimension returns to the recognition that social justice -- or to put the matter negatively, societal discrimination -- is critical to efforts to promote health. While the general relationship between health and rights -- such as the right to information, to education, to recognition as a person before the law, to freedom of movement, to the right to marry and found a family, to freedom of opinion and expression -- is clear, the mechanisms and interactions need to be better understood.

Finally, what is the meaning of the right to health? The right to health goes beyond access to quality health care, although this would be a great achievement for American society. The preamble to the constitution of the World Health Organization states that people have a right to the highest attainable standard of health, and that this is fundamental to world peace and security. At a larger level, the AIDS pandemic demonstrates the extent of global health-interdependence: An obscure event somewhere rapidly became a health crisis here and around the world.

Thanks to the generosity of the Swiss-based Association Francois-Xavier Bagnoud, the first academic center to focus exclusively on health and human rights was established in January 1993 at Harvard. The Francois-Xavier Bagnoud Center for Health and Human Rights (named after the young Swiss helicopter pilot who died on a rescue mission in West Africa in 1986) will link the academic strengths of research and teaching to field work that addresses real public health problems.

For me, the discovery of the inextricable relationships between health and human rights has been a gradual process, based on my work to fight epidemic disease and to promote health. I believe that the pragmatic idealism of physicians will add tremendous strength to a growing global capacity to prevent disease and promote health, as we seek to put health and human rights at the center of our human commitment.

In the modern world, the existence and acknowledgment of human rights as legitimate concerns require that health workers become human-rights literate.
The office of Leopold Hofstatter, M.D., is simple and tidy, almost modest. When he’s not there, two objects dominate the small space: a Webster’s unabridged dictionary on a desk stand and a large painting on the wall opposite.

The dictionary is symbolic of Hofstatter’s close acquaintance with language and the breadth of his interests. The painting, done by his first wife, Lilli, is more intimately significant. The portrait’s creator aside, it is the subject — a young man unmistakably with a mental illness, his eyes closed and a painfully blank expression on his pale face — that embodies Hofstatter’s dedication to service to others.

At 91 and sincerely modest, he clearly is uncomfortable being the subject of an interview. “I am just an ordinary human being, nothing extra,” he says, though he has influenced more than a half-century of psychiatry, worked to improve the lot of psychiatric patients, pioneered more restricted psychosurgical techniques and been named a fellow in the American Association for the Advancement of Science in honor of his contributions.

For almost a century now, his preference has been to stay busy, keeping out of the Bible more appealing and accessible to others.

During the hard days of World War I, Hofstatter preserved food for his family and applied a method by which their meals could be cooked, despite a shortage of gas for the stove. Young Leopold built a super-insulated chest that kept food cooking for four hours while he was at waltz and tango class with his sisters. “We’d come home to have rice boiled in milk with chocolate powder on top,” he says, delighted at the memory of having done well in adversity.

“I always have a project to work on,” Hofstatter says. He made a doorbell and the crude battery to power it for the apartment building his family occupied in Vienna. The building was constructed before the siege of Vienna by Turkish troops in 1683 and had no provision for electrical wires. But Hofstatter knew his family would appreciate the convenience of a doorbell, so he created one. His projects were done on the side while studying Latin, French and English in school, Italian, Spanish, Russian and Croatian on his own.

A sense of innovation inspired by common sense also has infused Hofstatter’s professional life and its projects. He was steered toward medicine by its purpose of serving people directly. A strong sense of anti-militarism born of the horror of World War I and his uncle’s duty as commander of a flame-thrower unit bolstered that choice.

Out of respect for his patients as human beings, Hofstatter years later was responsible for limiting the extent of surgery to the fron-
At every opportunity, he improved psychiatric patients’ morale by increasing the level of respect shown to them.

In early 1938, Hitler’s armies marched into Vienna. The date was March 11, Hofstatter’s birthday. He and Lilli soon left and shortly thereafter settled in St. Louis, where Hofstatter had obtained a research fellowship in neurosurgery with Ernest Sachs at the medical school. He taught applied neuroanatomy and, later, psychiatry to medical students.

During his long involvement in psychiatry, Hofstatter has witnessed many changes. His early specialty of psychosurgery is little practiced since the advent of psychotropic drugs. The paternalistic attitude that early psychiatrists sometimes adopted toward their patients is gone. Insulin therapy, which Hofstatter calls "a fraud from the beginning," was for a while accepted beyond anyone’s imagination. And hydrotherapy “has been given up, although it is beneficial,” he says.

“Some of the conditions that used to be common are almost unknown today,” he says. “For example, take congenital syphilis. Now, we treat syphilis early and effectively, so it no longer is passed along. I saw many tragic instances of general paresis of the insane, another rare condition today. We stopped its progression, but we couldn’t bring life back to the cells killed by invading spirochetes,” is his sad observation.

When he met von Economo, the scientist had contracted with the Soviet government to preserve for future study the brains of elite thinkers after their deaths. The plan was to examine the brain tissue microscopically to discover the source of their genius.

“Those people were completely unaware of the chemical and electrical processes that occur in cerebral activity, and there was very little to be learned from histological studies,” Hofstatter says.

Through it all, Hofstatter has kept pace with change. Today, he follows the development and application of brain visualization techniques like positron emission tomography (PET) and magnetic resonance imaging (MRI). He is particularly interested in applying them to the study of the effects of early childhood experiences on myelination and on social behavior. And he participates in a project for the St. Louis Science Center that will include history’s many great thinkers, writers, composers and others who have suffered from mental illnesses.

He spends part of his time caring for and playing the piano for his wife, Theresa, herself a pianist. On most days, Hofstatter goes to his small office to work on his projects. He repeatedly ponders one question: “I’ve always wondered and been surprised at the trust, confidence and respect shown me by my family, colleagues and superiors. I was fortunate to have the best teachers and examples to learn from and to be inspired by. I happened to stumble on a few things. I keep myself going. I just can’t help being interested,” he says, shifting the dictionary to sit squarely on his desk.

Hofstatter characteristically has avoided honors and awards, declining to join even most professional societies. Other rewards have been more important. To illustrate, he tells the story of how, when Lilli’s painting of the mental patient had been hanging on his wall for some time, he encountered the man in the portrait. Working as an elevator operator, the man had been treated successfully. “That’s what gives me satisfaction,” he says.
The Coleman Foundation Symposium, presented Friday, February 5, treated the subject “Molecular Oncology: Novel Approaches to Understanding and Treatment.” Among the dignitaries on hand were (left to right): Michael W. Hennessy, vice-president of The Coleman Foundation; John E. Hughes, president of The Coleman Foundation; Thomas F. Deuel, M.D., symposium organizer and moderator of the morning session; Jean D. Thorne, executive director of the foundation, and William A. Peck, M.D., executive vice chancellor and dean of the medical school. The Coleman Foundation Symposium, presented annually, rotates among six midwestern medical schools and focuses on recent discoveries in basic cancer research. Located in Chicago, the foundation has been a continuous supporter of the medical school.

During his career, Hodges organized radiology departments at the University of Chicago and the University of Florida, trained leaders in the field and developed innovative technological advancements, such as the phototimer. He taught physiology and worked as a Roentgenologist in China and returned to the Orient after his retirement.

The RSNA meeting, convened each year in Chicago, is the single largest scientific meeting held in the country.


Sixteen such scholarships had been established. The scholarships are the school’s major merit-based scholarship program funded by private support. Funded partially by annual gifts from alumni, former residents and other donors, they recognize beloved teachers. Each named scholarship provides a first-year recipient with $10,000 toward tuition costs. The medical school then matches the grant up to the full amount of tuition. The scholarships continue for the four years of medical education.

Leonard Berg, M.D., joined the faculty in 1955 as an instructor in clinical neurology and was named professor in 1972. Today, he is director of the Alzheimer’s Disease Research Center.

Robert C. Drews, M.D., professor of ophthalmology, has been on the clinical staff since 1966. In 1979, he served as the president of WUMCAA.

John Kissane, M.D., joined the faculty in 1958 and is professor of pathology in pediatrics. In 1970, he was selected Teacher of the Year by the graduating class.

J. Neal Middelkamp, M.D., professor of pediatrics, has been on the faculty since 1953. He was honored with an Alumni/Faculty Award from WUMCAA in 1988.

Established in 1989 by WUMCAA, the named scholarships are not based on financial need but on academic merit and the exceptional personal qualities required for the successful practice of medicine.

The School of Medicine has received a $1.35 million donation to fund research in the division of pulmonary and critical care medicine. The donation comes from the trust of Martin W. Schaefer, a Belleville IL native, who died in 1991 from emphysema, a common respiratory disease that destroys the lungs by causing inflammation of the connective tissue framework. Schaefer hoped a trust would further research and aid in the development of new treatments.

“Emphysema and other associated severe respiratory disorders constitute a group of diseases affecting an increasing segment of our adult and aging population,”

Schaefer Trust Donates $1.35 Million
David M. Kipnis, M.D., distinguished university professor in the Department of Internal Medicine, says, "The ability to expand our research activities in understanding the pathological events leading to these disorders and to devise mechanism-based therapeutic strategies to treat them represents an extraordinary opportunity for our scientists engaged in this area of clinical investigation."

Schaefer was born July 16, 1923, and attended public school in Belleville. He was drafted into the U.S. Army in 1942 and discharged in 1946, after which he joined the Army Reserve. He was called back into service during the Korean conflict and opted for a military career at the end of that war. He retired as a colonel in 1970.

The respiratory and critical care division is known for its research in asthma and pulmonary obstructive disease and has the largest lung transplant program in the world. The division director is Michael J. Holtzman, M.D.

AOA Holds Banquet

Leonard Slatkin, music director and conductor of the St. Louis Symphony Orchestra, was the featured speaker at the annual initiation banquet of the Washington University Chapter of Alpha Omega Alpha, held at the University Club on Wednesday, January 27.

Nearly 200 members and guests of the chapter attended the induction of 20 members into the medical honor society, the president of which is Kenneth M. Ludmerer, M.D.


Each year, the chapter elects one new faculty member and one new alumnus. This year, the new faculty member is Patricia L. Cole, M.D., assistant professor of medicine and associate dean for student affairs. The new alumnus is Alan J. Tiefenbrunn, M.D., associate professor of medicine.

AOA councilor John D. Davidson, M.D., coordinated the banquet arrangements that included entertainment by a string quartet composed of school of medicine students: Jacqueline Hoffman and Soham Roy from the Class of 1995 and Nicole Willeumier and Adam Eaton from the Class of 1996.

The AOA chapter will host visiting professor Al Tarlov, M.D., on April 22 and 23. Tarlov, of the division of health improvement of the Health Institute of the New England Medical Center, Boston, is expected to speak on health care reform.

Bequest Will Fund Arthritis Research

Washington University has received a $2 million bequest from the estate of Audrey L. Levin, according to an announcement by Chancellor William H. Danforth, M.D.

The bequest will establish an endowment in the Department of Medicine to fund one, possibly two, chairs to further research into arthritis. Mrs. Levin and her husband, the late Sam J. Levin, were internationally recognized philanthropists and art collectors. They contributed many works of art to museums in Israel and the United States, including paintings and sculptures to St. Louis University, Washington University and the St. Louis Art Museum.

Mrs. Levin was the founder of Audrey Levin Realtors, a successful real estate firm specializing in commercial property. She was a member of Washington University's William Greenleaf Eliot Society.

Danforth has called her one of her generation's great benefactors: "She showed us how to enjoy life's gifts while sharing them with others. I am thankful that she chose Washington University as a partner in doing good for the generations ahead."

Gervais D. Smith, M.D. '22

Gervais D. Smith, M.D. '22, worked as a general practitioner in Bolivar MO for 66 years. Now 96, he lives in a healthcare facility in Springfield where his wife of 52 years spends the day with him. She writes that he "has always been very proud to be a graduate of Washington University."

Joseph B. Kendis, M.D. '33, writes that he retired about five years ago and is "living the easy life now," after many years working in...
alcoholism and drug abuse both in private practice and at the Hyland Center at St. Anthony's Hospital in St. Louis.

Kenneth M. Amlin, M.D. '35, has moved to San Mateo CA after living in Arnold CA, at an altitude of 4,000 feet in the Sierra Nevada, for 21 years. He writes that he was "tired of being snowbound after heavy storms." He would like to hear from his classmates at 75 W. 5th Ave., San Mateo CA 94402.

E. Norris Robertson, M.D. '37, sends word that he and his wife, Mary, have been married for 56 years, residing in Oklahoma since the end of World War II. The couple has one son and one daughter, two grandsons and two granddaughters. Robertson is engaged in the private practice of ophthalmology and holds the rank of clinical professor of ophthalmology at the University of Oklahoma Health Center.

Harry E. Lichtwardt, M.D. '43 (December), retired from active practice in urology nine years ago when he was working as chairman of the Department of Urology at William Beaumont Hospital in Royal Oak MI, one of the 10 largest admitting hospitals in the nation. He serves on the Executive Committee of the American Urological Association and divides his time between Orchard Lake MI, and Naples FL. He and his wife, Genevieve, also visit their three grandchildren and two sons in California and Montana.

James O. Davis, M.D. '45, Ph. D., received the Distinguished Alumni Award from the College of Arts and Sciences at the University of Missouri on February 19. Davis, who retired in 1982, worked for many years at the National Heart Institute and did research that led to the development of enzyme inhibitors used in the treatment of heart disease. He served as chairman of the Department of Physiology at the University of Missouri beginning in 1966, and a professorship in cardiovascular research is established in his name there.

Robert H. Tanner, M.D. '47, has received the special service award from Memorial Community Hospital in Jefferson City MO. The award is presented for outstanding service to the hospital, the community and the surrounding area. A family practitioner, Tanner is a member of the medical staff at Memorial Community Hospital, served on the utilization review committee and the board of trustees. He is a life member of the hospital's board of governors and has served as president, vice-president and secretary/treasurer of the medical staffs at Memorial and St. Marys Health Center.

Lowell A. Gess, M.D. '51, reports that he "emerged unscathed from a military coup in Sierra Leone, West Africa," and planned to do more eye surgery at the Kissy UMC Eye Hospital in Freetown during January, February and March of this year.

Marvin E. Levin, M.D. '51, and Lawrence W. O'Neal, M.D. '46, have just published the fifth edition of the text The Diabetic Foot. The third editor is John H. Bowker, M.D., of the University of Miami School of Medicine. Recently, Levin was a visiting professor in Cairo as a guest of the Egyptian Diabetes Care Association.

Philip S. Crossen, M.D. '54, has retired from active practice but continues as medical director at Planned Parenthood of Lexington KY. He writes, "Doesn't pay too well, but it is very satisfying, and they don't fire me when we are away for extended time to Michigan in summer and Florida in winter."

Mary Ann Reynolds, M.D. '62, retired from private practice on December 31, 1992. Harry Reynolds, M.D. '60, continues to work part-time as a locum tenens general surgeon. They write that they hope to travel both in the U.S. and abroad. The couple resides in Turlock CA.

Jim Murdock, M.D. '63, and his wife (Marilyn) and children live in Eugene OR on a small mountain with Arabian horses, German shepherd dogs and Siamese cats. Jim is active in the surgical community at Sacred Heart General Hospital and keeps up his music, having performed with the Eugene Symphony. The couple has three daughters; Lynn recently graduated from Carleton, Elizabeth is a junior at Yale, and Katie is in her first year at Sewanee.

David L. Dunner, M.D. '65, is president of the Society of Biological Psychiatry for 1992-'93. Dunner is professor and vice chairman for clinical services in the Department of Psychiatry and Behavioral Sciences at the University of Washington. He edited the recent publication, Current Psychiatric Therapy (W.B. Saunders, Co., 1993). His wife, Peggy Zolbert Dunner, OT '64, operates an antique jewelry business near Seattle.

David C. Bisno, M.D. '66, sold his Atlanta ophthalmology practice in the spring
of 1992 and has since been enjoying studying the history of science at Dartmouth College and Harvard University. He reports that his daughter is an "aspiring, although unemployed," actress, and his son is a third-year rabbinical student.

Steven B. Raffin, M.D. '68, wrote a chapter for the 16th edition of the Merck Manual.

Charles L. Rich, M.D. '69, has assumed the position of chairperson of the Department of Psychiatry at the University of South Alabama. His previous position was with the State University of New York at Stony Brook. He also is editor-in-chief of the Annals of Clinical Psychiatry and was listed recently in the book, The Best Doctors in America.

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Wilfred G. Ellis, M.D. '82, has been awarded the AIDS Service Award from the State of Ohio for 1992. Ellis has been an advocate for his patients and committed to the local AIDS Task Force, as well as being an early supporter of the Ryan White initiative. He is chairman of infectious diseases at the St. Rita's Medical Center in Lima OH.

FORMER HOUSE STAFF

Robert Maltz, M.D., FHS in otolaryngology, has been appointed director of the Department of Otolaryngology at Jewish Hospital in Cincinnati. He also was elected recently to the Council of the Cincinnati Academy of Medicine.

John S. Spratt, M.D., FHS in surgery, is a Naval Reserve captain and a clinical professor of surgery at the Uniformed Services University for the Health Sciences in Bethesda MD. He recently attended the annual meeting and luncheon of the editorial advisory board and reviewers for the journal Military Medicine.

Fremont P. Wirth, M.D., FHS in neurosurgery, has been appointed a director of the American Board of Neurological Surgeons. The 14-member board, organized in 1940, is the certifying board for neurosurgeons in the United States. Wirth practices in Savannah GA, where he currently serves as secretary of the Georgia Medical Society.

Larry L. Mathis, HA '72, is president and chief executive officer of the Methodist Hospital System and its 10 member corporations, including The Methodist Hospital, a 1,527-bed tertiary care, education and research facility located in the Texas Medical Center in Houston. He is chairman-elect of the board of trustees of the American Hospital Association. Healthweek magazine named him one of 25 top multi, alliance and buying group executives in the nation, and Business Week named him one of the five best managers in nonprofit health services in the U.S.

Larry L. Mathis, HA '72

Calvin R. Robinson, HA '76

Calvin R. Robinson, HA '76, has been appointed to the position of vice president of operations for Meridia Huron Hospital in Cleveland. He resides in Cleveland Heights.

Jim Humphrey, HA '87, and his wife, Loraine, are expecting their first child in May. Jim is director of managed care at Corona Medical Center in Corona CA.

Rose J. (Catron) Flynn, NU '51, retired at the end of January from the Baptist Memorial Hospital System in San Antonio TX, after working there for 21 years. She says her plans are indefinite, but that she and her husband have lots to keep them busy, including enjoying their grandchildren.

Martha Sue Sublette Birk, OT '33, has lived and worked in Decatur IL since she married Carl P. Birk, M.D. '34, who practiced medicine there for 51 years. The couple raised three children and reports that many members of their extended family are Washington University alumni.

Anne Rothstein Anderson, OT '77, her husband, Jim, and her son, Paul, live in the shadow of Yosemite's high peaks in Sonora CA. Anne owns and operates a small therapy practice specializing in geriatric rehabilitation.

Mrs. George Basinger, PT '53, has completed 15 years as the director of physical therapy at the East Texas Medical Center — Pittsburg. She continues to serve the East Texas Regional Healthcare System by extending its physical therapy service to many other northeast Texas medical facilities.
IN MEMORIAM

William J. Harrington, M.D., former director of the division of hematology here and an internationally renowned blood specialist who made major discoveries about the mechanisms of blood disorders from experiments he performed on himself, died at his home in Miami in October. He was 68 years old.

Harrington apparently died while repairing a generator outside his home that had been without electricity and running water since Hurricane Andrew hit the area the week before.

M.K. King, M.D., Danforth Professor of Preventive Medicine and former dean of the medical school, says Harrington “was Carl Moore’s greatest pupil.” Both men performed experiments on themselves in the interest of advancing medical knowledge. In 1950, Harrington discovered that a substance in the blood of individuals with idiopathic thrombocytopenia purpura (ITP) destroyed their platelets. He made the discovery by injecting a pint of an ITP patient’s blood into himself. Almost immediately, his own platelet count dropped. He was admitted to Barnes Hospital where, within a week, his platelet count returned to normal, showing that the factor that caused ITP was in the blood.

At age 28, he became the youngest member ever elected to the American Society of Clinical Investigation. Later, he moved to the University of Miami, where he founded the Center for Blood Diseases, became the chairman of the Department of Medicine and founded the Ph.D./M.D. program. For 25 years, he worked to improve medical education in Latin America, and he made house calls for as long as he practiced. Harrington earned one of 70 Mastership awards ever granted among the 60,000 members of the American College of Physicians.

He is survived by his wife, Mary, a daughter, three sons and four grandchildren.

Robert A. Huckstep, M.D. ’48, died on November 28, 1992, at his home in Farmington MO. He was 71 years old. A community leader in Farmington, Huckstep had been committed to education and had served on the local board of education and the board of trustees of Mineral Area College for 15 years. He had been instrumental in the building of Farmington Community Hospital.

Though he had officially retired, he continued to work part-time at Medical Arts Clinic in Farmington.

Among his survivors are his wife, Mary, two sons, one daughter, one brother and three grandchildren.

G. Leland Melson, M.D. ’65, professor of radiology, died of cancer on November 10 at his home in Glendale MO. He was 53.

Melson was a member of the medical school faculty for 20 years. He was highly respected for his work as a teacher and clinician, as well as for his research on abdominal ultrasound imaging.

Melson received his medical degree from Washington University in 1965 and joined the faculty in 1972 as an instructor at the School of Medicine’s Mallinckrodt Institute of Radiology. He became chief of the clinical ultrasound division in 1977 and a full professor in 1983.

He received several honors during his career, including being named a member of the medical honorary society Alpha Omega Alpha and a fellow of the American College of Radiology. In 1989, he was recognized by the St. Louis Metro Area Sonographers for his contributions to the field of ultrasound.

He published more than 50 scientific journal and textbook articles and was an active member of several professional societies. He served on the Missouri Radiological Society board of directors, as vice president of Alpha Omega Alpha’s local chapter at Washington University and as a past president of the Greater St. Louis Society of Radiologists. He also served on a consensus-development panel for the National Institutes of Health.

A memorial service was held November 13 at Salem United Methodist Church in Ladue. Among Melson’s survivors are his wife, Brenda, one daughter, two sons, his mother, and a sister.

Jack R. Rhodes, M.D. ’45, died November 2 of natural causes in Sheridan WY, while he was attending a building dedication at the Sheridan Veterans Affairs Medical Center. He was 71.

Rhodes began his general surgery practice in Sheridan in 1953 and served 30 years on the staff of Memorial Hospital there, including holding the post of chief of staff. Rhodes closed his practice in 1983, joining the staff at Sheridan VA Medical Center. He retired earlier in 1992.

Rhodes was active in Boy Scouts, his church and fraternal and professional organizations. He was an avid fisherman and traveler and had just returned from a trip to England, Scotland and Ireland. His sudden death came as a shock. Survivors include his wife, Mary Elizabeth, two daughters, five sons, a sister and 13 grandchildren.

Call For News

Members of the medical school community with news for their colleagues are invited to send a note to Ruth Bebermeyer, Medical Alumni and Development Office, Box 8049, 660 S. Euclid, St. Louis MO 63110.

Please include mention of the variety and date of your affiliation.
An awards luncheon was held in the King Center on December 8, 1992, to recognize outstanding achievements by students in the 1991-'92 academic year. Nancy E. MacDonald received the CIBA-Geigy Award for Community Service and was presented with the complete CIBA Collection of Medical Illustrations prepared by Frank H. Netter, M.D. CIBA's Kevin Clark made the presentation. Honored along with MacDonald were medical students Michele L. Francoeur, Timothy J. McCulley, Lawrence S. Kaskowitz, Michael E. Ohl, William L. Lyons, Jennifer L. Paterson, Scott M. Pinter, Corina Jo Norrbom, Catherine Bradley, Stephanie B. Cox, Ryland E. Melford, Korwyn L. Williams, Marianne Ingels, Martha S. Terry, Mathias J. Kill, Lynne M. Champagne, Mark A. Koler and Tamara L. Densmore.
The birth of Raja at the St. Louis Zoo on Sunday, December 27, was assisted by staff in the endocrine laboratory of the Department of Obstetrics and Gynecology. Several elephant births in recent years have been complicated because zoo staff could not know exactly when the calf was due. But Janet Willand, Alice Hightower and Toni Broeker of the lab tested the serum progesterone levels of Pearl, the mother elephant, regularly. And on Saturday, the 26th, when Pearl's progesterone level dropped from the 500-600 picograms per milliliter it had averaged to 119 picograms, Hightower alerted zoo veterinarians that the birth was imminent. Pearl was then monitored closely, and her early signs of labor were detected. Raja has captured the city's affection.