Mary Russell was one of 30 young people taking part in the Program in Occupational Therapy's summer Discovery Program. At the St. Louis Zoo, she experienced some of the consequences of using a wheelchair. The program brings high school and college students interested in careers in occupational therapy to the medical school campus for a week to help them make more informed career choices. The students, from across the country, are exposed to occupational therapy as it applies to pediatrics, physical disabilities, mental health and independent living.
On The Cover:

Nerve-cell axons, stained orange, grow toward their motor neuron targets, stained green. Photos like this show William D. Snider, M.D., the mechanisms by which axons seek out their precise targets in a developing nervous system.

For more about the research, see the feature story on page 12.

The Small View

Physicians explore the clinical potential of a tool that can peer inside tiny fallopian tubes.

Looking For The Lazarus Factor

Neurotrophic factors may hold the secrets of nerve repair.

Exercising Control

The outpatient treatment of severe psoriasis sends the incurable disease into remission.

The Neuroscientist's Art

Images recorded in pursuit of an understanding of the nervous system stand alone as art.

Newsbriefs

Student Stage

Silhouette: David M. Kipnis, M.D.

Alumni Report
Atkinson Named Head Of Internal Medicine

John Atkinson, M.D., has been named chairman of the Department of Internal Medicine. The appointment, effective Oct. 1, 1992, was announced by William A. Peck, M.D., vice chancellor for medical affairs and dean.

Atkinson replaces David M. Kipnis, M.D., professor of medicine, who has held the position since 1973. Kipnis has been appointed Distinguished University Professor of Medicine and will divide his future activities among expanded research efforts in diabetes mellitus, undertaking special projects for the Department of Medicine and the dean and increased involvement in corporate and foundation interactions with the medical school. (See the "Silhouette" later in this edition.)

"The Department of Medicine at Washington University has a long tradition of outstanding leaders, most recently David M. Kipnis. Hence, the department has become one of the best in the nation, recognized for the scientific, educational and clinical contributions of its superb faculty. John Atkinson has the talent to build on that tradition well into the 21st century. He is a world-class investigator, a renowned teacher and a superb clinician who has the respect and admiration of students, house staff, trainees and faculty," Peck says.

Atkinson, professor of medicine and molecular microbiology, will leave his post as director of the rheumatology division. Louis Simchowitz, M.D., professor of medicine, will serve as the division's interim director. Atkinson will continue his research on the structure, function and genetics of the complement system, a group of proteins of the immune system.

Atkinson's research has played a key role in defining how the complement system is activated and in ways to control the damage complement proteins sometimes cause by attacking the body's cells.

Atkinson joined the Washington University faculty as an assistant professor of medicine and head of the rheumatology division in 1976. He became a full professor in 1984. Since 1976 he has been an investigator for the Howard Hughes Medical Institute. The institute supports medical scientists at academic medical centers and universities throughout the United States. Atkinson serves on the editorial boards of four medical journals, including the Journal of Immunology and the Annals of Internal Medicine.

Atkinson received his bachelor's degree from Kansas University in 1965 and his medical degree from the same institution in 1969. He completed his internship and residency at Massachusetts General Hospital.

Cloninger Honored With Awards

Robert Cloninger, M.D., Wallace Renard Professor and head of the Department of Psychiatry, is one of two recipients of this year's James B. Isaacson Memorial Award. The award was presented at the meeting of the International Society for Biomedical Research on Alcoholism in Bristol, England.

Cloninger shares the award with Michael Bohman of Umea, Sweden. The two have worked together on adoption studies in Scandinavia and are being honored for their work on genetic risk factors for alcoholism. They share the fourth Isaacson award, which was created in 1986 to honor scientists whose research contributions are crucial to basic or clinical medical advances in alcoholism and drug abuse.

Cloninger and Bohman's adoption studies allowed them in 1981 to identify two types of alcoholism. In type 1, the more prevalent, drinking begins in early adulthood, causes medical problems in later life, and is caused by both genetics and environmental factors. In type 2, which usually occurs in men and often in criminals, genetic tendencies are the primary cause.

Cloninger has investigated the genetic epidemiology of alcoholism.
Van Essen Heads Anatomy And Neurobiology

D avid C. Van Essen, Ph.D., formerly professor of biology at the California Institute of Technology, has been appointed professor and head of the Department of Anatomy and Neurobiology.

David C. Van Essen, Ph.D.

Van Essen is widely recognized for his research on how the brain organizes and processes visual information. His studies in primates have helped to demonstrate that more than 20 areas in the cerebral cortex are responsible for processing visual information. Using the tools of neurophysiology and computational neuroscience, Van Essen’s research has clarified how the various areas of the brain work independently and together to create the process of seeing.

The work of Van Essen and other neuroscientists has demonstrated that there are two general streams of information in the visual cortex: one dealing with fine detail and color, the other with movement and orientation in space. Van Essen’s current research involves a variety of physiological and behavioral experiments to define which areas of the brain control a particular perception, such as motion or color.

“As an internationally recognized neuroscientist, Dr. Van Essen represents a major addition to one of the strongest neuroscience programs in the world,” says William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine. “Dr. Van Essen is an award-winning teacher with administrative talent, and he will be an excellent leader for a great department.”

Van Essen received his graduate degree in neurobiology in 1971 from Harvard Medical School. He was a postdoctoral fellow at Harvard under David H. Hubel and Torsten N. Wiesel, who shared the Nobel Prize in Medicine in 1981 for their work on how mammalian brain cells analyze visual information.
$5 Million Collaboration Will Develop New Pharmaceuticals

Under a five-year collaborative agreement with Sphinx Pharmaceuticals Corporation, the School of Medicine will receive $5 million to develop new treatments for cardiovascular and inflammatory diseases. Richard Gross, M.D., Ph.D., professor of medicine, chemistry, and of molecular biology and pharmacology, will lead the project.

The collaboration will support research focused on developing drugs to control enzymes called phospholipases A2 (PLA2), thought to play a key role in heart attack, stroke, atherosclerosis, arthritis, asthma and other diseases.

PLA2 enzymes cause the release of arachidonic acid, which is converted into several potent regulatory molecules that effect a wide range of essential functions throughout the body. In heart cells, these regulators cause the tissue damage and irregular heart rhythm that accompany heart attacks. They also are believed to contribute to inflammation in several tissues.

One goal of Gross' research is to find inhibitors for PLA2 that will stop arachidonic acid release and avoid the "downstream" problems it causes. "What we are aiming for is a drug that operates at the beginning of this cascade to treat a multiplicity of problems with a single agent," Gross says.

Gross will focus on the three forms of PLA2 known to exist inside cells. He and his colleagues discovered two of these "intracellular" forms in 1985 and 1986.

PLA2 enzymes produced outside the cell have long been a research target but so far have not yielded useful drugs, Gross says. Studies over the past decade by Gross and others suggest that these intracellular forms are more likely to be the relevant pharmaceutical targets, he says. "We have very high hopes that successful agents can be found using these intracellular phospholipases A2 as probes to identify medicinally useful compounds."

Under the terms of the agreement, Sphinx will contribute at least $5 million to support the project during the next five years. Sphinx will receive licensing rights to two pending university patents and will hold licensing or option rights to the university's interest in future patents that arise from the research. In addition, Sphinx will hold exclusive development and marketing rights to candidate drugs that result from the collaboration. The university will receive a royalty on future product sales.

"We are pleased to enter into a research and development collaboration with Dr. Gross, who is one of the world's experts in the field of PLA2," says Clayton I. Duncan, Sphinx president and CEO. The Durham, NC, company is an industry leader in developing therapeutic drugs aimed at lipid-related enzymes. Its research programs focus on treatments for cancer, cardiovascular disease and inflammatory disorders.

At The Sticking Point

Streptococcal bacteria know that success in life is a sticky business. They have a remarkable ability to cling to throat cells with such avidity that monsoon-like sneezes and oceans of saliva fail to dislodge the bugs. And major illnesses like strep throat, pneumonia and scarlet and rheumatic fever are the result of this bug's penchant for our throats.

When streptococci float into the throat and anchor themselves, infection is virtually guaranteed. Until recently, scientists did not understand how streptococci cling to the throat. Now, in Proceedings of the National Academy of Sciences, scientists here report that they have discovered the key protein that group A streptococci use to grip cells.

Without protein F, streptococci can't cause strep throat, pneumonia or rheumatic fever, says the paper's lead author, Michael G. Caparon, Ph.D., assistant professor of molecular microbiology. The new evidence shows that Streptococcus pyogenes uses thousands of these proteins as tentacles to reach out and seize fibronectin receptors. Fibronectin is a sturdy, fibrous protein that is well connected to the meshwork that anchors cells, making it an appealing target for in-
Protein F grips fibronectin with a hold strong enough to withstand the coughs, sneezes and saliva that normally sweep away unattached bacteria.

Protein F might as well be super glue, judging from 20 to 30 million new cases of group A streptococcal infection each year in the United States. That rate of success translates into millions of days spent out of school or out of work for those infected.

Usually, penicillin is enough to stop the infection before strep make life considerably more miserable. Although researchers have yet to encounter penicillin-resistant streptococci, they predict that it won't be long before such strains are making the rounds. Drug-resistant strep could be a disaster, Caparon contends. Without treatment, streptococcal infection can progress to pneumonia or rheumatic fever, a disease that can destroy delicate heart valves.

Word from the front lines of research is even more ominous. Several types of streptococci that directly penetrate the skin to cause a devastating toxic shock-like illness recently have been isolated. This bad news undermines the importance of drugs that the bacteria can't outsmart. Theoretically, the discovery of protein F gives scientists a better chance at designing drugs that can stop strep adhesion to healthy cells. An "anti-adhesive" approach could work, Caparon says, but there's much more research to do before "no-stick" pills arrive on the pharmacist's shelf.

For now, the excitement of the discovery remains in the scientific community where — for the first time — scientists have a genuine streptococcal adhesive to work with. Scientists have sought strep's adhesive protein for years, but it remained elusive because tools couldn't keep pace with ideas. Many models of streptococcal adherence have been proposed, but all have been swept away by further research, Caparon notes.

The short shelf life of past adherence theories gives Caparon a healthy skepticism about his find. Though he knows he has identified an adhesion protein, Caparon remains unconvinced that his theory will stick. "It seems too clean," he says. "Bacterial adherence is such a complicated phenomenon that the protein F model seems too neat. Is this the last word? It's difficult to say. When anyone else has tried to make such strong conclusions, they have always eventually been shown not to be the case."
From Sweden To Normark

Staffan J. Normark, M.D., Ph.D., professor and head of the Department of Molecular Microbiology, is the recipient of the Goran Gustavsson Award in Medicine bestowed by the Royal Swedish Academy of Sciences.

The three-year, $500,000 award is named for Goran Gustavsson, a Swedish philanthropist who donated $60 million to the Royal Swedish Academy of Sciences in 1990 to reward outstanding achievement in medicine, molecular biology, physics, chemistry and mathematics. A committee at the academy selects award winners from a group of scientists nominated by its members.

Normark was awarded the prize in medicine for his contributions to the understanding of how bacteria cause disease. The award money will be used to further his research.

During more than 20 years of research, Normark has studied many types of bacteria, especially E. coli, a bacterium commonly involved in urinary tract infections and sepsis. Although E. coli is a regular inhabitant of the intestinal tract, when it spills into the blood or grabs hold of cells lining the urinary tract, it can become a major medical problem. The adhesive mechanisms that E. coli use to adhere to cells and initiate disease are not well understood, but Normark says the adhesins are a target for drug therapy. Normark and his colleagues in Sweden and the United States are currently developing "anti-adhesive" drugs to prevent bacteria from attaching to healthy cells.

Studying how bacteria protect themselves from host defenses and therapeutic drugs is another project destined to improve current drug design. Mutant strains of bacteria are resistant to the best antibiotics in the medical arsenal, and genetic studies in Normark's laboratory are yielding new insight into how bacteria become resistant. The research is currently supported by the National Institutes of Health and pharmaceutical companies.

Normark, a native of Sweden, came to the School of Medicine in 1989 from the University of Umea, where he was a professor of medical microbiology.

Leary To Direct Veterinary Affairs

Steven L. Leary, D.V.M., has been named assistant vice chancellor for veterinary affairs and director of the division of comparative medicine.

Leary's appointment, effective August 1, was announced by Theodore J. Cicero, Ph.D., associate vice chancellor for animal affairs and associate dean of the School of Medicine.

"We are delighted to have Dr. Leary join our faculty," says Cicero. "He has an impressive background in research and extensive experience in the planning and designing of animal research facilities."

Leary comes to St. Louis from the University of Alabama at Birmingham, where he was a professor of comparative medicine and director of the animal resources program. He will provide guidance on the care and use of animals at the university and will participate in decisions regarding the animal program and its facilities and procedures.

Highly regarded for developing and maintaining the animal resources program at Alabama-Birmingham, Leary's research interests are in arthritis, cancer and the comparative pathology of lab animals. He joined the faculty at the University of Alabama-Birmingham in 1986. Earlier, he served on the faculty at the University of Minnesota in the College of Veterinary Medicine and as a veterinary consultant at the Veterans' Administration Health Center in Minneapolis. He also has worked as a regional veterinary officer for Papua, New Guinea and has practiced veterinary medicine in Iowa and Illinois.

For the past three years, Leary has served on the accreditation council of the American Association for the Accreditation of Laboratory Animal Care and since 1990 he has been a member of the task force on future directions of laboratory animal medicine for the American College of Laboratory Medicine.
Antidepressants Help Diabetic Patients

Reporting the results of a four-year study, researchers here have demonstrated for the first time that antidepressant drugs can successfully treat clinical depression in diabetic patients.

In the past, although doctors may have prescribed antidepressant drugs for their diabetic patients with depression, there was no proof that the therapy would be effective because diabetic patients metabolize some drugs differently than those with normal blood glucose levels.

Depression is common in diabetic patients, according to Patrick J. Lustman, Ph.D., associate professor of medical psychology. "Diabetic patients are about three times as likely to suffer from major depression, and it’s often worse for them than for non-diabetic patients. In depressed people who aren’t diabetic, the symptoms tend to come and go. Diabetic patients get depressed and stay depressed," says Lustman.

Though their symptoms are more debilitating, Lustman says, "Depression is under-recognized in diabetics. About two-thirds of the internists who treat diabetic patients don’t recognize or treat depression." Those who do get antidepressant drugs usually receive the medication not for depression but for treatment of diabetic neuropathy.

Lustman says tricyclic antidepressant drugs have been proven effective as analgesics, but until now had never been studied to see if they actually worked as treatment for depression in diabetics. The new insight was reported at the 52nd Annual Conference of the American Diabetes Association in San Antonio, TX.

Studying patients with poor glucose control and major depressive disorder, Lustman and his team found that diabetic patients receiving the antidepressant drug nortriptyline for eight weeks were significantly less depressed than those who received placebo.

The antidepressant medication did not control blood glucose levels as investigators had hoped it might, though some of Lustman’s other work suggests that effective treatment for depression could result in better long-term blood glucose management. In a separate study on depression and blood glucose management, Lustman and co-investigators found that depressed diabetic patients often have problems with glucose levels simply because they aren’t as likely to comply with their prescribed treatment regimen.

"Depressed patients are less likely to monitor their blood glucose levels as they should," says Lustman. He speculates that management of depression with nortriptyline could have the added bonus of leading to better overall disease management for diabetic patients.

Gordon Receives Distinguished Achievement Award

The American Gastroenterological Association has presented the Distinguished Achievement Award, its highest honor for an investigator, to Jeffrey I. Gordon, M.D., alumni endowed professor and head of the Department of Molecular Biology and Pharmacology.

Gordon’s laboratory employs transgenic mice to examine the mechanisms that allow the intestine to acquire different functions in its various parts and how gut epithelial cells differentiate from stem cell precursors. Gordon and his colleagues also use genetic, biochemical and organic chemical tools to examine an enzyme called N-myristoyltransferase (NMT) that attaches myristic acid (a rare fatty acid) to proteins important in regulating cell growth, the viability of fungi that cause a variety of infectious diseases and the assembly of certain viruses.

These studies have allowed them to develop a new group of compounds that inhibit replication of the AIDS virus in human white blood cells in the laboratory. The new compounds resemble myristic acid and are transferred by NMT to proteins of the AIDS virus — blocking the virus’ ability to assemble. These compounds also may be useful for treating other infectious agents and may affect other pathologic conditions, such as cancer.

Jeffrey I. Gordon, M.D.

Gordon has received several other awards for his research, including the American Federation for Clinical Research Young Investigator Award and the National Institute of Diabetes and Digestive and Kidney Diseases Young Scientist Award.
by Kleila Carlson

The Small View

S
maller in diameter than a toothpick, a woman’s fallopian tubes are significant out of all proportion to their size. They are the tunnels through which eggs must travel to the uterus after being released by the ovary and so are an essential pathway in the complicated process of fertilization. Blocked by tubal disease — common in American women — these tiny tubes are at the root of the frustrating and emotional infertility dilemma suffered by millions of couples.

Assessing The Falloposcope’s Potential

The same minuscule size that makes fallopian tubes susceptible to blockage makes it difficult and sometimes impossible to accurately diagnose tubal disease. When disease occurs in the smallest segment of the fallopian tube, as it does one-third of the time, it has been impossible to view because the one- to two-centimeter diameter there is simply too small.

The aptly named falloposcope — a new diagnostic tool being investigated at the School of Medicine — may make it possible for physicians to explore what Daniel B. Williams, M.D., calls the “narrow and tortuous” region of the fallopian tube known as the proximal portion. The instrument may one day take the place of laparoscopy to perform techniques commonly used to help infertile couples conceive. Procedures such as gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer (ZIFT), both of which require gentle manipulation to place the sperm and egg inside the fallopian tube, may someday be performed using a falloposcope.

Early results of a multicenter study examining the safety and effectiveness of the instrument and how it is placed into the fallopian tube show promise. Researchers are optimistic they will have the potential to perform delicate surgery and diagnose tubal disease transcervically (through the cervix), eliminating the need for major surgery.

“The falloposcope will allow us to do a number of things we currently cannot do,” says Williams, instructor in obstetrics and gynecology and principal investigator of the study here. “It allows us to view disease, such as tubal adhesions, which we may be able to remove with very small lasers. We can assess the inside of the fallopian tube and inform patients ahead of time about their potential risk of ectopic (tubal) pregnancy. This is something we’ve
never been able to do before, because we couldn’t clearly visualize the early part of the fallopian tube.”

Williams, who came to St. Louis from California just over a year ago, has been working with the falloposcope for the past two years. He helped refine the technology while he was a fellow at UCLA- Cedars Sinai Hospital in Los Angeles. Late last year, the School of Medicine was approved to take part in a multicenter Food and Drug Administration (FDA) trial to test the instrument’s safety and effectiveness. It is the only center in Missouri involved in the project; institutions in the United States and Europe are taking part in the clinical study.

Williams’ study involved 10 women who were already undergoing laparoscopy for infertility. Two women had blocked tubes as a result of proximal tubal disease, and two had normal tubes. Tubal dysfunction was eliminated as the cause of infertility in those with normal tubes.

According to Williams, the proximal portion of the fallopian tube, which extends outward from the uterus, is frequently the site of obstructive disease. “Roughly 30 percent of all tubal disease results from proximal occlusion,” he says. “Until now, we haven’t been able to adequately assess this segment because it was too small to view. The diameter of the proximal portion is one to two millimeters or about one-third the diameter of the ampulla (where fertilization occurs in the fallopian tube), which is about six millimeters. It was difficult to develop a scope that could negotiate this particular region of the tube while providing good imaging.”

Because endoscopes have been unable to reach this area, physicians previously diagnosed tubal disease by radiographic imaging using radiopaque dye. Williams says such tests are limited because they don’t identify the type of tubal blockage or detect the presence of potentially damaging lesions that aren’t obstructive. “In order to provide proper treatment, we need to be able to distinguish between diseased tubes that are blocked due to inflammation or fibrosis and tubes that are plugged by mucus or tubal spasm.”

A large percentage of the tubal damage Williams sees results from chlamydia and gonorrhea, both of which are sexually transmitted diseases that can induce tubal damage or lead to damaging infections that may cause no outward symptoms in the patient. “Tubal disease is one of the major causes of infertility,” Williams says, adding that an estimated 3 million couples are affected by some form of infertility. “At least 30 percent of all infertility is the result of tubal disease.”

Falloposcopic techniques to diagnose and treat the damage that can result from tubal infection have been undergoing refinement since the late 1980s. The actual scope that seeks out the injury is a miniature version of the instrument used to uncover clogged arteries around the heart. Similarly, the balloon catheter used to position the falloposcope in the fallopian tube — a new technique which was also evaluated in the FDA study — is much like the one used with coronary angioplasty.

“The new system delivers the falloposcope safely into the fallopian tube by means of a balloon catheter that unfolds from within itself,” Williams explains. “The balloon is actually rolled within the end of the catheter and it unfolds from the catheter tip, like a carpet being unrolled on the floor. This eliminates any force that might occur between the balloon and the inner wall of the tube.”

The unfolding balloon, which follows the path of the fallopian tube, has a hollow tube down its middle that allows for placement of the falloposcope. When inflated, the balloon is about the diameter of a toothpick; the falloposcope that traverses its midsection is about the size of a sewing needle.

Williams says advancing technology in the diagnosis and treatment of proximal tubal disease is exciting for reproductive endocrinologists like himself. But what is likely to have even greater impact is the potential use of the

“At least 30 percent of all infertility is the result of tubal disease.”
“The falloposcope will allow us to do a number of things we currently cannot do.”

The falloposcope with assisted reproductive procedures, such as GIFT and ZIFT. Within the next six months, he expects to begin phase two of the FDA study which will assess the effectiveness of the falloposcope in performing transcervical GIFT. Other investigators are attempting transcervical GIFT both blindly or by using ultrasound to guide them.

GIFT is an assisted reproductive procedure that involves removing eggs from the female and sperm from the male and placing them together in the fallopian tube. A related procedure, ZIFT, involves positioning eggs that already have been fertilized in the laboratory in the fallopian tube. At this time, both GIFT and ZIFT require surgery using a laparoscope through an incision in the abdomen.

“The falloposcope would allow us to directly visualize where we are in the fallopian tube,” Williams says. “Fertilization normally occurs in the third segment (ampulla), so that’s where we want to place gametes and embryos.”

Another benefit to this instrument is that we may be able to avoid the cost of an operating room procedure and use of general anesthesia. GIFT or ZIFT would take from 15 to 30 minutes as an outpatient procedure, and there’s also the chance it could eventually be done in the office.

Williams says the falloposcope could be valuable when trying to decide whether to perform GIFT or ZIFT, or allow the patient to attempt pregnancy with her own fallopian tubes. “If we have a patient who has had two ectopic pregnancies in one tube and we perform a dye test that indicates her tubes are open, we still need to know the status of the inner tube. Is there scarring, adhesion formation or deciliation (loss of the hairs that beat the embryo toward the uterus), all of which could impede her chance at becoming pregnant.”

Between gloved fingers, the tip of the scope reveals its scale.

The physician’s-eye view through the falloposcope shows any blockages caused by tubal disease.

“One way to resolve this issue is to look inside the tubes, and if they appear normal, we can recommend that the patient attempt a pregnancy on her own. We have a couple of patients in this situation right now and are awaiting the outcome.”

Conversely, he says, if a problem were discovered inside the fallopian tube he could recommend GIFT or ZIFT to avoid putting the patient through other procedures that would be unproductive.

“Using the falloposcope in assisted reproductive procedures is in the early stages and we’re on the ground floor; but I’m optimistic that the technology will become more refined and evolve into an office procedure. This would greatly expand the applications of the falloposcope.”

Some centers in Europe are already using the falloposcope to experiment with transcervical GIFT. Williams says at present they are blindly feeding a catheter into the fallopian tube or using ultrasound to monitor the catheter’s whereabouts. Studies in Europe are four to five months ahead of those in the United States because governmental guidelines for human studies in Europe are less stringent than those in the United States, he says.

Williams adds that the most significant risk with the falloposcope is tubal perforation, which can occur if tiny wires or balloons are inserted through the catheter to open clogged tubes. Such an occurrence is rare, he says, adding that at this time the instrument is only used as a diagnostic tool, not in conjunction with treatment.
RESEARCHERS EXPLORE WAYS TO SAVE, REGENERATE NERVES

BY JIM KEELEY

Looking for the Lazarus Factor

The neurons in the brain and spinal cord are unforgiving. Any insult can be catastrophic. A stroke or back trauma can instantly sever connections nature has carefully orchestrated, leading to paralysis or even death. Sometimes, the insult is insidious, as when the body succumbs to old age or disease and produces less of the nutritive proteins that bathe and feed the nerve cells that cluster in the brain and spinal cord. Without a source of nourishment, those neurons stop talking to each other, wither and die. This may be what happens in degenerative conditions such as Parkinson's and Lou Gehrig’s disease.
William D. Snider, M.D., investigates proteins called neurotrophic factors that nourish nerve cells, may save them from death and even initiate their regeneration.

Despite concerted effort and the application of molecular biology, neurobiologists have not found a "Lazarus factor," a drug that saves neurons from death or initiates regeneration. The problem has been that the nerve connections leading from muscles to the spinal cord and then to the brain are so complex that they defy understanding. Only improved knowledge of the nervous system can point to the drugs that will restore wrecked neurons and shattered synapses.

Although spontaneous neuronal regeneration occurs in lower species, it's not likely that human neurons can fully recover from serious injury or degenerative disease by themselves. Help must come from researchers reaching into the nervous system and plucking out proteins that may be of use. And scientists are just now warming up to that challenge, having isolated about 20 neuronal proteins that can rescue cells from death, reverse degeneration and in some cases initiate regrowth.

The first of the proteins, called neurotrophic factors (the Greek trophe means nourishment), is now being tested at the School of Medicine on people with Lou Gehrig's disease (amyotrophic lateral sclerosis). And more trials of these drugs are expected soon for other diseases.

**RIVERS OF GROWTH**

In the neurobiology community — where the basic science of these proteins is worked out — bench scientists looking for clues to how nerve connections are forged and nourished are communicating with clinicians treating brain and spinal cord damage. That communication, both groups say, is the key to understanding nerve repair and how to remedy ailments of the brain and nervous system.

According to William D. Snider, M.D., associate professor of neurology, regeneration of nerve processes in the central nervous system occurs poorly if at all. "Right now we can only get extremely limited regeneration in lab models," Snider says. "We think of regeneration as more of a long-term goal." But Snider and other neurobiologists at the School of Medicine believe that if they can understand how nerve connections are formed during development and then maintained, they can make great progress in discovering how the body might naturally mend bad connections. "This is more than just interesting developmental neurobiology," Snider says. "In order for us to approach neural injury, we have to understand what makes nerves grow."

Scattered on the surfaces of Snider's office are hundreds of slides painted in neon red, electric yellow and vibrant green hues. Under the microscope, the
slides reveal rivers of color twisting and branching. These rivers are actually neurons injected with a dye that traces the course taken by neuronal processes as they snake their way to the rat spinal cord. Each slide is a map that allows Snider to follow the development of spinal cord circuits.

The dye, Dil (pronounced die-eye), is a godsend for neurobiology, Snider says. Without its brilliant color and ability to stain neurons and their axons — the part that projects away from the cell body — developmental neurobiologists would not have the maps they need to study the formation of nerve connections. Each slide tells Snider a little bit more about the creation of the nerve network that allows the brain, spinal cord and limbs to work together to sense pain, heat and pressure. Although his bench work is a long way from the neuromuscular degeneration Snider sees in the clinic, the research familiarizes him with neurotrophic factors that could be tomorrow’s medicines.

A theory that Snider is testing is that growth factors guide growing neurons to their targets. Scientists know that as a neuron grows it sends out an axon, a long projection that grows to a target. But it is still not known what causes an axon to home in on a specific neuron or a precise destination in the spinal cord. Snider believes that growth factors play a key role in this process. He theorizes that as the axon extends away from the cell body it may “feel” its way to its target by growing along a chemical pathway of neurotrophic factors secreted by the target cell. It’s as if if each neuron has a built-in homing device that locks on to a growth factor produced by the target it is supposed to reach. Once the target is reached, Snider hypothesizes that growth factors again exert control in establishing the complex circuitry necessary for normal nervous system function. Any disruption in the flow of growth factors to the developing neuron can be chaotic; neurons stop growing, retract their processes and die.

Snider recently demonstrated just how important neurotrophic factors are to specific populations of developing neurons in a report in the journal Neuron. The report shows that when dorsal root ganglion neurons — those neurons that relay information from limbs to the spinal cord — are deprived of nerve growth factor (NGF), they fail to reach their target in the spinal cord and die. An antibody to NGF injected into embryonic rats shuts off the flow of NGF at a crucial time. The investigations show that NGF deprivation causes a dramatic drop in the number of the particular types of neurons that sense pain and temperature.

Neurons injected with orange dye make a clear map of their paths as their processes grow toward their targets, dyed green in this photo.
The research reported in *Neuron* shows that the absence of a specific neurotrophic molecule can affect the survival of a single type of neuron. Furthermore, the results suggest that antibodies to NGF could be used to block pain sensations by interfering with nerves that project to the spinal cord, Snider adds.

**NOURISHING NEURONS**

The recent identification of neuronal growth factors has opened up a new area of research for neurobiologists. Scientists now can approach rationally the specific effects of a neurotrophic factor on a given type of neuron. Because there are more than 20 different nerve growth factors, and surely more to be found, researchers must understand their effects before they can approach clinical studies.

So far, the NGF family consists of three closely related growth factors: nerve growth factor, brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3). Snider believes it's possible that each member of the NGF family is responsible for the survival of a different set of neurons. "When all we had was NGF, we were limited in our studies. Now that we have these other growth factors, we should be able to learn more about how the peripheral nervous system is established," he says, about how nerve growth is nourished and guided.

It's been 40 years since Rita Levi-Montalcini isolated the first neurotrophic factor, NGF, in her lab at Washington University. Scientists immediately recognized that it might be possible to use NGF to push human nerve cells to repair themselves. In theory, nerve growth factors could be given to patients whose own bodies had stopped supplying them. Forty years later, the journey from theory to practice is still not complete. Researchers have found that getting growth from neurons in culture is a lot easier than prompting damaged nerves with growth factors *in vivo*.

Snider's developmental work is all the more important now that clinical trials of neurotrophic factors have begun. The more scientists can learn about how cells depend on specific factors for survival, the closer clinicians will be to prescribing appropriate nerve growth factors for diseases like Lou Gehrig's, Parkinson's, Alzheimer's and peripheral neuropathy. Understanding how the body naturally promotes and stabilizes the formation of nerve connections could lead to a "recipe" of growth factors for healing nerve cell damage.

There has yet to be a successful clinical trial of a neurotrophic drug, but optimism for these promising proteins is strong. Lately, research in this field has undergone its own regeneration. Biotech companies with hopeful-sounding names like Neurogen and Regeneron are supporting neuroscience research, hoping for a big payoff when neurotrophic drugs finally become clinically applicable. These companies and millions of Americans hope that proteins pulled from human nerve cells can rejuvenate sick neurons.

During development, neurotrophic factors are capable of marvelous feats. Why shouldn't they be able to help with motor neuron disease or Alzheimer's? Snider is optimistic that human trials of neurotrophic drugs will succeed, because he has watched these proteins form neuronal connections from scratch and remodel them if necessary. "If these first trials succeed — and it's my belief that they will — then you'll see an explosion in the number of neurotrophic drugs coming into the clinic," he says.
Exercising Control

by Juli Leistner

Severe Psoriasis Can’t Be Cured, But It Can Be Treated
The disease was winning. After 13 years of treating her psoriasis by herself, Nancy Neumann realized that she needed help. What had begun as a mild case of red, patchy scales on her legs gradually gave way to fast-growing, thick plaques all over her body. They flaked, itched, hurt and sometimes cracked and bled. At work, the 37-year-old nurse applied lotions to remain comfortable enough to finish the day. Her YMCA asked her to stop using the swimming pool. A cashier refused to take money from her hand.

To regain the upper hand, Neumann turned to the School of Medicine’s new Barnes West Dermatology Center for a carefully administered, whole-body treatment of tar and artificial light.

Psoriasis is a chronic, incurable skin disease that affects about one in 50 Americans, or 4 million people. It usually appears between ages 20 and 50. Although its cause is unknown, medical research tells us it stems from an overgrowth of skin cells. In its mild form, red scales typically develop on the elbows, knees and scalp. Outbreaks occur spontaneously or can be triggered by stress, bacteria or any trauma to the skin such as insect bites or shaving. In severe cases, scales develop into persistent, thick plaques that cover from 33 to 100 percent of the body’s surface.

Neumann, one of the center’s first patients, originally treated her psoriasis with over-the-counter medicated creams. Then about two years ago, the disease progressed to involve nearly her entire body surface. “It got to the point where it was uncomfortable as well as disfiguring. It was really interfering with my life,” she says. Last fall, she sought help from a dermatologist, but his news was not encouraging: Six to eight months of treatment with ultraviolet B (UVB) light — the sun’s tanning rays — would give her improvement but not remission. Then she was introduced to the school’s dermatology center through her psoriasis support group, a local branch of the National Psoriasis Foundation.

In the Goekerman method of treating severe psoriasis, patients receive controlled exposure to ultraviolet B light in a light booth.
The red scales characteristic of psoriasis are visible in photograph A. In B, a nurse carefully applies sticky, pungent tar medicated with salicylic acid. In Photo C, the treatment continues with the application of common plastic wrap. Photograph D, that of a different psoriasis patient's arm, reveals the success of the technique.

The center's tar therapy, called the Goeckermann method, is not new; the facility's hallmark is that it offers the Goeckermann therapy on an outpatient basis. Traditionally patients have received the treatment in three- to six-week hospital stays. But for the past five years or so, insurance companies have been reluctant to pay for the costly inpatient care. In 1987, Arthur Eisen, M.D., head of the dermatology division, and Ann Martin, M.D., assistant professor of medicine in dermatology, anticipated a problem and began looking for alternatives.

"Insurance companies were turning down psoriasis patients who really needed something more extensive than just seeing their doctor every three weeks. We were concerned about what we would do for these patients if it really came to be the case that they could not be hospitalized," Martin says.

The center opened in March, one of only 30 of its kind in the country and eight in the midwest. It gives patients more convenient care for about one-fourth to one-third the cost of inpatient care.

"This new center provides a very good alternative to hospital care without compromising effectiveness," says Karen Forsman, M.D., director of the center and instructor of medicine in the dermatology division. She and her staff treat patients with psoriasis on at least one-fourth of their bodies; psoriasis on 36 percent of the body would cover the entire trunk and buttocks.

Neumann drove one hour each day from her home in Imperial, MO, to be treated. "When I started treatment, I had psoriasis on the palms of my hands, on the bottoms of my feet, on my legs, on my arms, on my abdomen, on my chest, on my back, in my hair, inside my ears. There wasn't an area of my body that wasn't affected in some way," she says.

Patients receive a six-hour treatment each day, five days a week, for a total of 15 to 18 treatments. An initial exam by Forsman determines the amount of light and the strength of the tar needed. Then patients step into a light booth for
anywhere from 12 seconds to 12 minutes. Next, nurses use tongue depressors to swab on a sticky, pungent layer of tar over the patient’s entire body. The tar is medicated with salicylic acid that removes the scales. Nurses must be careful to apply the tar in the direction of hair growth; brushing the other direction can inflame hair follicles. Some patients are also wrapped in plastic wrap, which maximizes the tar’s effect by increasing its penetration into the skin. A tar shampoo goes on the patient’s head and is topped off with a shower cap. Then the patient slips into a scrub suit and bides time for four hours.

After lunch, patients remove the tar by soaking for 15 minutes in a warm bath dosed with mineral oil. Several careful cleanings remove the shampoo. Next they return to Forsman. She prescribes another dose of light followed by the second layer of tar. Patients put clothing on over the tar — Neumann invested in two black sweat suits — and drive home.

At home, the patients leave the tar on for a few more hours, shower it off, apply a third coat and sleep in it. “Then you get up in the morning, shower it off and start all over again,” Neumann says. Throughout the treatment, patients must resist the temptation to rub their skin; trauma from scrubbing, combs or fingernails can aggravate psoriasis.

The Goeckermann method was developed in the 1920s at the Mayo Clinic in Rochester, MN. It has remained one of the safest and most effective psoriasis treatments available, Forsman says, although precisely what mechanism the treatment uses to arrive at its effectiveness is not yet clear. The other possible treatments — including a medication called etretinate, the anti-cancer drug methotrexate, and PUVA therapy, which uses light in combination with the drug psoralen — carry side effects, can become toxic and require close monitoring by a physician, she explains.

Although the Goeckermann method does not cure psoriasis, it usually produces a temporary remission; patients must repeat the therapy from time to time. Studies show that by the end of the treatment, the majority of patients are free of plaques; 90 percent are still clear eight months later, and 73 percent are clear after one year, Forsman says.

Neumann was delighted with her results. Her skin was clear except for scaling on her nails and in her ears and a bit of redness where plaques had been.

Now, weeks later, the redness is nearly gone, and she continues with follow-up light treatments. “It’s been the best thing that could have happened to me. It was a very positive and rewarding experience for me to get treatment and have it be the success that it was,” she says.

Cases of psoriasis have been documented for 2,600 years, but its cause and cure remain undiscovered. Researchers suspect a genetic and immunologic origin; roughly one-third of psoriasis sufferers have a family member with the disease, Forsman says. The inflammation that comes with psoriasis could be due to the high levels of white blood cells, interleukin-6 and arachidonic acid found in psoriatic skin, she adds.

Various growth factors and polyamines — chemicals important in cell reproduction — are also abundant in psoriatic skin and may lead to the excess cell growth. And plaques seem to develop or worsen with streptococcal and yeast infections, Forsman says.

The need to understand and control the disease goes far beyond cosmetic concerns; severe psoriasis can be life threatening, stresses Martin. “When skin is diseased, all of the functions it performs break down,” she says. Psoriasis interferes with the skin’s role in controlling body temperature and providing protection from infection and dehydration. In addition to the physical toll, the disease can lead to feelings of shame and anxiety that can interfere with social activities.

But Neumann urges psoriasis sufferers not to be ashamed of their disease. “People with psoriasis should learn to try to control the disease and not let it control them. Because they are going to have to deal with it for the rest of their lives.”
Scientists and artists both use the word "study," usually with very different meanings. As the cover photograph of this issue makes plain, their two definitions sometimes converge.

Exploring the development and behavior of the hugely complex nervous system, neuroscientists record images of their observations and manipulations. Investigations go on at that essential level where neuron communicates to neuron through electrochemical junction, where nerve meets muscle, where receptors organize to receive information coded in chemical neurotransmitters.

Collectively, these are the operations and the messages and the junctions that define life. So it is no surprise that the scientific images beat with a vitality that lifts them out of the informational and into the aesthetic. In this pictorial, Outlook presents a few of the visions that inform the neuroscientist and may inspire us all.

\[\text{A snake's living muscle fiber is shown in blue-green; the nerve that innervates it is in orange and red. The axon can be seen leading to its target, and the individual button-like dots on the muscle are the synaptic "boutons" of the nerve end. Boutons possess two compartments — shown separately in yellow and red. The yellow stains the compartment that houses mitochondria; the red highlights the compartment containing the neurotransmitter that the boutons release.}\]

From the laboratories of Jeff W. Lichtman, M.D., Ph.D., and Robert Wilkinson, Ph.D.
Reaching out to other neurons, a healthy mouse nerve cell in culture is stained to show the structure of its processes. The irregularities near the ends of the spindly neurites are called spines and are the sites at which nerve-to-nerve communication occurs.

From the laboratory of Mark P. Goldberg, M.D., and Michael Bateman.

The large, striated structure here is a single mouse muscle fiber. The brown element is a neuromuscular junction, or synapse, the site at which nerve communicates with muscle. And the blue “dots” are cell nuclei. Their bright color is an indication that elements in the gene for a neurotransmitter receptor are being expressed principally here. The upshot is that muscle cell nuclei at the synapse are different from others; their expression of chemical receptors is one clue nerves may use to find their way to appropriate targets.

From the laboratories of Joshua Sanes, Ph.D., and John P. Merlie, Ph.D.
A stained slice of rat brain at low magnification shows the same "swirl" arrangement of neurons revealed by the arc pattern of the previous photograph. Here, individual nerve-cell bodies are visible, but their processes are not marked by the stain. In humans, this region of the brain, the hippocampus, is called the "seat of the soul." Closely connected to memory function, it is an area of the brain particularly susceptible to stroke.

From the laboratory of Robert Wilkinson, Ph.D.

Nerve cells are shown at high magnification in a living slice of rat brain. The cell bodies and their processes — axons and dendrites — are visible and can be observed as the nervous system matures. If the cells continue to behave as they would in the brain, observing them will instruct researchers about how the nervous system develops.

From the laboratory of Robert Wilkinson, Ph.D.

Pseudocolor defines the density of receptors on the membrane of a muscle fiber in a living mouse. The receptors are for acetylcholine, the neurotransmitter at the neuromuscular junction. During development, muscle fibers are at first innervated by more than one nerve. Subsequently, they undergo a change that leaves each muscle fiber innervated by only one nerve. As competing nerves are eliminated, the density of receptors on the muscle fiber beneath the losing input drops. In these two images, taken 17 hours apart, receptors disappear, as shown by the smaller peaks visible in the lower left.

From Rita Balice-Gordon Ph.D., and Jeff W. Lichtman, M.D., Ph.D.
Plaques and tangles invade the brain of an Alzheimer's patient. The larger plaques lie outside of cells and are deposits of beta amyloid protein that is thought to be toxic to nerve cells. The smaller, denser tangles are filaments within the nerve cells that have been damaged by the disease process. From the laboratory of Joseph L. Price, Ph.D.

Nerves compete with one another to innervate muscles. The battle is visible here between green- and red-stained nerves. Each picture is of different nerves and different muscles. Two nerves progress from being nearly equal at embryonic day 17 until one has become established and the other is in retreat by post-natal day 10 in the mouse. From Rita Balice-Gordon Ph.D., and Jeff W. Lichtman, M.D., Ph.D.

Blood vessels are shown in the brain of a mouse just before birth. Researchers believe the hairlike structures, called filopodia, join to form a continuous channel that supplies nutrients to the brain. From Carl Rovainen, Ph.D. and Thomas A. Woolsey, Ph.D.
Wrestling With Ignorance

by Cheryl S. Rucker

L

ike most medical students, I appro

ached my third year with some trepidation. I

had heard horror stories from blac

k students about receiving

both blatant and subtle racist attacks on the wards

and being unable to respond

or address the issue. Such

stories made me anxious, but

I remembered my high

school band director’s teaching. “Behind every problem

lies an opportunity.”

I solicited the opinions of several black fourth-year

students until I found some

one who had had mostly

good experiences and asked

her how she approached the

third year. A positive atti

dude, self-confidence, consis

tent reading and preparation

were the keys, she said. But

she agreed with other stu

dents’ advice — don’t look

for racist slights, and if they

happen, don’t blow your top.

In other words, don’t risk

getting a bad evaluation. The

awareness that third-year

evaluations were largely sub

jective and the thought that I

could be poorly evaluated

because of one person’s

prejudice scared me and iso

lated me from my mostly

white classmates, even as

early as the end of second

year, before spending even a
day on the wards.

I believe that positive in

cner thoughts do attract posi

tive daily experiences.

Resolved to maintain a posi

tive attitude, I donned my

freshly starched white jacket

and stuffed it with my new

stethoscope, spiral manuals

and name tag. Although it

was difficult to believe that I

actually knew anything, I

soon developed a comfort

able rhythm. My internal

medicine team was very ca

usal, and we often sat in at

tending rounds having lively

debates about current issues.

One day a team member

remarked, “Cheryl, you
don’t have a Southern accent

like most people from the

South.” This launched a con

versation about television

personalities who drop their

accents in order to compete

in that job market. Another

student matter-of-factly re

marked that Bryant Gumbel

didn’t talk like the black

men he grew up with.” I re

minded him that he worked

with me and that I didn’t talk

that way. He replied, “I’ll

bet when you’re around

black friends, you use a

black dialect.” Calmly, I pro

ceeded to tell him that all

blacks aren’t the same and

do not talk the same. I then

pointed out that his exposure
to black people had obvi

continued to get along —

perhaps even better — I re

tained a feeling that I could

not trust him.

My first surgical experi

ence was initially scary, but I

felt protected by the black

scrub nurses in the gyneco

logic operating room. They

would make sure I had

breakfast so that I wouldn’t
deficit during surgery, hand

me instruments before I

could ask, and willingly give

me information about which

attendings liked and disliked

students. As I moved on to
general surgery, I noticed a

change in the climate. The

white scrub nurses were of

ten brusque and terse with

me compared to the way

they treated my white, male

counterparts. For example,

when the nurses brought in

stools for the other “student

doctors” to sit on during sur

gery, I was inevitably ne

glected until my resident

reminded them that I needed

one as well.

On the last night of a sur

gery rotation, the resident

and I prepared to handle our

last case. As we were wait

ing for the anesthesiologist

to get ready for the case, I

hung around eagerly await

ing the ready signal that the

patient would be brought

into the operating room and

preparation for surgery

would begin. Soon, one of

the nurses signalled that the

OR was ready and called for

“As a black female physician,

I realize that these little struggles

will be an everyday part of my

medical career.”

continued to get along —

perhaps even better — I re

tained a feeling that I could

not trust him.

My first surgical experi

ence was initially scary, but I

felt protected by the black

scrub nurses in the gyneco

logic operating room. They

would make sure I had

breakfast so that I wouldn’t
deficit during surgery, hand

me instruments before I

could ask, and willingly give

me information about which

attendings liked and disliked

students. As I moved on to
general surgery, I noticed a

change in the climate. The

white scrub nurses were of

ten brusque and terse with

me compared to the way

they treated my white, male

counterparts. For example,

when the nurses brought in

stools for the other “student

doctors” to sit on during sur

gery, I was inevitably ne

glected until my resident

reminded them that I needed

one as well.

On the last night of a sur

gery rotation, the resident

and I prepared to handle our

last case. As we were wait

ing for the anesthesiologist

to get ready for the case, I

hung around eagerly await

ing the ready signal that the

patient would be brought

into the operating room and

preparation for surgery

would begin. Soon, one of

the nurses signalled that the

OR was ready and called for
the doctor. I replied, "I could start getting the patient prepped and draped." She looked at me with disdain and yelled after me as I walked down the hall. "No! I need a doctor, you’re not good enough.”

I struggled to hold back the tears. The circulating nurse apologized for the other’s comment. It was meant to hurt and it did, but I refused to let it show. My resident and I prepared the patient for surgery and we completed the case without incident. I managed to feel a sense of accomplishment despite the earlier disparaging comments of the nurse.

I was not alone when it came to degrading experiences. A black female classmate was completing her patient’s physical exam and emerged from behind the curtain wearing her white coat, a stethoscope around her neck, her ENT kit in hand, notebooks in her pockets, and a clipboard filled with journal articles. As she made her way to the door, the patient’s roommate, after licking his fingers, said to her, "Ma’am, did you make this chicken? Is sure is good!” She replied, "No, sir. I didn’t.” She fumed silently for hours, but when she told me about it, I smiled, then laughed. We realized it didn’t help to get angry every time others assumed we were cooks, clerks, janitors, or nurses.

I tried to console myself and my friend; maybe comments like that aren’t racial. Maybe the scrub nurse would have said that to any student; maybe that man would have said that to any woman. Blacks in the professional world deal daily with a constant lack of recognition and respect for their accomplishments. As a black female physician, I realize that these little struggles will be an everyday part of my medical career, and that I will constantly wrestle with stereotypes. My triumph is in rising above them and moving on to educate others.

Reprinted with permission from the Journal of the American Medical Association (JAMA), May 6, 1992; Volume 267, Number 17. Copyright 1992, American Medical Association.
That David M. Kipnis, M.D., can see into the future no longer surprises those who work with him. They have witnessed his vision become reality at the School of Medicine.

Stepping down from his administrative duties after two decades guiding the Department of Internal Medicine, Kipnis elevated the department to world prominence. He attracted sought-after scientific minds, forged new avenues of securing resources and bridged the division between basic and clinical sciences.

Washington University Chancellor William H. Danforth says of him, "Washington University School of Medicine would be a different and much lesser institution without David Kipnis. He has scientific understanding and vision and a gift for putting the right people in the right places. His deep affection for this institution and his example of commitment, accomplishment and dedication has inspired us all to greater heights."

Kipnis came to Washington University in 1955 as an American College of Physicians Research Fellow to study under Nobel laureate Carl F. Cori, M.D., and to pursue his own research in diabetes and endocrinology.

His work has been cited for many honors, including the Endocrine Society's Ernest Oppenheimer Award and the American Diabetes Association's Lilly Award.

Research remains his first love, but his position as an administrator has prevented him from being as active in it as he would like. Still, he says, skills that are applicable to scientific research do not go to waste in administration.

"I would say about 80 percent of my time is spent with administration, but the administration involves finding scientific talent, developing resources (laboratory space, equipment and financial support) that make it attractive for young people to come here, working with hospital administrators to develop strategies in a market-oriented health care system and sustaining a viable enterprise for the medical school and hospitals," says Kipnis.

Kipnis, whom Danforth calls a "genius for finance," has been a creative developer of resources that are increasingly difficult to come by. The Washington University/Monsanto Biomedical Research Agreement — the largest research collaboration between an American company and an American university — was engineered by Kipnis and the late Howard A. Schneiderman, former senior vice president for research and development and chief scientist at Monsanto. The agreement, first reached in 1982, currently extends through 1994. It amounts to nearly $100 million in research funding and supports 50 research projects involving 120 university scientists. It is one example among many.

Kipnis' business acumen has benefited his department as well as the school. The number of full-time faculty has increased nearly fourfold, from 46 to 160, including 110 physicians at Barnes Hospital, 38 at Jewish Hospital, and between 12 and 14 at the John Cochran Veteran's Administration Hospital. The department's total operating budget, which 20 years ago was $4.5 million, now approaches $110 million and accounts for 25 percent of the total research budget for all of Washington University.

The spectrum of research now ranges from the most fundamental science to the most clinical applied research. Kipnis was responsible for broadening research horizons because he believes interaction between the basic and clinical sciences is "essential to the intellectual viability of the Department of Medicine."

"Without the basic sciences and that kind of close, collaborative interaction, we would not be at the cutting edge that we are now," says Kipnis. He notes that more than half of the faculty in the department of medicine have joint appointments in basic science departments.

Longtime colleague and friend Carl Frieden, Ph.D., professor of biochemistry and molecular biophysics, says Kipnis' greatest accomplishment was laying the foundation for the cooperative spirit that exists between basic science and clinical medicine. "When he arrived there were a lot of people here who influenced his feelings about basic science and the importance of basic science to clinical work," says Frieden. "People like Arthur Kornberg and his associates, Paul Berg, Melvin Cohn, Dale Kaiser, David Hogness and others. I don't think there's any better department of medicine anywhere because there are so many people here who are doing good basic science. David has a real eye for selecting people who are able to do basic science and carry out basic research in a clinical setting, and that distinguishes the department from all others."

Kipnis says both branches of medicine have benefited from this bilateral influence, which is evidenced in the success of young scientists such as Jeff Gordon, M.D.,
David M. Kipnis, M.D.

who last year was named alumni professor and head of the Department of Molecular Biology and Pharmacology.

"David has a unique gift for being able to see the world through other people's eyes and yet not feel the need to impose his 'reality' upon them," says Gordon. "He has been able to use that talent to describe and create niches for young people in his department that allow them to evolve and develop in a way that is most meaningful to them, yet at the same time is conducive to their development of a feeling of competence. These things were possible because David derives great personal pleasure in the success of young people. For students and young faculty alike, the process of science is really a journey of self-discovery; I think that David gave many of us the courage to embark on the journey."

Kipnis says, "When you see that (success) happen, it's almost like being a parent. It's tremendously gratifying. In my own career, I was aware that the key people — people like Carl Cori — seemed to enjoy my success, I think he took great satisfaction and pride in my success, and I've had the same feelings for many members of this department."

That success breeds success is apparent in the Department of Medicine, one of only two in the country that boast four members of the National Academy of Sciences. In addition, Kipnis says the department has impressive representation in the Association of American Physicians and the American Society of Clinical Investigation.

Kipnis is as proud of the department's young scientists who are nominated for and win fellowships and awards, such as those from Burroughs Wellcome, Mar-
Penelope G. Shackelford, M.D.

specialty is pediatric infectious diseases and specifically the development of the immune system, completed a one-year internship at Case Western Reserve after her graduation, then returned to Washington University Medical Center for her residency in pediatrics and a fellowship in infectious diseases. Today, she works on antibodies to bacterial polysaccharides, the coat that allows bacteria to evade the body’s defenses.

Shackelford says she hopes to lead the alumni association in the theme that has been established over the last few years, seeking ways in which alumni can support current students. She sees three areas of effectiveness for alumni: recruiting students, furthering student exposure to clinical medicine in real-life settings and advising them in their career choices.

“Changes in the ways in which healthcare is delivered have made it harder for students to get full exposure to clinical medicine,” she says. “We’re highly specialized and often see only very complicated cases.” In response to that trend, she foresees a program in which students might spend time in the clinical offices of alumni, experiencing precisely what the more general practice of pediatrics or internal medicine, for example, is like. A network of alumni outside the existing faculty could help provide that exposure, she says.

In addition, Shackelford hopes to continue the alumni association’s support of student volunteer programs such as STATS (Students Teaching AIDS To Students), the drug education program and the Young Scientist Program.

She accepted the gavel from Ira J. Kodner, M.D., who completed his one-year term on June 30. Kodner presided over the annual meeting of WUMCAA in May, where he presented the new slate of officers and Executive Council members for 1992-’93 as recommended by the nominating committee. The nominations were unanimously approved.

The new officers and members are: vice-president — David W. Orthals, M.D. ’70; secretary-treasurer — Lewis C. Fischbein, M.D. ’74; council members to serve three-year terms — Stephen A. Kamnetzky, M.D. ’70; William J. Ross, M.D. ’72; Ernest T. Rouse, III, M.D. ’71; Emily L. Smith, M.D. ’68; and James Bobrow, M.D., former house staff; out-of-town council members — Stephen W. Van Meter, M.D. ’67; Sharon Van Meter, M.D. ’67; Captain Stephen B. Lewis, M.D. ’66; Jonathan M. Mann, M.D. ’74; and Gary S. Racheleffsky, M.D. ’67.

Alumni association members accepted a report of the financial assistance their organization had provided during the year:

• $120,000 to the Distinguished Alumni Scholarship Fund.
• Emergency and transition loans to students via the Alumni Student Loan Fund.
• $750 each for the student activity funds of the first-year class and the second-year class.
• $4,760 to cover the budget of the school’s chapter of the American Medical Students Association.
• $15,000 for the Young Scientist Program that provides the opportunity for economically disadvantaged high school students to spend a summer working in a laboratory under the direction of a student in the Medical Scientist Training Program.
• $1,350 for the Drug Education Project, in which medical students make presentations to elementary school students about the effects of drug use.
• $5,000 to the Academic Societies that allow faculty and students to participate together in educational and social events.
• $5,000 for a reception for graduates and their families.
• $30,000 to the Alumni Endowed Professorship Program. Currently, there are four such professorships. They are held by Jeffrey I. Gordon, M.D.; Alan L. Schwartz, Ph.D.; Douglas E. Berg, Ph.D.; and Robert D. Schreiber, Ph.D.
• $60,000 to Continuing Medical Education.

Kodner reported that the Executive Council also devoted attention to student-related concerns and student projects and to the avenues via which alumni can play roles in recruiting and advising students and in providing first- and second-year students with greater exposure to clinical medicine.
Challenge Met, Annual Fund A Success

The School of Medicine's annual fund drive — the yearly solicitation of support for the school — that ended at the close of June, resulted in a gift total of $942,418 for fiscal 1992. According to Hannele Haapala, director of annual giving, fully 69 percent of the total was given by alumni.

The annual fund set high-water marks in several areas this year. Overall, alumni gave eight percent more than they did in fiscal 1991, and participation was particularly notable among graduates of the Health Administration Program (HAP) and the Program in Physical Therapy (PT). Slightly more than 30 percent of all HAP alumni participated in the annual fund program, and more than 32 percent of PT grads responded. Among physician graduates of the school, almost 35 percent made gifts during fiscal 1992.

Haapala also noted that membership in all donor clubs — from the Century Club for donors of $100 or more to the Eliot Society for donors of at least $1,000 — increased during fiscal year 1992. Eliot Society members numbered 383, compared to 367 during the previous year.

Part of that increase was attributable to the Asa C. and Dorothy W. Jones Challenge, an effort to enlist at least 100 new members in the Eliot Society. The challenge was met, with 103 new members named during the year.

The challenge was issued by Dr. and Mrs. Jones, longtime supporters of the school, who matched gifts to the annual fund up to $100,000. Jones, M.D. '42, celebrated his 50th reunion this year.

Scholarships
Honor Beloved Teachers

The alumni association has selected the four distinguished alumni in whose names the first cycle of the Distinguished Alumni Scholarship Program will be completed. Hannele Haapala, director of annual giving in the Office of Alumni and Development Programs, calls the scholarships a way to recognize "beloved teachers."

Honored with scholarships in their names are: I. Jerome Flance, M.D. '35, clinical professor of medicine; David Goldring, M.D. '40 (1914-1992), professor emeritus of pediatrics; Charles W. Parker, M.D. '53, professor of medicine and molecular microbiology; and Jessie L. Ternberg, M.D. '53, professor of pediatrics and pediatric surgery.

These four highly regarded alumni — also outstanding members of the faculty — join the 12 others for whom existing scholarships have been established. The scholarships are the School of Medicine's major merit-based scholarship program, funded to a large extent by annual gifts from alumni and others. Each named scholarship provides a freshman recipient with $10,000 toward tuition costs. The medical school then matches the grant up to the full amount of tuition. Assuming that the students named remain in good standing, the scholarships continue for four years of medical education.

Established by the alumni association in 1989, the scholarships are not based on financial need but on academic merit and the exceptional personal qualities that contribute to the successful practice of medicine.

CLASS NOTES

'20s and '30s

Irwin B. Horwitz, M.D. '29, writes that he is "just loafing toward my 88th birthday and enjoying being lazy."

O. Elliott Ursin, M.D. '36, and his wife recently traveled with a small group to Russia. Sponsored by St. Olaf College and led by a professor of Far Eastern affairs, the trip was a success, Ursin reports.

Edward Alun Harris, M.D. '37, serves as professor emeritus in the Department of Pediatrics at the University of Alabama College of Medicine. He is active as a medical consultant to the disability determination unit of the Alabama State Department of Education. Widowed since 1984, he reports that he has five grandchildren and one great grandson.

J. Robert Mangum, M.D. '38, retired from the practice of medicine at the end of 1991 and remains in good health in Davenport, IA.

'40s and '50s


Alexander Ling, M.D. '44, has retired after 16 years as senior member of Northeastern Ohio Neurosurgical Associates, the largest and oldest neurosurgical group in metropolitan Cleveland.

Truett Bennett, M.D. '45, retired from his ENT practice in Hawaii and moved back to North Caro-
lina. There, he found a need for a physician in the tiny (population: 600) town of Oriental, so he began a solo general practice. He writes, "I am enjoying the change very much."

Paul F. Brown, M.D. ‘47, has retired from practice but does occasional locum tenens.

Robert R. Lyle, M.D. ‘49, reports that he continues to enjoy practicing family medicine three days a week and that he has 10 grandchildren.

William N. Chambers, M.D. ‘50, retired from limited practice in December of 1991. Since the death of his wife, Fran, in 1986, he has traveled the world solo and says he is "lucky to have a few good friends," with whom he plays bridge, poker, chess and the stock market.

Adrian M. Ostfeld, M.D. ‘51, the Anna M. R. Lauder Professor of Epidemiology and Public Health and Medicine at Yale University School of Medicine, has been elected a fellow of the Royal Society of Medicine in London. Ostfeld, recognized for distinguished contributions to the biomedical sciences, is one of 230 professionals in geriatrics and gerontology with society membership.

Gordon R. Heath, M.D. ‘52, practices pediatrics in Lakeland, FL.

Galen B. Cook, M.D. ‘55, president of Medical Logic International, (publisher of 52 items of clinical software) has announced an agreement with SRC Systems of San Antonio that will expand the exposure of the company’s products.

Joseph V. LeBlanc, III, M.D. ‘56, has retired from the post of corporate medical director at Phillips Petroleum Co. in Bartlesville, OK, where he and his wife continue to reside.

The new chair is expert in suicidology at the psychiatry department of the State University of New York at Stony Brook. Rich joined eight of his colleagues at that institution on the list.

Eric Zurbrugg, M.D. ‘70, and Jo Zurbrugg, M.D. ‘70, moved to Hilton Head Island late in 1991 with plans to start a pediatrics/pediatric neurology practice together there. The new office address: Hilton Head Pediatrics, 21 Mathews Drive, Suite #10, Hilton Head Island, SC 29926.

C. Leon Partain, M.D. ‘75, has been named chairman of the Department of Radiology and Radiological Sciences at Vanderbilt University Medical Center and radiologist-in-chief at Vanderbilt University Hospital in Nashville, TN.

Toby L. Litovitz, M.D. ‘76, authored a paper comparing pediatric poisoning hazards in 3.8 million exposure incidents and found that iron supplement pills — often mistaken by children for candy — were the single most frequent cause of pediatric unintentional ingestion fatalities. The New York Times reported the findings published in the journal Pediatrics.

Gary L. Baker, M.D. ‘77, was certified by the American Board of Plastic Surgery and received the Certificate for Added Qualification in surgery of the
hand from the American Board of Surgery in 1991. Previously, Baker was certified by the American Board of Internal Medicine and the American Board of Surgery. An assistant professor of plastic surgery at the University of Kansas Medical Center in Kansas City, KS, Baker is one of two plastic surgeons in the nation certified by four separate ABMS-sanctioned boards.

Carol Marie Mitchell, M.D. '79, was married to Thomas L. Marcus on October 18, 1991, in Waterloo, IL. She writes that she and her husband eloped 70 years to the day after her grandparents did the same thing.

Douglas Alan Munro, M.D. '83, writes that he was "finally" married in June of 1991 in Colorado. He continues his private practice of radiology in Santa Rosa, CA.

Paul Detjen, M.D. '84, has opened offices in Winnetka, IL, for the practice of adult and pediatric allergies and immunology. He is a board-certified allergist and also is certified by the American Board of Internal Medicine.

Sari R. Levine, M.D. '85, writes from Mountain View, CA: "Nothing could be better. I have a great job, wonderful associates and am enjoying each moment of post-residency private practice. I think I've found paradise."

Rachel Haft, M.D. '86, reports that she is "recently and happily" married to Jeffrey Brown. After visiting Israel and Egypt on their honeymoon, the couple now reside in Boston.

Bill Frank, M.D. '87, has recently finished his dermatology residency at Harvard Medical School.

Andrew Epstein, M.D., F.H.S. in cardiology, has been promoted to professor of medicine in the division of cardiovascular disease at the University of Alabama at Birmingham.

Ronald B. Miller, M.D., F.H.S. in internal medicine, left the private practice of nephrology to spend the 1989-90 academic year as visiting scholar at the Center for Clinical Medical Ethics of the University of Chicago and to direct the Program in Medical Ethics at the University of California—Irvine.

Edgar W. Percy, M.D., F.H.S. in pediatrics, has been in private practice in Lake Charles, LA for 31 years. He has been married for 52 years to his childhood sweetheart, the former Mary Alice Albright, and the couple have two children.

Bartolomeo J. Castelli, HA '82, and his wife, Deborah, had their first child, Vincent Joseph, on May 3, 1991.

Dale S. St. Arnold, HA '86, recently was appointed president and chief executive officer of Mount Carmel Health in Columbus, OH.

B. J. Kerr

Bernard J. Kerr, Jr., HA '88, a captain in the U.S. Air Force Medical Service Corps, has been selected for promotion to major. He completed the doctor of education degree at SIU-Edwardsville in 1991, and has recently finished an Air Force-sponsored post-doctoral fellowship in managed health care.

Connie Kraal Craigmle, PT '87, and her husband, Todd, announce the birth of a daughter, Monica Lynn, born in July 1991.
Elamay Mueller Jeffery, OT '48, and her husband sold their California home and flew off to Germany in early 1990 for 14 months. Upon their return, they settled in Tucson.

Laurie N. Schwarze, OT '82, is director of rehabilitation services in Queens, New York City. She and her husband planned to move to Dallas by the time this update reaches print.

Edna Sanders Eimers, NU '36, celebrated her 50th wedding anniversary on January 26, 1991, with all 24 descendants present.

Hope Mitchell Lewis, NU '36, plans a trip to Saudi Arabia in October to visit her daughter there.

Helen Bennett Paust, NU '48, planned to retire in 1990 but had an opportunity to work with post-traumatic stress disorder patients in Austin, TX, and accepted it. She says she plans to see how she feels about work at the end of 1992.

Mildred Lehman Hill, NU '53, asks that any alums interested in a reunion in 1993 write to her with suggested dates at #46 Whitmer Drive, Chesterfield, MO 63017.


Carl G. Harford, M.D. '33, and for many years a faculty member at the School of Medicine died Monday, May 18, 1992 after a long illness. A specialist in infectious diseases, he pioneered the study of viruses and worked to evaluate penicillin in the 1940s. A son, two daughters, a sister, a brother and three grandchildren survive him.

David M. Goldring, M.D.

David M. Goldring, M.D. '40, the renowned pediatric cardiologist who first became an instructor in pediatrics at the School of Medicine in 1940, died from lung cancer on May 26, 1992, at his home in University City. He had been a staff pediatrician at St. Louis Children's Hospital for more than 40 years.

Goldring founded the pediatric cardiology division at the hospital and, in 1956, helped design a heart-lung machine that first enabled surgeons to perform open heart surgery to correct congenital deformities in the hearts of children. He also pioneered research to define the causes of high blood pressure in children.

Despite his outstanding contributions to research, "he perhaps will be remembered most as a remarkably kind and gentle physician and teacher," says Arnold Strauss, M.D., director of pediatric cardiology at St. Louis Children's Hospital. An endowment fund for studies of congenital heart disease will be established in Goldring's memory, Strauss says.

In 1985, he was presented with the medical school's Alumni/Faculty Award, and in 1991, Goldring became the first recipient of the St. Louis Children's Hospital medical staff's highest honor, the Distinguished Service Award. He was active in many health organizations, serving as director of the Missouri Rheumatic Fever Program from 1949 to 1955; secretary treasurer of the American Pediatric Society, and president of the St. Louis Pediatric Society.

A memorial service was held on Sunday, June 28 at Graham Chapel, followed by a reception at Whittemore House. Among the survivors are his wife, Evelyn; a daughter, Nancy; two sons, Steven and Peter; two grandchildren, and his brother, Sidney Goldring, M.D., former head of neurosurgery at the medical school. 

James W. Willoughby, M.D. '47, died on May 27, 1992. He practiced in allergic diseases in Liberty, MO.

Maurice F. Attie, M.D. '75, was killed on Sunday, June 5, 1992, when he was struck by a car as he bicycled near his home in Bala Cynwyd, PA. An avid bicyclist, Attie was wearing a helmet when he was hit from behind. An associate professor at the University of Pennsylvania, he was a highly regarded researcher in endocrinology. In 1991, he won his medical school's award for excellence in teaching. He is survived by his wife, Barbara; daughters Alisa, a premed student, and Jessica; a son, Michael; his parents; a brother and a sister.
Medical Alumni

Classes of '33, '38, '43, '48, '53, '58, '63, '68, '73, '78, '83

Mark your calendars.
May 6-8 1993

Put Reunion '93 on your schedule now!

Details and registration materials will follow in January.
An unusually cool and pleasant summer prompted thoughts of an early fall at the medical school and stirred memories of scenes like this one from last year.