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Nerve Cells: Making the Right Connections

One of the most hotly debated topics in neurobiological research has centered around nerve cell connections in mature animals: To what extent, if any, are nerve-to-nerve connections malleable? The question is particularly intriguing to those who want to unravel the regulations governing the functions of nerve cells in the brain and spinal cord. But scientists' abilities to probe and prod nerve cells are limited by the cells' inaccessibility. Thus, research efforts have centered on developing a useful model of nerve cells outside the brain and spinal cord. If the rules governing the function of these model cells can be elucidated, then scientists may achieve insights as to how brain and spinal cord neurons establish interconnections.

As Washington University's Dale Purves described in *Outlook*, Spring 1984, the hardwired, computer-like scheme that is frequently cited to describe nerve cell interactions is not an accurate description of the early life of mammals. Instead, he says, nerve cell interconnections are really the result of dynamic events, in which some connections die out, and others form anew, in an ever-changing pattern.

Recently, Purves and postdoctoral fellow Robert Hadley obtained direct evidence to support this hypothesis. By examining a single nerve cell in a living animal at different time intervals, they were able to map the cell's dendritic processes — cellular extensions which receive input from other nerve cells. Some time later — up to three months — they located and photographed that same cell, visualizing it on both occasions via intracellular injection of non-toxic fluorescent dyes. Then, by comparing earlier composite photographs of that nerve cell, they were able to show that some processes had disappeared, and others had formed anew. This remarkable-sounding feat — actually finding a particular cell in an animal on two different occasions — is really not so difficult, says Hadley. A cell on the surface of a sympathetic nerve ganglion — a group of nerve cells in the animal's neck — can be recognized later by its unique size and shape. "We look for distinctive landmarks near the cell, such as blood vessels, so that we can locate the same cell later," points out Hadley.

Using this technique, Purves and Hadley were able to relocate a particular nerve cell: Armed with composite photos taken during both sets of experiments (the first ones done earlier), they create camera lucida drawings which show an entire cell and its processes in detail. A comparison of these reconstructions illustrates any changes which have occurred in the cell, as pictured here.

In creating these drawings, Hadley and Purves continue a tradition of painstaking artistic attention to detail begun a century ago by Santiago Ramón y Cajal. The latter's exquisitely detailed drawings clearly showed that each nerve cell is a discrete unit, not part of a continuous web of tissue — a theory held by leading neuroanatomists of the day. Yet Ramón y Cajal faced great difficulty. The new technology of photography was still too primitive to take pictures through a microscope. Capitalizing on and improving the staining techniques developed by Golgi, Ramón y Cajal had to mentally create a single neuron from his many different views of that cell. Compared to the techniques of Ramón y Cajal, those used by Hadley and Purves to capture neurons' dynamics seem advanced. However, a new era in neuroanatomy is about to dawn, spawned by the advent of computers. Jim Voyvodic, a graduate student working in Purves' lab, has written software that enables a computer to construct three-dimensional images of single neurons. Thus, a computer will measure changes in that nerve cell over time, eliminating the need to laboriously hand-draw a neuron's tree-like extensions.

Eventually, monitoring changes in neuron-to-neuron connections will suggest ways to elucidate the intracellular events that precipitate these alterations. Ultimately, this should lead to a better understanding of how our nervous systems change over time, as we grow and learn.
Tracking Mislabeled Molecules
Two rare lysosomal storage diseases have helped scientists solve one of the cell’s secrets: how enzymes are transported from where they’re made to where they’re needed. Children with these diseases lack a sugar “label” on their lysosomal enzymes, causing them to be routed incorrectly.

Nursing: Bedside and Beyond
No longer simply an adjunct to physicians, nurse-specialists provide a whole host of services extending beyond medical care. They have “borrowed” from the roles of physician, health educator, and social worker to carve for themselves new clinical niches that are depicted in this photoessay.

Tools of the Trade
Spinal surgery is performed with new and improved implantable systems on patients with scoliosis and other deformities. New spinal fixative systems do not sentence patients to weeks in a body cast, yet produce better results.

Beyond Cold Turkey
A treatment program for persons with chemical addictions is in place at Jewish Hospital. One of the program’s psychiatric consultants has had first-hand experience in facing — and overcoming — addiction.

Living Contact Lenses
A new surgical procedure spares certain patients from a corneal transplant or a lifetime of blurred vision because of inadequate correction from eyeglasses. Epikeratophakia has been performed on adults and children, with good results.

Studentstage: HAP
Personal Outlook: Daniel Hartl
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The Alumni Report
Silhouette: Floyd Bloom
Class Notes
two kinds of cell-specific protein antibiotics. The two kinds of cell-specific protein antibiotics could be different in their sensitivity to the different therapeutic agents.

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Cell Traffic: Ins and Outs, featured in the summer 1985 issue of Outlook, explored the work of two research teams at the School of Medicine who are mapping the route by which cells take in and transport substances.

The laboratories described in “Cell Traffic” concentrate on proteins that enter the cell from the outside and then have to be directed to the right location. But what about proteins made within the cell — what routing system directs them to the correct locations? This cell trafficking scheme is being mapped in the laboratory of Stuart Kornfeld, M.D., professor of biological chemistry and medicine.

“Many of us are interested in how proteins are targeted to their correct destination in the cell,” says Kornfeld. “Proteins have signals built into them that allow them to be shipped. We are trying to decipher these signals.”

Remarkably, some of the same mechanisms are used to sort and deliver materials from outside the cell, as well as those made within cells. And snarls in the systems can lead to crippling, even lethal, disease.

One such group of diseases has a remarkable connection with Washington University. During the last decade, several graduates of the School of Medicine, as well as current and former faculty, played pivotal roles in hypothesizing — and proving — the defects causing certain rare disorders, lysosomal storage diseases, in which undigested “garbage” accumulates and is stored in cells. Along the way, their advances disproved the prevailing theory about how these diseases occur, and generated key ideas about a cell’s workings, ideas that have been capitalized on by investigators in other fields.

Working Out the Details

How do proteins manufactured by cells get shipped to the right address? Kornfeld’s group has grappled with this problem. His research team has investigated proteins called glycoproteins. How do these proteins, bound for jobs in lysosomes — the cell’s “garbage disposals” — get to their eventual workplace in the lysosome?

“This system of targeting lysosomal enzymes for lysosomes is unique in the sorting schemes for proteins made in cells,” he points out. “Proteins destined for other locations in the cell, such as the nucleus or mitochondria, have labels consisting of amino acids, not sugars. Sugars are involved in targeting lysosomal enzymes from their site of synthesis to the lysosomes, and in the uptake and sorting of proteins presented to the cell from the outside, such as was described in the article on cell traffic.”

Kornfeld and his collaborators have been able to piece together a detailed scheme that explains how these proteins reach their cellular destination. Once shipped to lysosomes, glycoproteins assume their rightful role as lysosomal enzymes — proteins that chop up substances brought to that organelle for disposal. What’s more, the breakdown of this cellular routing system results in certain diseases.

Such breakdowns are serious: “Lysosomal enzymes are important for host defense and other functions. They destroy worn-out cellular components, remodel tissues, and degrade substances taken in by the cell,” explains Kornfeld, a hematologist on staff at Barnes Hospital. Lysosomes are crammed full of enzymes that do the dirty work of disposal. In lysosomal storage diseases, at least one of these enzymes is missing. “There’s a lysosomal storage disease associated with almost every one of these enzymes,” he adds.

“The majority of lysosomal storage diseases, like Tay-Sachs or Gaucher’s diseases, involves the absence of a single enzyme, not a whole host of enzymes,” Kornfeld continues. “But the rarest of these diseases, in which multiple enzymes are missing, have been the most fruitful in allowing us to unravel how the cell carries out sorting.”

The cell handles the logistics of sorting and shipping much like commercial express couriers. After proteins are manufactured, they go to a central sorting facility: the cell’s Golgi apparatus. The Golgi are arranged in stacks, much like pancakes. In the Golgi, sugars are removed from, and others are added to, newly synthesized proteins. All glycoproteins begin with the same sugar structure. But Kornfeld has found that lysosomal enzymes undergo further sculpting to transform their sugar component into a shipping label that will get the enzymes out of the Golgi and headed toward the lysosomes.

If any of the labelling or shipping procedures goes awry, then the lysosomes won’t have their full complement of enzymes. And when this happens, lysosomal storage diseases result.

The most deadly lysosomal disease is called I-cell disease. First identified in the late ’60s, the disease is characterized by the unusual appearance of skin cells from affected persons. The cells are crammed full of dark, dense inclusions—globs of undigested garbage. These inclusions are referred to by the name “I-cells.” I-cell disease primarily affects connective tissue, the nervous system, and organs like kidney and heart. Lysosomes of
children born with this condition lack their entire range of enzymes. Such children usually die of heart failure or pneumonia before reaching puberty.

In I-cell disease, cells do indeed make lysosomal enzymes, but the problem arises in shipping them out of the Golgi membrane. During the sorting process, the enzymes get into the wrong bin. Instead of being shipped to the lysosomes, enzymes are dumped outside the cell, which explains why serum from these children contains these errant proteins.

Leaky Lysosomes

In the early 1970s, NIH scientist Elizabeth Neufeld, Ph.D., and postdoctoral fellows Scott G. Hickman, M.D. ’70, and later, Larry Shapiro, M.D. ’71, began to study how I-cell disease originated. “At the time that Neufeld and Hickman did their work,” remembers Kornfeld, “the best explanation was the ‘leaky lysosome’ theory — the suspicion that lysosomal enzymes leaked out of the lysosomes and into the serum.”

Hickman, now assistant professor of medicine at WU, says that Neufeld had some extraordinary insights: “First, she suggested that large enzymes could be taken up by cells, and at the time, many people doubted this could happen. Second, she thought that there were actual recognition markers on these enzymes which targeted them to lysosomes. We helped to show that this recognition marker was in fact a sugar. But to be honest, we failed to come up with the exact mechanism of the disease.”

Hickman and Neufeld thought that the high levels of lysosomal enzymes in the serum of affected children meant that these proteins were secreted into the bloodstream, then later picked up by cells and somehow transported to lysosomes. In reality, says Hickman, “lysosomal enzymes are targeted directly to lysosomes after they’re produced. For the most part, they’re not secreted.” It remained for another researcher, then on the faculty of the School of Medicine, to discover this vital bit of information.

William Sly, M.D., at Children’s Hospital until January 1984, and now chairman of the Department of Biochemistry at St. Louis University, found that lysosomal enzymes have a particular shipping label, a phosphate-containing sugar, that targets them to lysosomes. Following up on Sly’s work, Neufeld was able to show that I-cell lysosomal enzymes are defective because their shipping labels are missing. The sugars on the defective enzymes are not phosphorylated, and it’s that process which tags the proteins destined for lysosomes. If I-cells are exposed to normal enzymes (enzymes with phosphorylated sugars), these glycoproteins enter the deficient cells and are shipped to the lysosomes.

The cell handles the logistics of sorting and shipping much like commercial express couriers. After proteins are manufactured, they go to a central sorting facility: the cell’s Golgi apparatus.

This information put Kornfeld’s team on the track of the cell’s shipping clerks — resident enzymes in the Golgi apparatus. Golgi enzymes catalyze the addition of phosphate to glycoproteins destined to become lysosomal enzymes.

However, the Kornfeld team’s research turned up more than cellular shipping clerks. It has helped to create, in great molecular detail, a map of the cell’s sorting system.

A System for Sorting

The Golgi’s shipping clerks are not a homogeneous work crew; some phosphorylate lysosomal enzymes, and others trim the glycoprotein’s sugar component. This two-step process produces a distinctive shipping label that is recognized by receptors in the Golgi membrane. These receptors are like cellular “barges,” picking up and steering glycoproteins from the Golgi membrane toward lysosomes. En route, each loaded receptor enters an acidic compartment where the receptor dumps its load. Sly showed that the now-bare receptor hurries back to the Golgi, while the unloaded cargo travels on to the lysosome.

But even in the best sorting systems, things can go astray. Sometimes, properly labelled enzymes destined for lysosomes are bumped along by the crowd in the Golgi and fail to connect with their receptors. Lost in a sea of proteins, they are inadvertently dumped outside the cell.

But even these can be salvaged. Properly labelled glycoproteins, even if in an abnormal location outside the cell, can be recognized by receptors that have left the Golgi for the cell’s outer membrane. These receptors recognize the errant proteins, grab them, and shuttle back to the lysosomes.

The Golgi’s enzyme shipping clerks are the culprits behind I-cell disease and another less serious lysosomal storage disease, pseudo-Hurler polydystrophy. The defect in both cases is the same: It’s in the enzyme that phosphorylates proteins destined for lysosomes. In I-cell disease, the enzyme is inactive. And in the majority of patients with pseudo-Hurler polydystrophy, the enzyme is only weakly active. “Even two percent activity can support life,” Kornfeld points out.

In the remaining patients with pseudo-Hurler polydystrophy, the defect is clear: It’s the first step in the phosphorylation process, when the Golgi enzyme “docks” with the glycoprotein destined for the lysosome. This docking positions the two proteins so that the phosphorylating enzyme can sculpt the sugar component of the glycoprotein destined for the lysosome. But in this subset of patients, the two proteins can’t dock. If a sugar chain drifts into the right position, the phosphorylating enzyme can do its job, but it can’t grab the lysosomal enzyme and maneuver it into the right position.
A Failsafe Mechanism

A surprising finding has emerged from this work. Up to now, researchers have assumed that lysosomes are all pretty much the same. But these organelles may have differences detectable to molecules. The Golgi hold two different types of receptors that ferry glycoproteins to lysosomes. These receptors might recognize different types of lysosomes — all lysosomes might not be created equal.

Working with Bernard Hoffman, a visiting scientist from France, Kornfeld has found that there are two distinct receptors that bind lysosomal enzymes via the sugar marker discovered by Sly. “Both receptors reside in the Golgi,” says Kornfeld. “The fascinating question is, why has the cell developed two receptors that bind the same ligand? Our working hypothesis is that these two receptors take lysosomal enzymes to different classes of lysosomes. That is, we’re proposing that the lysosomal system may be more complicated than people had appreciated. Not all lysosomes are identical — they may have different complements of lysosomal enzymes within them, in order to carry out different functions that lysosomes perform.

“Why don’t we find patients who have defects in the receptor?” muses Kornfeld. “Persons who can’t make the receptor should end up with the same clinical syndrome as somebody who doesn’t have the phosphorylating enzyme. I think that the answer is that there are two receptors, so if you’re missing one, the other can compensate. Two receptors provide a fail-safe mechanism, whereas if a key enzyme is knocked out, the whole system collapses.”

Screening

Both I-cell disease and pseudo-Hurler polydystrophy are autosomal recessive, so parents of affected children are carriers of the gene. “Each parent carrier has about half the normal enzyme activity,” Kornfeld says, “but the range of activity can be fairly broad.”

His laboratory is one of few in the United States to screen for the enzymatic defect in the two diseases. Physicians nationwide send samples to Kornfeld for assay. Thus, patients can be tested and accurately diagnosed, and suspected carriers can be screened, providing helpful information before they pass on a gene for lysosomal storage diseases.

Yet the development of effective clinical therapies for these diseases is not an immediate prospect, according to Kornfeld. However, he tempers his bleak outlook with optimism generated by the work in his and other labs. Very sensitive assays can effectively detect I-cell disease or pseudo-Hurler’s syndrome prenatally.

“Some indirect assays are very accurate,” Kornfeld points out. “High levels of extracellular lysosomal enzymes, and the characteristic changes in the cells — the inclusions — can show, with 98 percent probability, if the fetus is affected. Our direct enzyme assay is much faster than these current methods, and is 100 percent certain. But the current ways aren’t bad."

Physicians like Kornfeld and Hickman do not treat children with I-cell disease or pseudo-Hurler’s syndrome, yet are devoting great investigative energy to basic questions about the cell and its inner workings, delineating the glitches causing these diseases. The payoff is more than just new knowledge about these rare diseases. It extends into and outside Washington University, in countless other laboratories. Neufeld’s original hunch in the early ’70s that led to an understanding of I-cell disease also stimulated other researchers endeavoring to understand how many kinds of proteins are recognized and routed. “Now,” says Kornfeld, “many people look for signals on the protein they’re investigating, signals that allow particular proteins to be recognized and directed to the right place.”

The work on Golgi enzymes, begun by Tabas, Reitman and Vargi in Kornfeld’s lab several years ago, has also generated a ripple effect. “This work allowed researchers in many labs to dissect the Golgi apparatus,” explains Kornfeld. “Until very recently, no one had any idea where particular enzymes were located in the Golgi. Nobody knew if all its ‘pancakes’ did the same job. The work of Tabas, and later, Reitman and Vargi, prompted investigations which eventually showed that the enzymes which did the first phase of sculpting are on the bottom of the stack. The enzymes which did the intermediate jobs are in the middle, and so on. So this work has helped us to understand how the Golgi apparatus is organized.”

These basic discoveries can, in turn, generate clinically useful work. “My belief is that if you understand the pathophysiology of any disease, you’re more likely to arrive at a rational treatment,” summarizes Kornfeld. “In the end, understanding the basis of lysosomal diseases will result in rational approaches to clinical therapies. You can’t count on luck.”
Today's nurses can choose from a wealth of options not available to clinicians of an earlier era. In addition to primary nursing, nurses can select from a variety of expanded roles, both in and out of hospitals. Nurse practitioners work with some degree of independence in a private practice setting. A nurse-clinician or clinical nurse has a bachelor's degree but may opt for further education, earning a master's degree in some clinical specialty. Thus prepared, a clinical nurse-specialist can take on a variety of duties.

Not everyone is eager to embrace more independent nursing roles. One division chief wasn't sure that a nurse-specialist would be helpful; he needed some convincing.

"I began with a bias," admits Joseph J. Volpe, M.D., chief of pediatric neurology. "That bias said that physicians should carry out activities related to patient care decisions, and that nurses—even specially trained nurses—can't be expected to have the background to exert judgment in clinical situations. So, with that bias, I've been exposed to our division's nurse-specialist, Val Tasch. She has totally changed that bias, without even trying."

Volpe explains that Tasch skillfully performs duties traditionally done only by physicians, such as conducting a neurologic exam and formulating a diagnosis and reasonable plan for management of the patient's problem. "But she does other things that physicians often don't do," continues Volpe. "She patiently counsels a family, explains a child's illness and its impact on their lives and how to deal with that, gives details about treatment—items that physicians rush over."

"Clinical nurse-specialists perform many functions traditionally done by physicians," says Teresa Vietti, M.D., chief of pediatric hematology/oncology. "They measure and administer chemotherapy, perform lumbar punctures and intrathecal therapy, and monitor protocols." In addition, Vietti continues, the clinical nurse "can pick up where physicians leave. They can answer the questions parents were unable to ask the doctor, or repeat information that the parents were unable to absorb because they were in a state of shock upon hearing that their child has cancer."

Outside the hospital, the nurse-specialist can continue medical monitoring, and furnish education and support to the child and parents, as well as to the community beyond. Says Alan M. Robson, M.D., chief of pediatric nephrology: "We can cut down on hospitalization for nephrotic syndrome by educating patients about their disease.

"Illness in one family member has a tremendous impact on the whole family," concludes Robson. "If you focus only on the sick member, you do the whole family a disservice."

Clinical nurse-specialist Anne Richardson works with end-stage renal patient Michelle Stevens before surgery to implant a fistula, a prerequisite for dialysis.

Photographer Cheryl Ungar spent several months following Anne Richardson, nurse-specialist in pediatric nephrology. These pages depict a sampling of Richardson's activities as she works with physicians, patients, their families and communities. Richardson is but one of the growing community of clinicians in nursing to whom Outlook pays tribute with this photo essay.
Upper left, Richardson meets Michelle's teacher (left) so that she and Michelle's classmates have the opportunity to ask questions. Richardson finds that teachers often have misconceptions about dialysis:
"They'll say things like, 'There's no room in my classroom for the [dialysis] machine.' Teachers often feel that the students should be isolated at home, with tutors; school nurses can get panicky."

Lower left, Richardson confers with renal service physicians at Children's Hospital (from left): Michael C. Chobanian, Richardson, H. William Schnaper, and Charles P. McKay.

Left, Richardson also counsels patients like Brian Page who've had a kidney transplant. Nephrology is one of many services at Children's Hospital that enlists the help of nurse-specialists. The others include adolescent medicine, allergy/immunology, neonatology, neurology, pulmonary medicine, psychiatry, and general surgery. In addition, a clinical nurse-specialist works with all prospective in-patients and their parents. In each case, the clinical nurse-specialist performs distinctive duties, some of which are unique to a particular service.

Below, Alan Robson, chief of pediatric nephrology, says that Richardson's role in patient education has reduced hospitalization.
Like so many other things, the spinal column attracts little attention until it stops working. Its 26 small bones — ranging in size from a shot glass to a small fist — are stacked in serpentine form, each separated by a thin gasket-like seal.

Keith Bridwell surgically corrects spinal deformities arising from tumors, paralytic diseases or scoliosis.
It looks simple enough, but it's not. The hollow column and skull together form a "safe" in which the body protectively locks away all that makes us human. This bony safe insulates the transmission of electrical nerve impulses to the brain, allows us great freedom of movement — even holds our entire skeleton in place. In many ways, the spine is our pillar of strength.

No surprise, then, that some physicians have spent their lives devising better ways to promote healing of a deformed, diseased or injured spinal column. The latest techniques — including several being used at Washington University Medical Center — are surgical; new metal devices that can be implanted on the vertebral column allow quicker and better correction of some complex problems, including spinal deformities and fractures.

These simple-looking pieces of stainless steel hardware, which include rods, wires, hooks and bolts, can actually be used to reconstruct spinal columns that have been eroded by malignant tumors. Even patients with paralyzing diseases like muscular dystrophy or cerebral palsy can be helped; the instruments make their weakened spines stiffer and straighter.

"Spinal deformity surgery has really evolved in the past three to five years," says Keith H. Bridwell, M.D., assistant professor of orthopedic surgery and a spinal deformity surgeon at Barnes and Children's hospitals. "We are always looking for better ways to correct the spine and allow the patient to get back to a normal life more quickly," he says. "These newer systems are more secure, provide more and safer correction, and patients rely less on casts and braces."

Bridwell is one of a few hundred surgeons — there are more than 15,000 orthopedic surgeons in the country — who perform only these spinal surgical procedures. At present, he averages four cases a week (200 cases a year). Says Bridwell: "A spinal deformity surgeon must average at least 100 cases a year to be really good at it."

**Instruments**

The new fixation systems have evolved from the Harrington rod, developed by Paul Harrington, M.D., in the early 1960s. In the early years of spinal surgery, before the Harrington rod, surgeons used bone grafts to fuse injured or deformed bones of the spinal column with little or no additional internal support for the repair. After the operation, the patient went right to bed — sometimes for months — to give the fused vertebrae time to heal. But while the spine mended, other parts of the body deteriorated; among the most serious complications were pneumonia, muscle atrophy and depression. Many patients required subsequent operations. And the longer they stayed in bed, the longer it took them to get back on their feet. When they did get up, they had to wear a body cast — a cumbersome, uncomfortable jacket of plaster — for several more months.

The Harrington rod, a metal pole one-quarter inch in diameter with a hook on both ends, cut the recuperative bed rest to several weeks because it was placed on the spinal column, alongside the vertebrae that were being fused, for supplemental support. But a patient still had to wear a cast for several months for additional protection. The cast itself caused other problems. For example, patients with poor sensation and circulation developed serious ulcersations when the cast rubbed against their skin.

The newest instruments — the Zielke (Zil-kee), Luque (Lou-key) and Cotrel-Dubousset (Cotrel-Doo-bow-say) — provide even more support, reducing the need for casts. Designs are based on biomechanical properties of the vertebrae, spinal cord and surrounding muscle layers. Sometimes the instruments are used in conjunction with the Harrington rod, which remains the most popular instrument worldwide for correcting certain spinal deformities.
Bridwell says the Zielke system is the best choice to correct scoliosis in the lumbar area. Invented by German physician Klaus Zielke, the system uses screws to attach a rod to the anterior vertebral column (unlike the Harrington rod, which is applied posteriorly). With Zielke instrumentation, fewer vertebrae need to be fused, allowing the patient a more nearly-normal spine. Often, nearly 100 percent correction is achieved, while about 50 percent is achieved with the Harrington rod system.

Luque instruments are used in the thoracic (ribcage) and lumbar areas of the spine, Bridwell explains. Popularized in the late 1970s by Mexican physician Eduardo Luque, the system uses wires to attach the rods to each vertebra. The wires provide additional strength and stability because they attach the rod at several levels, rather than just at the top and bottom. However, the operation is technically demanding because the wires must be passed just a breath away from the delicate spinal cord.

The Luque technique is most popular for patients who are already partially or completely paralyzed, such as some who suffer from spina bifida (a birth defect in which the vertebrae form an open canal instead of a closed tube), cerebral palsy or muscular dystrophy. The technique improves their posture by making the spinal column stiff and straight, which in turn lessens the difficulties of sitting and breathing.

Correcting Scoliosis

Scoliosis is the most common spinal deformity. There are dozens of types, some severe enough to be life-threatening, and most can be corrected. In idiopathic scoliosis, for example, spinal curves of 20-40 degrees or more are often corrected because they increase at the rate of one degree per year even after skeletal growth stops, causing disability in adulthood.

At Washington University, Bridwell often corrects paralytic scoliosis with a combination of Luque wires, two Harrington rods and new pelvic instrumentation called a “sacral stop,” also invented by Zielke. “The sacral stop is in its evolutionary stages,” says Bridwell, “but it might provide better fixation and correction for the paralytic scoliosis patient because it combines good pelvic fixation with the ability to correct the deformity by both distraction and lateral traction.”

The Cotrel-Dubousset (CD) system is slowly but surely gaining popularity. Designed by two French physicians — Yves Cotrel and Jean Dubousset — it was introduced in this country barely a year ago.

The technique uses two rods, linked together with two or three transverse rods and attached to the spine with eight to 10 hooks. Unlike the smooth Harrington rod, the CD rod has several thousands of diamond-shaped notches that allow multiple hook adjustments. Currently, the system is used in the thoracic and lumbar areas of the spine. “It is the most complex, but also the most secure and rigid system to come along,” says Bridwell. “It affords less reliance on external support than all the others.”

Washington University Medical Center was the fourth medical center in the country to use this system. Bridwell uses the new instrumentation systems on adults and children.

Monitoring During Surgery

Surgery to correct scoliosis usually takes about four to five hours. As a precaution, the patient’s spinal cord is monitored to avoid any injury during surgery. In some procedures, there is danger that the cord will be stretched when the vertebrae are adjusted. “Spinal cord monitoring is used for all spinal deformity surgery at Barnes and Children’s hospitals,” says Bridwell. “Before it was available, surgeons had the anesthesiologist wake up the patient with the wound wide open, and then they asked the patient to move his feet and toes.”

Bridwell says the wake-up technique worked reasonably well; patients were awake enough to respond, but sufficiently anesthetized to experience no pain and remember nothing. One problem, however, was that the monitoring was done only after the surgical procedure was complete. “It was all or nothing,” he explains. “We had to do what we were going to do, then wake the patient up to check.”

“Scoliosis monitoring is now quite similar to EKG monitoring for the heart,” Bridwell says. “By placing electrodes in the hands, feet and scalp (just beneath the skin), the spinal cord’s impulses can be monitored safely and effectively.”

After surgery with the newer tools, such as CD rods, patients rest in bed for just a few days. By the third to fifth day, they can sit at the edge of the bed; a short while later, they can walk. Most go home by the tenth day. And though some patients must wear a custom-made removable brace, many go home without any external support. Young patients can usually go back to school after three weeks; adults can often return to work within six weeks. Most patients are back to 95 percent activity within a couple of months, and full activity after the fusion heals, which takes about two years. Many have no perceptible loss of flexibility, and Bridwell says the patient shouldn’t be able to feel the instruments because they lie beneath several layers of muscle.

Scoliosis surgery is complicated surgery, says Bridwell, “and the bigger the surgery, the bigger the risks. Older patients recover more slowly than younger ones. Scoliosis surgery is only rarely done on patients beyond age 60.”

The likelihood of paralysis is small, reports Bridwell; the rate is less than 0.7 percent. Infection occurs in only one percent of patients, and the risk of pseudoarthrosis (failure of the fusion to solidify) depends on variables like the patient’s age and deformity.

Non-surgical methods to correct spinal deformities have not evolved as rapidly as surgical alternatives. For example, electrical stimulation of spinal muscles has been attempted instead of bracing. However, studies suggest that it is not likely to be as successful as bracing. Bracing remains the treatment of choice for small curves (20-40 degrees) in skeletal immature patients. Bracing will not correct the deformity, but may prevent worsening.

“More spinal deformities can be corrected now with less risk to the patient, and a faster return to normal life,” says Bridwell, who foresees continued improvement in ways to correct orthopedic problems of the spine. “Undoubtedly, more innovations and applications will occur in the next few years, even further refining the art of spinal surgery.”
Lucas Van Orden had it all: M.D. and Ph.D. from Yale, editor of a prestigious scientific journal, full professor, published author, researcher, lecturer, husband, and father of four children. Van Orden had climbed to what seemed to be the pinnacle of achievement when, in early 1975, he lost his foothold.

"I was giving lectures to medical students on alcoholism and drug abuse," he recalls, "while so intoxicated I couldn't remember I had done it."

In March 1975, after a blackout that erased the preceding month from his memory, Van Orden went into treatment and stopped drinking and taking drugs altogether. After a year's recovery, he decided to make treatment of the alcohol- and drug-dependent person a major focus of his career. Now completing a psychiatry residency at Washington University Medical Center, he serves as a consultant to Jewish Hospital's unique program for alcohol and chemical dependency.

The Jewish Hospital Alcohol and Chemical Dependency Program, begun in November 1984, is the first drug treatment unit in St. Louis to be located within an academic medical center. The program offers a unique type of care to the alcohol- and chemical-dependent person, care which treats not only the substance addiction but the complex physical and psychological consequences of that addiction.

Collins E. Lewis, M.D., medical director of the program, explains: "We don't just treat people with straight alcoholism or chemical dependency. We have patients who are depressed, suicidal, schizophrenic, and manic. We're comfortable treating all psychiatric disorders, as well as the many physical disorders that accompany alcoholism and drug abuse. Our program is different from others in that we don't just treat substance abuse in isolation."

Like Van Orden, the majority of alcoholics are a far cry from the stereotype of the homeless and jobless wino. Yet that image and its stigma persists despite the facts: 95 percent of the estimated 10 million alcoholic Americans have jobs, families, and ties to the community.

In fact, reflects Van Orden, it is precisely those trappings that enable an alcoholic to cover up his problem. "The thinking is," he states, "well, after all, he's successful, he can't be an alcoholic." And particularly for the professional, that's just not true because he needs to be successful to camouflage his alcoholism.

"No one is immune," says Lewis, assistant professor of psychiatry. "One may think of alcoholism as an infectious disease: People have different predispositions. Nearly everyone is exposed to alcohol. However, only a few go on to develop serious problems."

Alcoholism's widespread and seemingly random occurrence has made it difficult for researchers to pinpoint specific biological or psychological causes. But two groups have emerged as particularly susceptible, accord-
ing to Lewis: people with a family history of alcoholism, and those who as youngsters develop a pronounced pattern of antisocial behavior, such as skipping school, fighting, shoplifting, or running away from home. For these individuals, he says, the best preventive against developing alcoholism is awareness of their vulnerability. "These people have to be educated," he emphasizes, "and warned that they have an increased risk of developing serious drinking problems."

Just as there is no typical alcoholic person, there are no clear-cut guidelines for determining when drinking becomes alcoholism. A popular misconception is that light drinkers are immune from alcoholism. Lewis stresses that it is not the amount of alcohol consumed, but the degree to which it disrupts one's life, that identifies the alcoholic.

Today, alcohol disrupts lives at a much younger age, and those who become alcoholics are more likely to abuse other substances as well. Alice Noel, A.C.S.W., director of the Jewish Hospital Alcohol and Chemical Dependency Program, has worked with substance abuse since 1970. "Compared to 10 years ago," she observes, "people coming into treatment are much younger and much more affluent, and a lot sicker, than I remember them to have been. These younger patients are also more likely to be 'polydrug' users — they're into cocaine, tranquilizers, PCP — there's a whole menu of things they use."

In the Jewish Hospital program, Lewis and Noel work with a staff of physicians, psychiatrists, nurses and social workers. They are trained to identify and treat the special medical and psychological needs of the substance-dependent person, training that Lewis also offers to the staffs of all the medical center hospitals. The program's location within Jewish Hospital, and its affiliation with the medical center, makes the many resources of those institutions available for diagnosing and treating the special complications of substance abuse.

The advantages of the program are evident in the case of a middle-aged man who was recently admitted to Jewish Hospital for what appeared to be a strictly medical problem — blood in his urine and stools. Examination revealed the "classic" symptoms of heavy, prolonged drinking: cirrhosis and liver failure, jaundice, and severe inflammation of his stomach lining and pancreas. The man admitted that he had been drinking heavily for over 20 years.

His medical problems were brought under control, and he was placed in the hospital's alcohol and chemical dependency program. The in-hospital program enabled him to make the transition from medical to psychological treatment of his drinking problem without disruption, and allowed his physician to closely follow his recovery. In a less comprehensive alcohol treatment program or a hospital without such a program, Lewis points out, patients would be treated for their medical problems, then referred to a private therapist or released for treatment in an outside alcoholism program. "The continuity of care would be disrupted," he explains, "and it would be much more difficult for a physician to follow a patient's progress."

Patients admitted to the program must first undergo a carefully monitored period of detoxification. Detoxification is a crucial first step, allowing time for the toxic effects of the alcohol or chemicals to subside so that treatment of medical complications can begin. It is followed by a thorough psychiatric evaluation, one-on-one therapy with a psychiatrist, and group sessions. Breaking the psychological addiction to chemicals is the most difficult step of treatment, and one which requires a concentrated and continued effort. The Jewish Hospital program limits the number of participants in order to allow individual attention and to emphasize each person's responsibility for his own recovery.

"One of the things the patients have told us," says Noel, "is that they managed to just sit through other programs that were much larger. We ask people to do things, because recovery requires a behavior change. So someone who may have been sitting back, listening passively to lectures in another program, has demands put on them in our program."

One important demand is that the individuals learn new behaviors and acquire skills that will help them fill the free time they used to spend drinking.

"Because," explains Lewis, "once a person has been drinking and then stops, what is he going to do with all that free time? Our occupational and recreational therapists are not just playing games, they're teaching people to develop ways that are incompatible with drinking to spend their free time. One of our goals is to prevent relapse by teaching skills that people can take with them when they leave us."

Individual meetings between a recovering alcoholic and therapist allow a personalized approach to treatment, as well as opportunities for private discussions of concerns. Group sessions provide support through the exchange of common experiences and help the recovering person learn to say no to alcohol when confronted with business or social situations in which drinking is an accepted, even expected, fixture. Patients are also taught techniques for coping with stressful or anxious moments that would formerly have been relieved by a drink.

Van Orden believes that the group approach has yet another valuable role to play in the alcoholic's recovery. "What people find when they come into a chemical dependency program is that they have a hu-
Alice Noel and Collins Lewis are program director and medical director respectively of Jewish Hospital's Alcohol and Chemical Dependency Treatment Program. Recently, the program became affiliated with the St. Louis Area Chapter of the National Council on Alcoholism. The year-old program provides inpatient and outpatient treatment for substance abuse and its attendant medical and psychological problems.

van Orden says that families often mistakenly believe that simply eliminating the alcoholic's drinking problem will be enough. "The family says, 'If you fix the drinking, everything will be OK.' And what usually happens is that the alcoholic has had some sick behavior, and the family

Mary Silva is the editor of "Health Views," the newsletter published by the medical center.
One of the latest advances in ophthalmology is dramatically improving the outlook and eyesight of patients with severe vision problems not corrected by eyeglasses or contact lenses. An innovative surgical technique, epikeratophakia—or the "living contact lens," as it's sometimes called—provides a corrective lens made not of plastic or glass, but of human corneal tissue.

"It's like having contacts sewn on," says Stephen R. Waltman, M.D., professor of ophthalmology, who has helped test the procedure's effectiveness. "It's a simple, safe procedure, and it's successful."

"We cut a niche on each side of the patient's cornea, place the living lens on top, and sew it in. The patient's cells grow into the new lens, so that in time it becomes part of the patient's body."

Light enters the eye through the cornea, the transparent window that covers the iris and the pupil. In a normal eye, the cornea helps focus light rays precisely on the retina, producing a clear image that is transmitted to the brain. Nearsightedness is often the result of a cornea that is too highly curved, causing light rays to focus at a point in front of the retina; in farsightedness, the cornea is not curved enough, so that light rays focus behind the retina. Astigmatism, or blurred vision, occurs when the curve of the cornea is irregular, so that light rays don't focus on a single point.

These errors of refraction can usually be corrected by glasses or contact lenses. But contact lenses and even "coca bottle glasses" don't always significantly improve vision for patients who have had cataracts removed, people who are extremely nearsighted, and patients with keratoconus, a disease that destroys eye tissue and causes the cornea's natural curve to bulge. For these visual problems, epikeratophakia is an option.

In epikeratophakia, the living lens corrects vision by altering the curve of the patient's cornea, bringing about a change in the refractive power of the eye. The procedure is reversible, and is done at minimum risk to the patient because it does not invade the central optical zone of the eye.

Epikeratophakia is based on a technique developed in 1958 by a Colombian physician, José Barraquer. Barraquer, seeking a treatment for his cataract patients who did not respond well to glasses or could not tolerate hard contact lenses, devised a way to remove the patient's own cornea, slice it in half, freeze and reshape it, then place it back on the eye.

Twenty years later, New Orleans ophthalmologist Herbert E. Kaufman and his colleagues refined the procedure for use with donor corneas. Their other key contribution was to develop a storage method that permits the living lens to be commercially manufactured and distributed. Those two steps have made epikeratophakia viable as a remedy for severe visual handicaps.

The first step in the procedure is to measure the patient's corneal curve and calculate the corrective power required. Then, the ophthalmologist orders the living lens. To make the lens, a donor cornea is ground down and shaped so that it provides the necessary refractive power, then frozen and stored for surgery. The lenses are supplied by the California-based American Medical Optics.

When the lens arrives, generally four weeks after it is ordered, the patient enters the hospital for surgery, which can be done under local or general anesthesia. The lens is rehydrated just prior to the operation. After anesthesia is administered, the ophthalmologist removes the epithelium—the membrane that protects the patient's cornea—and makes a tiny cut on each side of the cornea. The living lens is tucked in and secured with a series of sutures. The patient stays in the hospital about three days and can return to normal activities in four weeks. In about four months, vision stabilizes and sutures can be removed. Insurance covers the costs, about $2,000 for surgery and another $3,000 for the hospital.

In the two years that epikeratophakia has been available on an investigative basis in the United States, some 600 cases have been done nationally. Waltman and his partner, assistant professor of ophthalmology Lawrence A. Gans, M.D., are among approximately 100 physicians who perform the procedure, though almost 300 have received the necessary training.

Living lens surgery has a limited applicability, Waltman says, but it is very effective. Waltman and Gans have performed seven of the surgeries since January. All of the patients have healed without complications and are starting to see well. One patient was a one-year-old who had a cataract removed; another had severe myopia that has been 90 percent corrected; and five were facing corneal transplants because of keratoconus.
Stephen R. Waltman is one of 100 U.S. surgeons who perform epikeratophakia. The procedure uses a quick-frozen donor cornea, carefully shaped to provide the corrective power required, which is sewn onto a patient's defective cornea.

"Epikeratophakia is certainly much safer than a corneal transplant, when the wall of the eye must be replaced," Waltman says. Five to ten percent of corneal transplant patients reject the new tissue, he points out. With epikeratophakia, there is no rejection: medication used in the surgery destroys living cells that cause rejection, and in addition, a partial rather than entire cornea is used. Also, epikeratophakia patients recover much quicker than corneal transplant patients, who must remain inactive three to four months after surgery.

For 21-year-old David Elfline, one of Waltman's patients, seeing truly is believing. Because of keratoconus, he had a corneal transplant in his right eye in July 1984, and epikeratophakia in his left eye last April. He much prefers the living lens surgery.

"I would recommend it," said Elfline, who had the operation under local anesthesia. "I was up and around in three weeks. I couldn't overexert, but I could drive, go back to work, and basically do anything I wanted." He reports that he has slight astigmatism, but that it is clearing. His vision, 20/40 at this point, improves each day. If it continues to improve, he may not have to wear glasses or contacts.

That's a much happier experience than he had with the full cornea transplant, which Waltman felt was a necessary risk because of the advanced state of the disease in the right eye. Elfline remained inactive for three months after the operation, and in the fourth month nearly lost the new cornea due to rejection. That near-rejection prompted Waltman to suggest that a living lens be placed in Elfline's other eye.

Because epikeratophakia is so safe, it has been very effective in infants and children with congenital or traumatic cataracts. "Very young children who have had cataracts removed are unable to wear contact lenses because their eyes are still growing, and they're too young to take care of the lenses," Waltman notes. "The living lens is an excellent solution." In children, he adds, recovery time is even quicker — sutures can be removed in two weeks.

One-year-old Jon Richardson, who received a living lens in July, still has trouble feeding himself because he can't focus on his food, but his parents know he sees more than he ever has before. The little boy, one of Gans' patients, had surgery in March to remove a cataract so dense that it not only blocked vision in his left eye, but turned the eye inward. The operation was performed under general anesthesia.

"We're not sure yet what Jon's vision will be, but at least he's seeing something, and his eye doesn't turn in anymore," comments Jon's mother, Lisa. "Right now, tests show he can focus three feet away, but before and after that point, his vision is blurry."

She and her husband Randy have been putting ointment in Jon's eye each night since he had the living lens surgery. He also wears a patch on alternate days to strengthen his right eye. Once Jon's vision is stable, Gans will write a prescription for glasses, the final step to normal eyesight.

"The surgery," says Lisa, "has definitely been worth it."

Surgery to correct refractive errors — nearsightedness, farsightedness and astigmatism — has flourished as a subspecialty in ophthalmologic practice, notes Waltman, who also offers radial keratotomy, the controversial surgery to correct low degrees of nearsightedness. In the last six years, almost a quarter of a million myopes have put aside their glasses and contacts in favor of radial keratotomy, an issue among ophthalmologists because it is done chiefly for cosmetic reasons. Waltman foresees less debate among ophthalmologists, and a rapid increase nationally in patient requests for the procedures, as refractive surgery becomes recognized as an alternative to glasses and contacts to correct vision problems.
HAP: THE SECOND GENERATION

What has one Irish nun, two accountants, and three medical technologists? (There's also a telecommunications director, a physical therapist, and an air pollution control engineer.) Still need clues? Try a CRT computer operator, an American Red Cross volunteer coordinator, and a paramedic. Give up? This unusual mix of professions is a cross section of students in the School of Medicine's Health Administration Program (HAP). And this broadly based student population accounts for the program's richness, says James O. Hepner, Ph.D., the program director since 1967. Hepner points out that Washington University was one of the first medical schools in the country to offer a curriculum to train persons who wish to enter some area of health care administration.

"The HAP program got its start in 1946," says Hepner, "when the late Frank Bradley, an alumus of the School of Medicine who was then president of Barnes Hospital, taught classes for 10 or 15 students."

Bradley created a training program that consisted of nine months of instruction and a residency. Today, full- and part-time HAP students attend classes for four semesters. (Part-time students must complete their academic work within five years after enrollment.) During the summer, they gain clinical experience in an internship. And following their fourth semester, they are expected to take a residency — an entry-level job, monitored by a preceptor — that often leads to permanent employment.

"There have been many changes in the program over the years," says Hepner. "For example, there is now a strong quantitative base to the curriculum, taught by full-time faculty. There is a strong component of human resources management, and health care environment. There is also an element of strategic planning for health care."

Now, the program has five full-time faculty members, all of whom are engaged in research. In addition, some of the part-time instructors are among the medical center "superstars": Ronald G. Evens, M.D. (president, Children's Hospital and director, Mallinckrodt Institute of Radiology); Robert E. Frank (CEO, Barnes Hospital); and David A. Gee (president, Jewish Hospital). Prominent attorneys, accountants and others from the St. Louis business community round out the diverse faculty Hepner has assembled.

In fall 1984, Introduction to Health Information Systems was added to the HAP curriculum. Coordinated by Stuart B. Boxerman, D.Sc., associate professor in the Health Administration Program, the course is taught by personnel from McDonnell Douglas Health Information Systems Company. The class, originally instituted as a one-hour, pass/fail option, has been upgraded to a two-hour offering. "To the best of my knowledge," says Boxerman, "we are the only academic program to have on-line access to a major vendor's hospital information system. Every one of our graduates needs a minimum level of hands-on proficiency in data processing."

In addition to innovative courses such as this, another change in the program has occurred in the composition of the student body, says Julie Holmes, formerly the assistant director of HAP. Before World War II, hospital administration was primarily a women's field, occupied principally by religious sisters and nurses. With the war and the GI Bill, this changed. "Now, women are re-entering the field," she says. "This year's entering class is about half women."

One of the women in the second-year class has a background that is unusual, even for HAP. Patricia Bates, a native of Little Rock, Arkansas, just finished a two-year stint in Washington, D.C., as a legislative aide to U.S. Senator Dale Bumpers of Arkansas. Bates, who began her career as a status intern on Bumpers' staff and worked her way up through the ranks, specialized in issues and legislation affecting health care, particularly of the elderly.

"I've always had a fascination with older people," she says. As a teenager, she used to go to nursing homes just to visit the people living in them. "That's when I got interested in the long-term care aspect," she remembers. "I became aware of the increase in the aged population and the impact it would have on the health care field. So my visits to nursing homes served two purposes — they were informative, but they were also something I enjoyed."

Her early interest in hospital administration was supported by her father, a physician, and her mother, a former teacher who retired 25 years ago when Patty — the first of four children — was born. As the teenager who loved to visit nursing homes grew older, she decided to make health care management her career. At Davidson College in North Carolina, Bates enrolled in an independent study program that permitted her to concentrate on the field of long-term health care. Her summers at the Arkansas Gerontology Center, and an internship at the University of Arkansas Medical Center, led to a thesis on the importance of hospital discharge planning in the health care of the aged.

The HAP program got its start in 1946, when the late Frank Bradley, an alumnus of the School of Medicine who was then president of Barnes Hospital, taught classes for 10 or 15 students.

With this long-standing interest in, and preparation for, a career in health care management, how did the stint with Senator Bumpers come about?

"I knew I wanted to get my MHA," says Bates, "but I wanted to delay it for awhile and spend a year in Washington. So I went to D.C. and started knocking on doors. I went to Bumpers' office and used it as my home base. They set me up with contacts on the Hill, and health care agencies, and lobbying groups on aging issues. After spending a week there, they said, 'Put your resume in with us — we'd like to talk with you.' So they ended up hiring me for the summer as an intern, working on health care legislation for them and analyzing various bills.

"They wanted me to stay on the permanent staff," Bates continues, "so I extended my stay. I really progressed quickly and was able to get involved in a lot of different issues. The end of my stay, though, was really the highlight."
Senate Majority Leader Robert Dole (R-Kan) had sponsored a bill to cut $3.5 billion from the Federal budget by increasing the states' portion of their Medicaid expenditures. "The cutback in Federal funds was to be made up by the states," says Bumpers. "But the states came to us and said they simply didn't have the money. The real effect of this measure would have been a significant cutback in medical services to Medicaid recipients.

"Patty handled our entire effort to defeat this proposal. She contacted other Senate staffs and lined up 15 senators to speak against the bill. Due largely to Patty's help, we were successful in blocking it.

"Patty is one of the most persistent and knowledgeable aides I have ever had," adds Bumpers. "She is also one of the warmest, kindest and most sensitive persons I have ever known. Every member of my staff, and that includes me, admires and respects her."

Bates was clearly forging an exciting, rewarding career for herself in Washington, but she realized that she was at a decisive point: either stay on in Washington, or return to school for her MHA. She doesn't regret that she opted for the latter.

Besides Washington University's reputation as a premier training ground for health care administrators, and its commitment to the preceptor-sponsored residency, Bates was also impressed by the school's willingness to provide financial assistance to students. Recently, she was selected as the first recipient of the Robert E. Frank Scholarship in Hospital Administration, which was established in 1984 through a $25,000 gift from the Barnes Hospital Auxiliary.

The scholarship provides only a portion of her tuition costs, so Bates is working as a research assistant to Hepner, who has received a grant from the Hospital Corporation of America to examine HCA's human resources management practices and policies. "HCA is the largest multi-hospital system in the world," reflects Bates, "and although I expect to eventually be a part of a not-for-profit, voluntary system, I think that there's a lot to be learned from a for-profit like HCA."
In his 1975 presidential address to the American Society of Human Genetics, Victor A. McKusick remarked that genetics is involved in answering all three questions that constitute medical practice: What is wrong? (diagnosis), What is going to happen? (prognosis), and What can be done about it? (treatment). However, genetics goes a step further and asks a fourth question: Why did it happen? In the answer to this question, says McKusick, lie prevention and scientific progress. What's more, therein lies the secret of genetics' attractiveness. In the Division of Biology and Biomedical Sciences at Washington University, approximately two-thirds of applicants for graduate study and research indicate an interest in genetics. These students distribute themselves among many preclinical and clinical departments in pursuit of their own subspecialty interests: biochemical or molecular genetics, microbial genetics, immunogenetics, population genetics, neurogenetics, psychiatric genetics, pediatric genetics, and many others.

Modern genetics represents a confluence of basic science and clinical application not seen in medicine since the exciting days that followed the discovery of antibiotics. Unlike such fields as biochemistry, which originated as a medical discipline and later spread into the rest of biology, genetics originated apart from medicine and is a relative latecomer. As a relevant clinical discipline, genetics was not recognized until about 1960 when, during a few exciting months, reports appeared demonstrating the chromosomal basis of three relatively common, well-known syndromes. One of these — Down's syndrome — results from an extra copy of chromosome 21. These and other discoveries in genetics were the clinical culmination of several advances of the 1950s. Among these were the concept of the molecular basis of disease and the perfection of procedures for the biochemical study of urine, blood, tissue samples, and chromosomes. The therapeutic possibilities of genetics were demonstrated dramatically with the successful dietary prevention of the profound mental retardation associated with the inherited disorder phenylketonuria (PKU).

Since 1960, genetics has become increasingly integrated into medicine. Today, most major medical schools in the United States include a department of genetics or some comparable administrative unit; more than 75 percent of U.S. medical schools require at least one genetics course in the curriculum. At Washington University Medical Center, the field is represented by the James S. McDonnell Department of Genetics, which was established in 1975. However, many clinical and preclinical departments have also contributed to the development of genetics by appointing staff members trained in genetic subspecialties. Broadly defined, genetics at Washington University Medical Center presently includes more than 65 faculty members distributed among more than 15 clinical and preclinical departments. Uncommon foresight and cooperation among independent departments enabled and sustains the development and integration of genetics at Washington University.

As a matter of history, it should be pointed out that Washington University was also among the leaders in the origins of modern genetics as a basic science. The current phase of molecular genetics began in the early 1940s with informal interactions between Max Delbrück, Salvador Luria, and Alfred Hershey and others, at a time when Hershey was a member of the Washington University faculty. Their pioneering work was focused upon a group of viruses that infect bacterial cells. They demonstrated that these tiny particles possess genes like those of other organisms, including humans, genes which determine inherited characteristics and which can undergo spontaneous change through mutation. Most important, Hershey and collaborators provided one of the earliest demonstrations that the chemical building block of genes is DNA.

For their pioneering work, Delbrück, Luria and Hershey were awarded the Nobel Prize in 1969. Alfred Hershey was merely the first of a long line of Washington University laureates and luminaries who advanced the field of genetics.

Genetics as a clinical discipline received a tremendous boost in recent years through the development of recombinant DNA procedures, which are remarkable in their power to identify and manipulate individual DNA molecules. In the future, the library of probes may extend to those disorders derived from a genetic predisposition: Alzheimer's disease, schizophrenia, diabetes, and many congenital abnormalities. The use of probes to isolate and identify particular genes has recently been improved by associate professor of genetics Maynard F. Olson, Ph.D. He and his colleagues have perfected a new type of apparatus that separates large pieces of DNA. The DNA segments can serve as probes to detect other, more complex genetic diseases.

Those who have contributed to the development of genetics and its integration into clinical specialties — inside and outside of Washington University — have reason to be proud. The success of this enterprise can stand as a symbol of the dynamics of modern medicine and biomedical research: biomedical sciences feeding upon each other, nourishing themselves. It is also an example of a superb institution building creatively upon a strong tradition.

Daniel L. Hartl, Ph.D.
James S. McDonnell Professor and Head, Department of Genetics
Six division chiefs and directors have been appointed at Washington University Medical Center. Fred C. Chu, M.D., has been named director of pediatric ophthalmology. Philip E. Cryer, M.D., is the director of the division of metabolism and endocrinology in the Department of Medicine. Wayne Flye, M.D., Ph.D., has joined the surgical faculty as professor of surgery and director of the organ transplantation program.

Fred C. Chu

Philip E. Cryer

Wayne Flye

R. Gilbert Jost

Roderick P. Lusk

John A. McDonald

Krause Named Pew Scholar

James E. Krause, Ph.D., assistant professor of neurobiology, has been named one of the first Pew Scholars in the Biomedical Sciences by the Pew Memorial Trust of Philadelphia.

The Pew Scholars for 1985, all junior faculty members at 17 medical schools and research institutes in the United States, were selected because of their outstanding promise in basic science or clinical research to advance human health. Each of the scholars will receive a total of $200,000 over the next four years as en-

Chu heads the Children's Eye Care Center at Children's Hospital, where he is responsible for examining and treating children with visual disorders and "crossed" eyes. He is an assistant professor of ophthalmology and of ophthalmology in pediatrics. Chu's research interests include the application of computers to the study of eye movement disorders.

Cryer succeeds William H. Daughaday, M.D., who will continue in his position as the Irene E. and Michael M. Karl Professor in Endocrinology and Metabolism. At the School of Medicine, Cryer is professor of medicine and program director of the General Clinical Research Center (GCRC), a federally funded unit that supports biomedical research in humans. Cryer is also director of the Clinical Research Facility at the medical school's Diabetes Research and Training Center. He is on staff at Barnes Hospital and a consulting physician at Children's Hospital.

Flye comes to St. Louis from the Yale University-New Haven Medical Center, where he was professor of surgery and director of organ transplantation and immunobiology. His primary area of interest is in liver transplantation. He has performed transplants in over a dozen patients at Barnes Hospital since joining the School of Medicine.

Jost will coordinate Mallinckrodt's diagnostic services. On staff at MIR since 1975, Jost is professor of radiology and head of the diagnostic radiology computer division. He is staff radiologist at Barnes and Children's hospitals.

Lusk, assistant professor of pediatric otolaryngology, came to Washington U. from the University of Iowa College of Medicine. His research interests lie in laryngeal physiology, reconstructive and augmentive surgery, and voice disorders.

McDonald, associate professor of medicine and assistant professor of biochemistry, researches certain of the lung's adhesive and supportive molecules during experimental and human lung injury. He is also on staff at Jewish Hospital.
Krause’s research is an examination of the cellular biochemistry and physiological regulation of peptide neurotransmitter substances in the central nervous system. He will use a model system of substance P-secreting neurons in the basal ganglia of the rat.

His primary goals are to identify and describe peptide neurotransmitter biosynthesis and mechanism of action, and to learn more about how these processes are regulated biologically and mechanistically. His studies will provide a better understanding of basal ganglia substance P neurons, which are reportedly related to two neurodegenerative disorders, Parkinson’s syndrome and Huntington’s chorea.

Krause joined the faculty at Washington University School of Medicine in 1984. He received a Ph.D. in physiological chemistry from the University of Wisconsin in 1980.

Olk Elected to Retina Society

Assistant professor of clinical ophthalmology, R. Joseph Olk, M.D., has been elected to membership in The Retina Society, a national honorary organization for retina specialists.

Olk is one of 11 American ophthalmologists chosen this year by the society, which was founded in 1968 to encourage the exchange of information about diseases of the retina, the sensory membrane that lines the inner eye. The society’s 150 members were selected for their medical and surgical experience, literary contributions and retinal experience.

Olk, who is in private practice with Retina Consultants, Ltd., in St. Louis, is on staff at Barnes and Children’s hospitals and at St. Luke’s Hospital. He joined the faculty of the School of Medicine in 1981 as an instructor in clinical ophthalmology, after a one-year fellowship in retina-vascular disorders at the Wiltner Eye Institute at Johns Hopkins University. He is a 1975 graduate of Rush Medical College, and completed his internship and ophthalmology residency at Rush Presbyterian-St. Luke’s Medical Center in Chicago. He was a fellow in retinal-vitreous disorders at Barnes Hospital from 1979-1980.

Olk has delivered lectures and published more than 30 papers on diseases of the retina and vitreous. He is a member of more than a dozen medical societies, including the American College of Surgeons, the American Academy of Ophthalmology, the Pan-American Association of Ophthalmology and the Vitreous Society.

Daughaday and Lacy Elected Fellows of AAAS

Two internationally recognized faculty members have been elected fellows of the American Association for the Advancement of Science (AAAS).

William H. Daughaday, M.D., Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism, and Paul E. Lacy, M.D., Ph.D., Robert L. Kroc Professor of Diabetes and Endocrine Diseases, are among 312 association members who have been named 1985 fellows. The AAAS, formed in 1848, is the nation’s leading general scientific organization with almost 136,000 individual members and 285 affiliated scientific societies and academies of science. In electing fellows, the AAAS honors members who have made scientifically or socially distinguished efforts to advance science or its application.

Paul E. Lacy

Daughaday was honored for work that is known worldwide. His research has brought about a better understanding of basic hormonal action, especially in showing that some of growth hormone’s actions are mediated by the insulin-like growth factors, the somatomedins, and that adrenal corticosteroids are transported in plasma by a specific binding protein. He stepped down earlier this year after 34 years as director of the division of endocrinology and metabolism of the Department of Medicine, but continues as Karl F. Fessler and as director of the Diabetes Research and Training Center. He is on staff at Barnes and Jewish hospitals.

Lacy is internationally recognized for his diabetes research. He is noted especially for his recent efforts to control diabetes by transplanting insulin-producing cells from cadaver pancreases to diabetic patients, a procedure that temporarily and safely produced detectable levels of insulin in four of the seven patients treated. Lacy is credited with significantly advancing immunology, organ transplantation and the search for better diabetes treatments. Earlier this year, he stepped down as head of the
When Stephanie Talton returned to high school after her summer vacation, she was a little richer and a lot wiser.

Stephanie, a 17-year-old senior at Hazelwood East Senior High School who plans a career in medicine, spent eight weeks working in a laboratory at the School of Medicine as part of the Minority High School Student Research Apprentice Program. The nationwide program, sponsored and partially funded by the National Institutes of Health, is designed to involve minority high school students in biomedical research.

This summer, which marked the fifth year of the program at the School of Medicine, almost 400 students applied for 11 available slots.

Stephanie and 10 other St. Louis-area students worked in separate laboratories, earning minimum wage for a 37.5-hour workweek. "We encourage the students to look at health and science as a career," says Robert Lee, Ph.D., assistant dean for minority student affairs. "And we encourage them to get all the education they can. It's a working and learning experience.

School of Medicine administrators recruit the students by contacting administrators at about 75 St. Louis-area schools. Students who are recommended must be interviewed by a nine-member School of Medicine admissions committee. If they are accepted, they are assigned to a program advisor, or "mentor," within each department, with additional supervision by a medical student and laboratory assistant or medical resident.

This year, the mentors were faculty members in cardiovascular surgery, microbiology and immunology, genetics, internal medicine, psychiatry, anatomy and neurobiology, general surgery, obstetrics and gynecology and pediatrics. One student worked in the biomedical computer lab. The program has been so well received by faculty members in past years that some students have been invited to work part time during the school year.

During the eight-week session, the students perform a variety of tasks, all related to scientific investigation. In addition, they are required to take an anatomy/physiology course and write a research paper.

The student with the highest academic score is often invited to assist with the program the following year.

Stephanie, who had never been inside a laboratory before, received the highest academic score this year and says the overall experience was a good one for her. "During the first week it took me a while to get the hang of it and to get the big picture," she says. "But it taught me self-discipline and independence. I had to know what I was doing. And I would do it again."

For information about next year's program, call Rosalind P. Denson, Ph.D., program coordinator, at (314) 362-3633.

New Heart Research Center Funded

Researchers from the School of Medicine have been designated as part of a new national initiative to improve the application of research findings on ischemic heart disease. This new national initiative spearheads the Federal government's attempts to use recent research findings in a number of disciplines to influence changes in behavior and lifestyle.

Washington University has received funding from the National Heart, Lung and Blood Institute to establish the nation's first National Research and Demonstration Center (NRDC) in ischemic heart disease. The local center teams cardiology researchers from the School of Medicine with investigators from the behavioral sciences in several university colleges and schools to compare conventional programs for combating heart disease with social, educational and behavioral approaches that may improve patient compliance.

Investigators within the NRDC will study heart disease, with the goal of lowering risk, in three projects: one to increase medication use by recovered heart attack victims; one to encourage early treatment of incident heart attack; and one to examine work-implemented programs for lowering the risk of heart attack.

For the medication study, researchers will compare effectiveness of one-on-one counseling for recovered heart attack victims with that of educational videotapes for patients, their spouses and families. Results with both methods will be measured objectively to detect improvements in medication usage.

The early treatment program will be conducted through the Medical Care Group, and is designed to examine ways to speed responses of people potentially at risk of heart attack, and also to improve the response of medical care systems. Traditional patient education techniques will be used with one group, while another group will learn through practice drills and other behavioral interventions.

In the work-site study, a standard, pre-packaged educational program will be tested for effectiveness in comparison with a broad-based plan that workers help to develop and implement. The medical objective is to reduce the risk of heart attack through both behavioral and biological changes, for example, by lowering cholesterol intake and stopping smoking.
Burton E. Sobel, M.D., professor of medicine and director of the cardiovascular division, is the principal investigator of Washington University's NRDC. NRDC leaders include Edwin B. Fisher, Ph.D., associate professor of psychology, directing psychological research; Gustav Schnelldorf, M.D., professor and acting head of the preventive medicine department, the NRDC laboratory; and Kenneth B. Schechtman, Ph.D., instructor in preventive medicine, responsible for biostatistics.

The government is supporting NRDCs only at institutions already designated as Specialized Centers of Research (SCORs). SCORs — funded by the National Heart, Lung and Blood Institute — exist at more than 50 institutions and are devoted to clinical research in many different specialties. At Washington University's cardiovascular diseases SCOR, which is under Sobel's direction, 40 investigators from 12 departments study the heart's response to ischemic injury and seek new therapies for heart disease.

Older Volunteers Sought for Hypertension Study

Researchers are seeking older men and women for a study on whether exercise can lower high blood pressure. The study is being conducted by the Department of Medicine and is supported by a grant from the American Association of Retired Persons. Principal investigator is James Hagberg, Ph.D., a research associate professor who has specialized in the effects of exercise on aging.

"High blood pressure is a major health problem in men and women over the age of 60," Hagberg said. "Exercise is often proposed as a possible alternative to drugs for lowering blood pressure in people with moderate elevations in blood pressure." The Washington University study is designed to learn how much exercise training might lower blood pressure in older people.

For this study, researchers need men and women aged 60-70 who have mild to moderate hypertension (blood pressures in the range of 150-170/90-95). They must be healthy otherwise and must not be taking any blood pressure medications.

Subjects in the control group will be studied twice, once at the beginning of the program, and again after one year. Two groups of subjects will take part in a nine-month exercise training program; one group will exercise on its own after an initial three-week period, and the other will exercise three to four times a week under medical supervision at the School of Medicine. Both groups will be studied before the exercise program begins, and again at its conclusion.

Testing will include studies of the participants' heart function and other possible causes of their increased blood pressure. All testing will be free, and all results will be made available to the participants and their physicians.

Further information is available through Hagberg at (314) 362-2392.

The Gerty T. Cori Predoctoral Fellowship and Prize for 1985 has been awarded to Ursula M. Bond, a student in the Division of Biology and Biomedical Sciences. This award, named in honor of Nobel Prize-winner Cori, was established by Sigma Chemical Company. Awarded to a student in biochemistry, it provides a stipend and a monetary prize which is to be applied toward some aspect of the student's academic endeavors.

Bond received her undergraduate degree in biochemistry from Trinity College in Dublin. Before embarking on her graduate studies at Washington University, Bond had worked at the National Institute for Medical Research in London, and at Trinity College. Her work in the laboratory of Milton J. Schlesinger, Ph.D., professor of microbiology and immunology, has resulted in a scientific milestone — the discovery of a set of proteins produced specifically in response to stress. By applying heat shock or other stressors to cells, Bond has elucidated that these proteins are produced because of selective activation of the ubiquitin gene.

Each year since 1984, the steering committee of the Division of Biology and Biomedical Sciences' Molecular Biology graduate program selects a student from either the Ph.D. or M.D./Ph.D. program to receive this award. Last year's recipient of the Gerty T. Cori Predoctoral Fellowship and Prize was Mark S. Boguski, a student in the M.D./Ph.D. program.

Boguski earned the bachelor of arts degree in natural sciences in 1976 from Johns Hopkins University. His undergraduate research was conducted at NIH, Hahnemann Medical College, and at the Johns Hopkins Institute of the History of Medicine. At Washington University, Boguski has conducted research in the laboratory of Jeffrey I. Gordon, M.D., associate professor of biological chemistry and medicine. Boguski has cloned the gene for two apolipoproteins, A-I and A-IV, involved in lipid metabolism and transport.

Boguski has used many computational methods to determine the structure/function relationships of these proteins, as well as their evolutionary history.

"Mapping the Beat," an article in the spring 1985 issue of Outlook, has won first place in the Reader's Digest University of Missouri Competition for Magazine Writers (Published Category). The article, written by Linda Sage, Ph.D., freelance writer specializing in science, described the heart mapping procedure used during surgery to correct heart rhythm disturbances.

Sage, a stringer for The Economist, is teaching a science writing class in the Washington University evening school, University College. She has been a frequent contributor to Outlook.
The Norman J. Stupp Foundation has created a special fund to support work in geriatric neurology at Washington University. Through annual contributions, the Stupp Foundation Fund for Research and Education in Geriatric Neurology will support scientists and educators who specialize in impairments that are the result of multiple strokes and other dementias. Those impairments include deterioration in mental function, mood and behavior, and often create burdens for caregivers. The geriatric neurology team will devote special attention to problems of patients, their families, and the staff at Bethesda-Dilworth Memorial Home in St. Louis.

The Stupp Fund is established through the Department of Neurology and Neurological Surgery at the School of Medicine. William M. Landau, M.D., professor and head of the Department of Neurology, will administer the fund with advice from members of the university’s Memory and Aging Project, directed by Leonard Berg, M.D. Landau and Berg are both staff at Barnes, Children’s and Jewish hospitals.

The Norman J. Stupp Foundation, established in 1954, has channeled its contributions to Bethesda Hospital and Homes and to Boys Town of Missouri. It also provides scholarships in civil engineering at Washington University.

Stupp, who died in 1979, was a native of St. Louis who received a degree in civil engineering from Washington University in 1922. He joined the Stupp Brothers Bridge and Iron Company, founded by his grandfather in 1856, and with his brother expanded its operations considerably. He was a recipient of the Distinguished Alumni Award from Washington University.

Stupp was a longtime board member of St. Louis Shriners Hospital for Crippled Children, and board member and chairman of the board of Bethesda Hospital and Homes. He was also a leader in his national fraternity, Kappa Sigma, an active Master Mason, and a member of the Scottish Rite and the Moolah Shrine.

Daniel W. McKeel Jr., M.D., a pathologist at Washington University School of Medicine, is working with the St. Louis-based computer company Management Techniques, Inc., to develop a unique computerized system for autopsy records. The system is believed to be first in the country to automatically cross-index the two leading systems for classifying and encoding anatomic pathology and clinical diagnoses. If successful, it could be adapted by health care institutions nationwide as a means of increasing the precision of diagnoses and the classification of diseases.

The model system will be created under a $50,000 Small Business Innovation Research grant awarded by the National Institutes of Health (NIH) to Management Techniques, Inc. McKeel, director of the Division of Autopsy Pathology at the School of Medicine, is project consultant. His essay in the summer 1985 Outlook described the national decline in autopsies and the effects of that trend.

In the next few months, McKeel and Robert Levitt, president of Management Techniques, hope to develop and implement a comprehensive management information system for autopsy records. The system will automatically encode, retrieve and correlate clinical and pathological diagnostic data.

Computer software will code records using the two major classifications of diseases — Standard Nomenclature of Medicine (SNOMED) and International Classification of Disease, Version 9, Clinical Modification (ICD-9-CM). The software will be transferrable to major computer systems, and will be efficient in a distributed network of microcomputers.

After completing the model system, McKeel and Levitt will be eligible to apply for a phase II grant, which would provide funding to develop a product for commercial marketing.

The Small Business Innovation Research program was created in 1982 to stimulate technological innovation within the small business community. The small business sector with an increased role in federal research and development, and attract private capital to commercialize the results of federally funded research.

McKeel and Levitt applied for the grant after attending a special conference sponsored by the Regional Commerce and Growth Association.

Management Techniques, Inc., operates as both a computer services and a software development company in the bi-state area. The company has acquired broad experience in dedicated multiuser and networking computer systems.

McKeel also is an associate professor of pathology and co-director of the Washington University Diabetes Research and Training Center Morphology Core Laboratory. Funding for his academic pathology research has included two Biomedical Research Support Grants, an individual three-year Research Grant Award from the NIH, and a five-year Research Career Development Award.

Arthur W. Toga, Ph.D., administrator and director of the Laboratory of Neuro-Imaging (LONI) at Washington University School of Medicine, has received a grant from The Whitaker Foundation to support his research on brain function.

The three-year grant totals almost $150,000. Toga plans to visualize changes in brain activity, measuring their relationship to changes in behavior. To do so, he will use autoradiograms, "pictures" of brain metabolism made with x-ray film, as described in "Window to the Brain," a feature in the fall 1985 issue of Outlook.

He will analyze the autoradiograms through digital image processing, one of the forms of computer-based analysis for which LONI was established. Digital image processing allows scientists to interpret visual data by transforming them into numbers, which can then be translated into clearer images for further study.

The Laboratory of Neuro-Imaging, which opened in 1984, aids research in a number of departments at the School of Medicine. The laboratory has technology similar to that of NASA, whose computers enhance satellite pictures of the earth's surface. A scanner digitizes light transmitted through
or reflected from a wide variety of images. The digital data can then be stored, manipulated or projected as two- or three-dimensional images. Also, LONI can provide easily read color-coded images, and composite images for measuring changes over time.

Toga has been a research assistant professor in neurology at Washington University since 1980. He joined the faculty in 1979 as a research instructor, after completing a yearlong postdoctoral fellowship with the Department of Neurology. He received a doctorate in neurosciences from St. Louis University in 1978.

Professional memberships include the American Association for the Advancement of Science, Society for Neuroscience and the National Computer Graphics Association. Toga has published a number of articles and abstracts on his research in neuroscience and computer science journals.

Michael J. Noetzel, M.D., assistant professor of pediatrics and neurology and director of the Birth Defects Center at St. Louis Children's Hospital, has received a Clinical Investigator Development Award from the National Institute of Neurological and Communicative Disorders and Stroke. The Clinical Investigator Development Award, a career development award mechanism, is designed to provide support for individuals with high potential for academic research careers. The award is for a five-year period and will allow Noetzel to continue his research on the role of nerve cell filament proteins in the developing nervous system. He is currently investigating how these unique nerve proteins function in the immature brain and, in particular, how they promote growth of nerve cells.

The libraries at Washington University School of Medicine and the University of Nebraska are joint recipients of the Frank B. Rogers Award for Information Advancement from the Institute for Scientific Information (ISI).

The award, given annually by the Medical Library Association, recognizes an outstanding contribution to the use of technology in delivering health sciences information. Barbara Halbrook, associate director of the medical school library, and Simon Iglinski, Ph.D., director of the Washington University Medical Computing Facility, received the award on behalf of Washington University at the association's 85th annual meeting.

The award is named for Rogers, who was director of the U.S. National Library of Medicine from 1949-63 and a pioneer in computer applications for management of biomedical information.

Washington University received the award for the development of OCTANET, a telecommunications network in the midcontinental region for document delivery. OCTANET serves over 600 libraries in Colorado, Kansas, Missouri, Nebraska, Utah and Wyoming. The database for biomedical serials, which is accessed for interlibrary loans throughout the six-state Midcontinental Regional Library Network, was developed and managed by the Washington University School of Medicine Library in cooperation with the Medical Computing Facility.

OCTANET is one of several programs in technology research and development at the School of Medicine Library. Recently, ISI awarded the library a contract to develop Current Contents — the major computer service used by scientists to keep up with developments in their fields — for faculty, staff and students at Washington University Medical Center. Current Contents reproduces the tables of contents of scientific journals and distributes them in weekly compilations.

The institute also is providing some $140,000 in support services, along with a database covering the physical, life, clinical and agricultural sciences. The library and Medical Computing Facility will develop software for accessing Current Contents through its computerized bibliography system, and will study information needs and uses for research, teaching and patient care.

Steven J. Rose, Ph.D., director of the Program in Physical Therapy, has been named a Catherine Worthingham Fellow of the American Physical Therapy Association (APTA).

Rose, who is also co-director of the Department of Physical Therapy at Irene Walter Johnson Rehabilitation Institute, was recognized for national leadership in advancing the science, education and clinical practice of physical therapy. He is the sixth physical therapist to be honored with the fellowship, first awarded to former APTA president Catherine Worthingham in 1982.

Earlier this year, Rose was named to the APTA President's Commission on University Relations, which was formed to promote physical therapy training in higher education. He received the association's Lucy Blair Service Award in 1983.

Under Rose's direction, Washington University has established a model program that not only trains entry-level physical therapists, but also allows practicing physical therapists to pursue master's degrees by combining clinical practice with research.

Washington University School of Medicine is one of four institutions in the U.S. to be awarded $3.4 million as a Sen. Jacob Javits Center of Excellence in Neuroscience. The program, sponsored by the National Institute of Neurological Diseases and Stroke, stipulates that "the centers should be dedicated to finding the cause, prevention and cure for neurological diseases, and be designed so that multidisciplinary teams of the most capable scientists address fundamental issues of nervous system structure and function."

Gerald D. Fischbach, M.D., Edison professor and head of anatomy and neurobiology, and Dale Purves, M.D., professor of neurobiology, will direct the Center at the School of Medicine. Other researchers in the Center include Jonathan Cohen, Jeffrey Lichtman, John Merlie, Joshua Sanes, and Mark Willard.

Fischbach has pointed out that in the fall issue of Outlook, he was cited as the sole recipient of this award. The editorial staff regrets this error.
"I wanted to see one student become a doctor, to follow that person through at least four years of medical school, and really get to know them."

With this in mind, Stella Koetter Darrow approached Washington University School of Medicine, and she's not been disappointed. Her gift in 1978 to establish the Albert F Koetter, M.D., Scholarship Fund, has launched more than one young doctor. Currently, Laura Rokusek — a medical student from Rockford, IL — is the beneficiary of Mrs. Darrow's generosity. For Rokusek, like most students at the School of Medicine, the Koetter Scholarship has removed one major obstacle that might have prevented her from realizing a life-long dream — becoming a doctor.

Rokusek's path to medical school was not an automatic one. The youngest of three children, she does not come from an academically inclined family. Rokusek was able to attend Washington University as a National Merit Scholar, graduating with a degree in biology. She wouldn't have been able to afford medical school, she says, without the Koetter Scholarship: "One summer, I worked three waitress jobs — all different shifts — just to help make ends meet."

Rokusek is also an Olin Fellow, one of many medical students who are beneficiaries of the Mr. and Mrs. Spencer T. Olin Fellowships for Women.

As a third-year student, Rokusek relishes her clinical rotations. Recently, she finished her ob/gyn rotation and describes what it was like to deliver a baby: "The father was present in the delivery room for this birth. It was his first delivery experience, despite the fact that it was the family's third child.

"He was so moved by the experience that he cried, and I must admit that I felt like it too. Delivering the baby was definitely the high point so far."

Rokusek says that the patients on whom she's had to practice have been very supportive: "When I did my pediatrics rotation, I had to insert an IV. Luckily, I happened to be working with some older patients at Children's Hospital, 20-year-olds with cystic fibrosis. After a few unsuccessful attempts at getting the needle in, I was ready to give up. But they wouldn't let me. 'Keep trying, you'll do it,' they said, and I did.

"It's great to put into practice some of the things I learned in my first two years. I'm getting to the point where it's close to feeling natural to be taking care of patients, like this is really something I was meant to do."

Rokusek meets periodically with Mrs. Darrow, to have lunch and just generally keep in touch. Mrs. Darrow thinks that this type of personal involvement with a student "is very satisfying. It's exactly the kind of thing I originally had in mind when I established the scholarship."

The scholarship is a tribute to Mrs. Darrow's father, Albert F Koetter, M.D. A graduate of a German medical school, he was a staff otolaryngologist at Barnes Hospital and other private hospitals in what is now the Central West End, when he died of cancer at age 46. His young daughter, then age 7, never forgot her father. Later, when she and her sister Wilma graduated from Washington University, they established a link with the school that would always hold great significance for them.

The Koetter scholarship is one of many that support doctors-in-training. Mrs. George M. Powell established a similar endowment in appreciation for the medical education received at Washington University by her husband George M. (M.D. '32) and son George K. (M.D. '64). Besides friends of the university like Mrs. Koetter and Mrs. Powell, alumni of the School of Medicine have also gotten in on the act. For example, John R. Lionberger, M.D., '38, established a medical student scholarship fund in 1982. "A top priority is funding for medical student scholarships," says John C. Herweg, M.D., associate dean of Washington University School of Medicine. "Washington University will continue to attract, enroll and educate talented young men and women, irrespective of these students' socioeconomic status. But to do this, increased scholarship support is crucial."

Students entering in 1985 could graduate with an $80,000 debt or more; annual costs are nearly $20,000. The Eliot Society has developed a new program to help fund student loans and ease the burden of debt for medical students. For each Eliot Society member who donates $2500 or more, an interest-free loan of $1500 will be made to a student. The loan will be named for the donor, and the student and donor will be able to meet each other at a special annual dinner.

In addition, the executive council of the medical alumni association has decided to match, dollar for dollar, all Eliot Society gifts to this new program, up to $50,000. "This will add up to $100,000 or more in new funds for interest-free student loans," explains Nicholas T. Kouchoukos, M.D., '61, president of the medical alumni association.

For Stella Koetter Darrow, establishing the scholarship was just one of many philanthropic efforts. Her career as a librarian, working for the St. Louis public library system, stimulated her interest in helping the latter. In addition, she was a founder of Washington University's Bookmark Society, in which she remains active, and she is also a member of the Eliot Society.

"Establishing the scholarship was really my husband's idea," she remarks. "You ought to do something for the university while you're still alive," he said, "so that you can get some personal enjoyment out of it." Looking over at Rokusek, Mrs. Darrow paused for a moment: "I think he had a very good idea."
Researchers usually do not literally sacrifice their lives to science. But Floyd Bloom, M.D. ’60, nearly earned that unusual distinction. The incident occurred at the Salk Institute during his collaboration with Nobel Prize winner Roger Guillemin.

“One morning, just the two of us were in the laboratory,” remembers Guillemin. “This was in the very beginning of our work together, and I was totally unaware that Floyd is extremely allergic to rats.

“As we were doing our experiment, Floyd was bitten by one of these rats,” continues Guillemin. “Literally in seconds, he was in absolute shock and fell to the floor. I took care of him for a few minutes until he started coming around.

“We were supposed to go to an administrative meeting at the institute after finishing the experiment. So I called the executive secretary in administration, and I remember telling him, ‘Phil, I have a small problem. Dr. Bloom and I were working here and he just passed away.’ I corrected myself and said, ‘He just passed out.’” Guillemin, a native of France, laughs at the memory of his linguistic difficulty, saying, “From that time, it was mentioned as one of the small problems with my English.”

The incident didn’t deter Bloom, however. He and Guillemin shared a collaboration that the latter calls “remarkably successful and constructive, and so pleasant humanly and intellectually.”

They were pioneers in isolating and characterizing the then-new brain proteins called endorphins, so named because of their morphine-like effects.

“My efforts were complementary to his,” recounts Bloom. “He is a world expert in identifying and isolating new peptides. My laboratory determines which cells in the brain make those peptides, and how those cells use these molecules to communicate a message to other nerve cells. So it was an ideal relationship for him to determine the chemistry of the endorphin peptides, and for my group to map them and determine their cellular and behavioral effects.”

Endorphins are one of three classes of molecules, called neurotransmitters, that enable nerve cells in the brain and elsewhere to communicate with each other. Besides endorphins, molecules such as amino acids can act as neurotransmitters. Another group of molecules called monoamines also enables nerve cells to communicate. All three types of molecules — monoamines, amino acids and endorphins — effect changes in nerve cells.

“The three chemical categories of neurotransmitter differ in their function and in the structures of the cells that make them and use them,” explains Bloom. “The amino acid transmitters are the most prevalent ones throughout the brain. They produce the typical excitatory or inhibitory signals.
It’s like playing the piano with and without the foot pedal,” says Bloom. “By depressing the foot pedal, you can accentuate the music, making it more resonant, louder or sharper. You are not changing the keys that have been played, but you are changing the way in which hitting the keys produces the desired goal of making music. Monoamine systems, and endorphins, work sort of like those foot pedals—they enhance the quality of the signal that is coming across to a nerve cell, and they modify the way that cell responds to its signals.”

Bloom’s goal in working out the brain’s neurochemistry is, as he phrases it, “understanding how disorders of the mind arise from abnormalities in the process of chemical neurotransmission. Ultimately, for me, true understanding of the nature of a chemical neurotransmitter and the circuit that makes it and the circuit that responds to it, means to determine its potential role in behavior.”

Yet this won’t be attained, Bloom points out, until we determine the complete catalog of all neurotransmitters in brain cells’ library, together with the extent of these neurotransmitters’ effects. “We’re at least fighting with two hands behind our back,” he says. “Because we have an incomplete list of brain transmitters, we have an incomplete list of the circuits involved in mental illness and the nature of the changes in specific forms of mental illness. But when you ask the right question, things become simpler.

“It may well be that some new neurotransmitter that has never been discovered will have a very compelling relationship with a certain type of schizophrenia. By simulating the effects of that neurotransmitter with a drug, or antagonizing its effects, we will be able to treat this mental illness in a way that is quite powerful.”

Bloom and others will be able to complete the entries in the catalog of neurotransmitters much faster, thanks to the technology of genetic engineering. This technology is a shortcut that bypasses the tedious, time-consuming methods of protein purification traditionally used by scientists. (Guillem once had to process hundreds of thousands of sheep hypothalami just to obtain one milligram of the peptide he was isolating.) Genetic engineering permits researchers to begin with any peptide, or even mRNA—the template cells use to make proteins. Then, using recombinant DNA techniques to create bacterial “factories,” scientists can quickly manufacture adequate amounts of a protein of interest.

Bloom’s work in cataloguing brain peptides through analysis of mRNA “has opened up a whole new area of investigation,” says out long-time collaborator Paul Greengard of Rockefeller University.

This new technology can speed the cataloguing of the brain’s library of neuropeptides like the endorphins, leaving Bloom more time for other research interests. Now in La Jolla, California, at Scripps Clinic and Research Foundation as director of preclinical neuroscience and endocrinology, he heads several research groups. One investigates the effects on brain cells of substances such as lithium (used in the treatment of manic-depressive illness) and antidepressants. In addition, Bloom continues his long-standing research on alcoholism.

Bloom’s wide-ranging research has earned him national recognition, including election to the National Academy of Science. Most recently, he was named a fellow of the American Association for the Advancement of Science. His honorary degrees from Southern Methodist University, Hahnemann University, and the University of Rochester attest to his prominence.

“He’s a brilliant person, very imaginative, creative and original,” says Greengard, himself a world-famous neuroscientist. “He’s got about as deep and broad a knowledge of neuroscience as anyone. He’s always being asked by colleagues to represent our profession in various ways, such as speaking to Congress. And not only does he have a broad knowledge of neuroscience, he utilizes many different techniques to solve a problem.”

“He’s remarkably productive,” points out Samuel Guze, M.D., vice chancellor for medical affairs at Washington University, “and he’s been willing to tackle problems that have special technical obstacles.”

This ability to tackle obstacles served Bloom in good stead during a particularly trying time in his life. His wife became ill and died, leaving him a young son and daughter to raise. The illness and the grieving which followed, remembers Guze, much affected Bloom: “But characteristically, he handled it very well.”

A few years ago, Bloom married Jody Corey, a neuroscientist whom he met at a scientific meeting. “She always wanted to go to medical school,” remarks Bloom, “and now she is.” A fourth-year student at University of California at San Diego, she plans to become a neurologist. His two children are both grown now and leading successful lives, so that Bloom can freely and vigorously pursue the scientific questions that interest him. He makes time for few pursuits outside the laboratory, but he relishes running and has participated in several half-marathons (13 miles).

Bloom doesn’t think it the least bit unusual that an M.D. should forsake clinical work to do neuroscientific research. He credits the late Edward Dempsey, Ph.D., former chairman of the Department of Anatomy and Neurobiology at WU and dean of the School of Medicine, with great influence: “It was his recommendation that led me to continue to pursue brain research, rather than returning to my residency program.

“What typified the Washington University student of my generation, in contrast to students at other medical schools, was the faculty’s desire to establish in our minds a way to analyze critically what other people taught us. Being able to sift the wheat from the chaff, being able to focus on critical issues, has been something that has played an important role in whatever kinds of success I’ve had. I think my basic philosophy in research came directly from the exposure I had as a student at Washington University. And that is to ask important questions in a way clean enough to get a yes or no answer.”
**30s**

Paul O. Hagemann, M.D. '34, has been named vice chairperson of the Washington University Planned Giving Committee.

Clark Porter, M.D. '35, was honored by the Michigan chapter of the American Academy of Family Physicians for 50 years of private practice. After interning at St. Louis City Hospital, Porter spent a year with the Illinois Conservation Corps as camp surgeon. He moved to Michigan where he entered general medicine (later, family medicine) which he practiced until his retirement in 1980. He lives on St. George Island, Eastpoint, FL, and extends greetings to all his classmates.

**40s**

Willard B. Walker, M.D. '46, has been re-elected for a second year as the part-time representative to the Executive Faculty of Washington University School of Medicine. The council is the school's governing body.

Walker joined the School of Medicine faculty as an instructor in surgery in 1953, and was named associate professor of clinical surgery in 1971. After graduating from the School of Medicine, he completed internship and residency in general surgery at Barnes Hospital.

For 25 years Walker served as a surgical consultant and supervisor of surgery at Homer G. Phillips Hospital. He is now on staff at Barnes and Children's hospitals. He is president of Gateway Vascular Society, and a member of the American College of Surgeons, AMA, Southern Medical Society, and other professional societies.

Sidney Goldring, M.D. '47, professor and head of neurological surgery at the School of Medicine, has completed a yearlong term as president of the American Association of Neurological Surgeons. The association, founded in 1931 as The Harvey Cushing Society, is the primary organization for neurological surgeons in the U.S. Goldring delivered his final address to the association during its annual meeting in Atlanta and traveled to Hawaii this fall as the honored guest at the annual meeting of the Congress of Neurological Surgeons.

**50s**

Richard H. Morrow, M.D. '58, is secretary of the Scientific Working Group on Epidemiology in the Special Programme for Research and Training in Tropical Diseases, World Health Organization. He is also visiting lecturer at the Harvard School of Public Health. He resides in Switzerland.

**60s**

Philip W. Majerus, M.D. '61, professor of medicine and biological chemistry at Washington University, is one of five recipients of the second biannual Distinguished Career Award for Contributions To Hemostasis, awarded by the International Congress on Thrombosis and Haemostasis.

Robert H. Waldman, M.D. '63, is Dean of the University of Nebraska College of Medicine in Omaha. He took office on July 1, 1985. Formerly, he was head of medicine at the West Virginia School of Medicine.

Waldman, who served as acting dean of medicine at West Virginia, received his undergraduate degree from Rice Institute. After earning the M.D. from Washington University, he took a residency in the Osler Medical Service at Johns Hopkins. Subsequently, he was a clinical associate at the National Institute of Allergy and Infectious Disease.

James M. Hammond, M.D. '66, has been promoted to professor of medicine at The Milton S. Hershey Medical Center of the Pennsylvania State University.

B. Leonard Holman, M.D. '66, has recently been named a fellow of the American College of Radiology. Holman is on staff at Brigham and Women's Hospital in Boston and resides in Chestnut Hill, MA.

**70s**

Dennis Cooper, M.D. '71, has been a participating ophthalmologist on the Eye Van, sponsored by the University of Arizona and the state ophthalmological society, for eight years. The Eye Van is equipped to provide medical eye care to residents of rural Arizona and Indian reservations. Says Cooper: "I usually see more sick eyes in two to three days on the van in Navajo country than in a month in my office in Scottsdale."

**Former House Staff Notes**

Victor Goodhill, M.D., F.A.C.S., was a member of the house staff in otorhinolaryngology from 1938-39 and has returned to Washington University many times as a visiting professor.

He has been chief of otologic surgery and otorhinolaryngology at UCLA since the School of Medicine was established in 1964. Currently, UCLA is building the Victor Goodhill Otorhinolaryngology Research Center.

Goodhill has retired from private practice to concentrate on teaching and research.

Donald E. Riesenberg, M.D., F.H.A., has joined the editorial staff of the Journal of the American Medical Association (JAMA). He is the AMA's eighth Morris Fishbein Fellow in Medical Journalism. This yearlong fellowship gives recipients the opportunity to develop their skills as medical writers and editors. Eventually, Riesenberg hopes to establish a full-time career in medical journalism.

**Medical Center Alumni Association**

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Dark inclusions — globs of undigested garbage — dot this electron micrograph of a placental cell. The fetus has I-cell disease, and its defective lysosomes cannot process waste material. I-cell disease arises when any of the transport, sorting or labelling procedures for proteins go awry. Enzymes destined for use in the cell’s lysosomes are not properly labelled; thus, these organelles cannot function. See story, page 2. (Micrograph by George Hug, formerly a postdoctoral student of the late Carl Cori)
Figurines make it easier for clinical nurse-specialist Anne Richardson to create therapeutic play sessions with children who have kidney disease. During these sessions, children with nephrotic syndrome can act out their anxieties and achieve insights about their condition that would be impossible otherwise. See story, page 6.