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Computer-aided molecular design yielded this model of the crystal structures of the first nine residues of emerimicin, a peptide antibiotic that forms pores in membranes. See newsbrief on page 3.
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On the Cover:
New evidence challenges the long-held belief that the brain “wires” itself together by forming permanent connections between its cells. Studies by Dale Purves, M.D., suggest that, like Tinker Toys, the connections between brain cells are constantly being formed, torn down and rebuilt. Such findings may eventually change the way scientists study the nervous system and how they view certain nervous disorders. See story on page 12.
American Academy of Arts and Sciences Elects Three

Three faculty members at the School of Medicine have been elected as fellows of the American Academy of Arts and Sciences, one of the nation's oldest societies of leaders in science, scholarship, the arts and public affairs.

The new fellows are Gerald D. Fischbach, M.D., Edison Professor of Neurobiology and head of the Department of Anatomy and Neurobiology; Stuart A. Kornfeld, M.D., professor of biological chemistry and medicine; and Philip W. Majerus, M.D., professor of biological chemistry and medicine.

“These three men are at the forefront of their respective research, and all have been recognized internationally for their contributions to science,” said Samuel B. Guze, M.D., vice chancellor for medical affairs at the School of Medicine. “Their election as fellows of the American Academy of Arts and Sciences is clearly appropriate, because it is an honor meant for those with the most outstanding of accomplishments.”

Fischbach, director of the Center for Cellular and Molecular Neurobiology, was elected to the academy in recognition of his pioneering studies of the development of embryonic neurons and muscle cells in tissue culture and the formation of functional connections between them.

Fischbach and his associates are investigating events that occur within a few hours after an embryonic nerve cell contacts an embryonic muscle. A cluster of receptors that recognize the transmitter acetylcholine, which is released by the nerve, appears on the surface of the muscle exactly at the point of nerve-muscle contact. Fischbach believes that the nerve instructs the muscle, in some way, to increase the production of new acetylcholine receptors and to insert them at the appropriate place.

His team has isolated a molecule from brain tissue that may be responsible for this instructive or nourishing effect. He is currently purifying larger amounts of the molecule and further characterizing its actions.

This molecule, or class of molecules, may be important not only at the neuromuscular junction, but also at synapses within the brain. Knowledge of its composition will enable Fischbach and his research group to synthesize it and eventually show where and when in the nervous system the molecule is active. Ultimately, this work could improve treatment for chronic degenerative disease of the nervous system.

Fischbach came to Washington University in 1981 from Harvard Medical School, where he was professor of pharmacology. He received a medical degree from Cornell University Medical School and a bachelor's degree in mathematics and chemistry from Colgate University.

Kornfeld is interested in how these proteins are targeted to their correct destination in the cell, since the cell makes hundreds of different proteins that have to be sent to many different destinations. Signals built into the proteins allow this to occur. Kornfeld's work involves trying to decipher the signals to determine how proteins get sent to the correct location.

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

Majerus is co-director of the division of hematology-oncology. His research involves defining the mechanisms by which a blood cell responds to signals within its environment both to evoke responses inside the cell and to modify its surroundings.

Work in his lab uses biochemistry and molecular biology techniques to define the pathways involved in generating cell messages. He and his colleagues recently discovered several new enzymes and metabolites involved in this pathway and are further exploring these and other new reactions. Another project involves the study of an endothelial cell protein, thrombomodulin, which is a natural anticoagulant molecule.

Majerus pioneered the clinical research that first indicated that aspirin, taken daily in low doses, could help prevent possibly fatal thrombosis (blood clotting) in kidney dialysis patients, without harmful side effects. His
work suggested that aspirin might prevent clotting among patients who had already suffered one such occurrence, and that healthy persons might take aspirin on a regular basis to reduce the possibility of a heart attack. That preliminary work was confirmed earlier this year when Harvard University announced results of a follow-up study that involved 11,000 doctors nationwide who took an aspirin or placebo every other day.

Majerus joined the faculty at Washington University in 1966 after serving as a research associate in biochemistry at the National Heart Institute. He received a medical degree from Washington University in 1961 and completed undergraduate studies at Notre Dame University in 1957.

The American Academy of Arts and Sciences, founded in 1780, conducts studies that reflect members’ interests and respond to societal needs. There are currently 17 faculty members at Washington University who are academy fellows.

Garland R. Marshall, Ph.D., professor of pharmacology and of biological chemistry, has received the 1988 Award in Medicinal Chemistry from the American Chemical Society's Division of Medicinal Chemistry for his pioneering contributions to the field of computer-aided drug design.

Marshall was among the first to design molecular computer models that can be used to quickly predict the likelihood of a good "fit" between new drugs and their receptors. These models can save traditional chemists months or years of wasted time by being able to accurately predict what will work and what will not.

Marshall founded Tripos Associates, the pioneer in molecular modeling software, serving as its president and chairman until 1978 when it merged with Evans and Sutherland Computer Co.

This past year he co-founded a new journal, the Journal of Computer-Aided Molecular Design, of which he is editor-in-chief. At the university, where he serves as the director for the Center for Molecular Design, Marshall's personal research interests center on molecular recognition and the integration of spectroscopic data with theoretical chemistry as it relates to drug design.

Marshall earned his Ph.D. at the Rockefeller Institute, where he studied under R. Bruce Merrifield during the infancy of solid phase peptide chemistry. He came to Washington University in 1966, and has since made significant contributions to peptide chemistry and to the determination of the receptor-bound conformation of peptides.
There’s more to light than meets the eye, according to researchers at Washington University, who recently discovered that visible light helps suppress immune responses in the eye that might otherwise destroy sight.

In virtually all other areas of the body, invasion by a foreign substance triggers an inflammatory reaction that damages surrounding tissues as well as foreign material, according to Thomas Ferguson, Ph.D., an immunologist who serves as an assistant professor of ophthalmology at Washington University School of Medicine.

"If you get a poison ivy reaction on your skin, for example, you’ll notice that the tissue becomes ugly and swollen," he says. "That fine; your skin can heal. But if you damage the retina or some other part of the eye, you lose vision." Such is the case in retinitis, a disease that destroys the retina, and uveitis, which is one of the five leading causes of blindness.

Unlike the skin, the healthy eye exhibits an apparent lack of immune response and a "willingness" to accept foreign tissue, according to Ferguson. The high success rates for corneal transplants are a prime example. Transplanted hearts, kidneys, livers and other organs, in contrast, must be protected from their recipients’ immune systems with special anti-rejection drugs.

Scientists have similarly found that tumor cells, when placed in the eyes of laboratory animals, will grow there unaffected, eventually killing the animals. Such observations initially led investigators to believe that normal immune responses are simply not present in the eye. It was later found that the eye contains immune responses, but that they are actively inhibited.

Two things led Ferguson to suspect that this suppression of the immune response might be caused by light. First—it had been known for many years that ultraviolet light suppresses immune responses in skin and cell cultures. Second—Nobel Prize-winning work by Hubel and Weisel in 1981 illustrated light’s profound and necessary effect on the development of vision. Hubel and Weisel found that animals raised in the dark did not develop vision normally and that animals raised in the light with one eye covered were severely visually impaired in the covered eye.

To test the possibility that light might also be linked to the suppression of the immune system in the eye, Ferguson and members of his research team injected mouse spleen cells into the eyes of mice that had been raised in the light and those that had been raised in the dark. While the eyes of the mice raised in the light did not exhibit an immune response to these foreign cells, the eyes of the dark-raised mice did. This new evidence demonstrated quite clearly that immune responses are indeed present in the eye, but that they are suppressed in animals that have been raised in the light.

Ferguson and his fellow researchers were then interested in whether or not light causes a permanent suppression of the immune system, or if this suppression could be reversed. When they injected spleen cells into the eyes of light-raised mice and then placed them in the dark, Ferguson and his colleagues successfully abolished the suppression of the immune system after only 18 hours in total darkness.

When these mice were re-exposed to light for more...
than a day but less than a week, suppression was re-established. Obviously, light has a definite and profound effect on the eye’s immune response, and this effect can be experienced at any point in an animal’s development.

This effect can be seen most dramatically in a variation on a classic experiment with herpes simplex I. When this virus is injected into the right eye of a mouse, the eye is preserved. But 10 days later, the virus moves into and destroys the retina of the left eye.

Ferguson and his co-workers discovered that if they adapted the mouse to the dark for two weeks and did the same experiment, the virus did not enter the left eye, but was completely wiped out. “We knew we had something here,” Ferguson says. “We had completely altered the course of the disease by adapting it to the dark. We had changed the course of viral retinitis.”

Ferguson still needed to determine whether these effects of light were direct or indirect. “When you take an animal out of its normal light/dark cycle, that causes hormonal and other changes in the animal that could also affect the immune response or its suppression,” he explains.

To rule out these indirect effects of light, Ferguson and his research team injected spleen cells into the eyes of mice, sutured the eyes shut and then put the mice back into a normal room with 12 hours of light and 12 hours of darkness. They got the same results as they did by placing the entire animal in the dark, proving that “what we were seeing when we put an animal in the dark was happening to the eye, not to the whole animal.”

Although it was somewhat of a surprise, Ferguson learned that it was not ultraviolet, but visible light that has this direct effect on the eye’s immune response. The conventional fluorescent bulbs used in most of the studies consisted mostly of visible light, with no infrared light and very little ultraviolet. Consequently, Ferguson’s experiments were repeated with an incandescent light source that emits only infrared and visible light. These experiments suggested that only visible light was necessary for the suppression of the immune response.

What does it all mean? “If this is important for the eye in general, not just in mice, one might envision something like phototherapy,” Ferguson says. But first, scientists would need to determine the wavelength or wavelengths of light that have this suppressive effect.

Ferguson would also like to better understand the mechanism through which light suppresses the immune response. He and his colleagues have already found what they suspect to be an inhibitor within the transparent fluid between the lens and the cornea, or the aqueous humor.

If researchers could determine what this inhibitor is, they may better understand what happens when the suppression goes away (in uveitis and retinitis) and eventually even produce a drug that could control the immune response within the eye.

### Majerus Elected Member of the Institute of Medicine

Philip W. Majerus, M.D., professor of biological chemistry and medicine at Washington University School of Medicine, has been elected a member of the prestigious Institute of Medicine of the National Academy of Sciences.

Majerus is one of 40 new members of the institute, which was created in 1970 to examine public health policy matters.

Terms for new members began July 1, bringing the organization’s total membership to 474. There are currently 14 faculty on staff at Washington University School of Medicine who are active members. Majerus was also recently elected to the American Academy of Arts and Sciences.

### Grants for Asthma Research

Michael J. Holtzman, M.D., assistant professor of medicine, has been awarded more than $1 million to study the causes of asthma and other inflammatory lung diseases. Holtzman will receive funding from two five-year grants, one from the National Institutes of Health (NIH) and the other from the American Lung Association.

His research focuses on the biochemistry of cells lining the lung airways. The cells are in direct contact with the environment and might be responsible for protecting the airways, he says. He hopes to learn if and how they contribute to an inflammatory response when certain particles in the environment—such as dust, pollen and mold—are inhaled. The explanation for diseases that involve inflammation of the airways—for example asthma, bronchitis and cystic fibrosis—may lie in the normal or abnormal responses of these airway-lining cells.

The NIH’s Heart, Lung and Blood Institute has given Holtzman an $831,000 grant to support his studies. Also, he is one of two recipients nationwide of a Career Investigator Award from the American Lung Association. The $175,000 award is given annually to scientists whose work shows exceptional promise for treating lung disease.

Before joining the faculty at Washington University in 1987, Holtzman was an assistant professor of medicine and a staff member at the Cardiovascular Research Institute at the University of California, San Francisco. He has lectured internationally and has written numerous scientific papers on his research.
The latest studies of a vaccine designed to protect children from bacterial meningitis and other life-threatening diseases reveal an unusual regional variation in the vaccine's protective efficacy.

Three reports published in the Sept. 9th issue of the Journal of the American Medical Association (JAMA) indicate that efficacy of the Haemophilus influenzae type b (Hib) polysaccharide vaccine varies widely. According to one report, it is highly effective in Connecticut, Dallas County, and greater Pittsburgh, resulting in an 88 percent reduction of disease among children in those areas. A study of six other areas—Los Angeles, New Jersey, Tennessee, Missouri, Oklahoma, Washington state—conducted by the federal Centers for Disease Control (CDC), puts the vaccine's efficacy at an average of 41 percent. However, the vaccine is totally ineffective in Minnesota and may even be associated with a trend toward increased risk of disease among vaccinated children. The protective efficacy rate of the polysaccharide vaccine is minus 55 in Minnesota.

"Never before has a vaccine shown such striking differences in how it works in different parts of the U.S.,” says Dan Granoff, M.D., professor of pediatrics at Washington University School of Medicine. “The reasons for the regional differences are not yet clear, but these findings have important implications for how vaccines should be tested before they are approved and licensed.”

Granoff, who also serves as associate professor of microbiology and immunology at the School of Medicine, helped devise the Minnesota study and evaluate the data. He is a former chairman of the Infectious Disease Committee of the Missouri Chapter of the American Academy of Pediatrics.

"We've satisfied ourselves that the efficacy fluctuations are not due to chance or to differences in the quality of vaccine used in different regions, and that there are no obvious differences in the populations tested in each geographic region,” says Granoff, director of the infectious diseases division at Children's Hospital, a sponsoring institution of the Washington University Medical Center. "At this point, we can postulate that the discordant results with the Hib polysaccharide vaccine could be due to several circumstances, including genetic and environmental factors.”

According to Granoff, there is a precedent for geographical or populational specificity in vaccine protection: live polio vaccines do not always work well in some tropical countries because other viruses that block the action of the live vaccine may be present in the intestinal tract of the population.

The Hib polysaccharide vaccine was licensed in the U.S. in 1985, based on efficacy data from tests done in Finland. At first, the vaccine's only drawback seemed to be its inability to protect infants younger than 18 months of age, the group most commonly stricken by Hib disease.

When the vaccine became available in Minnesota in August 1985, the Minnesota Department of Health began monitoring reports of Hib disease. During the subsequent 28 months, 88 cases of Hib disease were identified in children 2 to 5 years of age, the group targeted for vaccination. Of these 88 cases, 36—or 41 percent—occurred in vaccinated children, indicating, when compared to figures from age-matched children in a control group, that the polysaccharide vaccine had no effect in preventing Hib disease in Minnesota children.

In response to preliminary findings from Minnesota’s case-controlled investigation, the American Academy of Pediatrics recommended that the vaccine no longer be used in Minnesota. In December of 1987, a new and stronger Hib vaccine was approved and licensed. It is recommended for children from 18 months to 5 years of age. But the conventional polysaccharide vaccine, which is three times less expensive than the new vaccine, is still on the market.

Granoff, who participated in evaluating the new vaccine, says that its use could eventually double the number of preventable cases of Hib disease.

Hib is a highly contagious bacteria that strikes one out of every 250 children under age 5. Besides meningitis—a leading cause of mental retardation and acquired deafness among children—Hib can also cause blood poisoning, pneumonia, crippling arthritis, and epiglottitis, an inflammation of the throat that can lead to suffocation. Seventy-five percent of Hib cases occur in children younger than 18 months, with infants under 12 months at particular risk. Five to 10 percent of children who contract meningitis die; another 20 percent have mild to severe retardation.

Addendum

The summer issue of Outlook reported work by assistant professors of medicine and pharmacology James B. Lefkowith, M.D., and George F. Schreiner, M.D., Ph.D., demonstrating that a diet lacking essential fatty acids make the kidneys of organ-donor rats less susceptible to organ rejection. The investigators would like to acknowledge their co-workers in this research: Wayne M. Flye, M.D., Ph.D., professor of surgery and of microbiology and immunology; Elizabeth M. Brunt, M.D., instructor of pathology; and Kenneth E. Korber, medical research technician.
Medical school was the farthest thing from David Chiara's mind 11 years ago when he dropped out of high school to ski the Western Rockies.

Skiing was all Chiara wanted to do from the day he donned his first pair of skis and broke his first leg at the age of seven. And while his hometown of Redding, California may not be the ideal winter wonderland for skiing—temperatures sometimes reach 130 degrees in summer—Chiara is quick to point out that Redding has produced three World Cup skiers.

There, the skiing on Mt. Shasta and Lassen is mostly freestyle—a category of competition developed since the early 1970s by such greats as Eddy Ferguson and Karen Huntington. Freestyle, which was held at the Olympics for the first time this year, features the three disciplines of mogul skiing, ballet and aerals. It is an extremely dangerous form of skiing, expensive to sponsor in the U.S. due to the high cost of insurance.

Chiara's own love for skiing snowballed during his high school years, during which he skied approximately 50 days each year. Summer jobs in construction helped fund this expensive pastime until, to his parents' chagrin, he quit school and went to Utah for two years to live as a "ski bum." He landed a part-time job as a night maid at the Cliff Lodge in Snowbird, which left him plenty of time to ski the amateur circuit by day. Skiing an average 100 days per season, Chiara remained in Snowbird for two seasons until he lost the ligament in his left shoulder and developed back problems. Burned out by a mountain that is so steep it "wins more than you do," Chiara retired from skiing at the tender age of 19.

With his career on the slopes at an end, he decided to try his hand at collegiate tennis. It seemed like the logical thing to do at the time, Chiara explains. "My left arm was gone and I play tennis with my right."

He enrolled at Shasta Junior College in Redding for two spring semesters, selecting easy courses just so he could play on the tennis team. Yet barely into his second season, he developed tendonitis in his right arm and wound up serving underhand for almost the entire season. His coach sent him to the '49ers team doctor, but to no avail. That was when Chiara decided to go to medical school.

Like the sports he'd pursued, Chiara has found medical school challenging and competitive, but in a different way. "From the time I quit high school to the time I started college, my brain had just about turned off," he says. Yet it was the same drive that sped him through the moguls that led him up the road in academics, and the ex-ski bum soon became an ex-ski bum with straight A's.

Chiara's own personal research interest is in the area of neurology. He hopes to one day study neuroscience at the molecular level to figure out how neurons work.

Chiara still skis whenever he gets the chance, and has taken up tennis again. Although he believes he may even be a better skier now, he has lost the competitive drive. "One of the reasons I skied before was that I liked the thrill of being on the edge," he says. "It's very impractical to ski like that now. I'm not as open to the idea of falling as I used to be."
Susan Deiters started attending classes at Central Institute for the Deaf (CID) when she was 3 years old. Unlike most deaf children in this country, she was not taught sign language, but speech.

To this day the 18-year-old and her parents are grateful. If she had been taught sign language, Susan would have to rely on an interpreter to communicate with people who don't know sign. She couldn't have been mainstreamed into public school at the age of 13 and it's very doubtful that she would be reading eight grade levels higher than the national average for the deaf, which is third grade.

In fact, Susan recently participated in a nationwide study that shows compelling new evidence that teaching the deaf to speak—before they learn to sign—helps them to attain their highest educational levels.

In the study, contracted by the National Institutes of Health, CID researchers found that among 100 16- to 17-year-old profoundly deaf adolescents who had been taught speech, average reading scores were a full five grade levels higher than the national average for the deaf.

“What we found especially interesting is that 30 of the 100 were reading at or above the 10th grade level. That means they were functioning for all practical purposes like normal-hearing adolescents, which is rather outstanding considering the severity of their deafness,” says Ann Geers, Ph.D., principal investigator for the study.

Susan, like other profoundly deaf people, would not be able to understand speech if she hadn’t had special training. Even when fitted with the most powerful hearing aid, she is only able to hear some sounds.

The CID evaluation of oral education that she took part in was accompanied by separate but related NIH-funded studies of total communication—a combination of speaking and sign language—carried out by Gallaudet University in Washington, D.C.

Gallaudet researchers measured reading skills in deaf children with deaf parents and those with normal-hearing parents. Researchers at both institutions looked for elements such as hearing ability that set good readers apart from those who didn’t read well.

Knowledge of the English language was the primary factor influencing the de-
As a result of learning to speak at an early age, Susan Dieters reads eight grade levels higher than the national average for the deaf.
development of reading and writing skills in the sample of orally educated hearing-impaired adolescents, according to co-investigator Jean Moog, principal of the school at CID.

Speaking Ability Key to Reading Ability

"The major predictor, the factor we were supposed to ferret out, was what most predicts reading ability." Moog says. "It's not socioeconomic status. It's not hearing loss—within the profound range, if you have a little more hearing, you don't read better than somebody who has less. It's not I.Q.—the very bright students didn't read better than the normal students on the average.

"What appeared to make the most difference was their facility with English: the extent to which they mastered vocabulary, understood syntactic structure and how to form complex sentences, how to write.

students are taught a combination of speaking and sign language in total communication programs.

Deaf children in total communication programs don't read as well, Geers says, because in many signing programs, deaf children are not given intensive instruction in speech and language, and therefore don't learn English very well. Furthermore, she says, if deaf students are to reach their full potential in the hearing world, they must be taught to speak at an early age—before signing is learned.

Oral Communication programs such as CID’s teach deaf children to communicate by using various hearing devices to maximize their limited hearing, reading lips and speaking.

Of the 20,000 profoundly deaf youth under age 21 in the United States, only about 10 percent are currently taught through this method. The majority of

CID teacher Betsy Brooks sounds out the letter “f” for pupil Ashley Vickers. Oral instruction at CID is intensive, requiring small teacher-to-student ratios.

them, how to speak them, and how to understand them when they were spoken.”

Oral communication programs such as CID’s teach deaf children to communicate by using various hearing devices to maximize their limited hearing, reading lips and speaking.

Of the 20,000 profoundly deaf youth under age 21 in the United States, only about 10 percent are currently taught through this method. The majority of

that's primarily what accounts for their reading skills.” Geers says.

In order for Susan and the other teens to participate in the CID study, they had to be profoundly deaf and to have been profoundly deaf before they learned language. They had to have been educated in an oral setting only, and to have a normal I.Q. with no other significant educational handicaps.

"We know the students we train at Central Institute for the Deaf achieve higher reading scores than the national average,” says Geers. “But in this study we were looking at kids from all over the country, so we didn’t really know what to expect."

Results showed that the average child in the study was rated as reading and comprehending paragraphs at the 8th grade level. Deaf students of deaf parents in the Gallaudet study achieved reading levels at mid-sixth grade, and deaf students with hearing parents taught in total communication programs were at high fifth grade level. All scored higher than the national average of third grade, though, which researchers attribute to the fact that these students had been screened to eliminate additional handicaps that could affect reading scores.

As expected in the total communication programs, deaf students of deaf parents fared better than those with hearing parents, probably because deaf parents begin signing fluently with their children during infancy, whereas hearing parents who want to sign must learn a new method of communicating with their child.

But Moog stresses that though students in total communication programs may become proficient at signing, most are not learning to speak well. She bases that on data from this reading study as well as another NIH-sponsored study conducted at CID in which 300 profoundly deaf children—150 from total communication programs and 150 from oral programs—were tested for spoken English skills.

Results showed that by the age of 8, the spoken language of children in oralprograms was 30 to 40 percent better than those educated in total communication programs. In both studies, the children tested were comparable in age, hearing impairment and intelligence.

Talking Well Enough to be Understood

“The theory of total communication is to teach signing and talking together to give children the benefit of taking information through whatever system suits them. The implication is that they will learn to both sign and talk,” says Geers.

“But our studies show that children are not learning to talk and sign together. Some are learning to sign, but they are not learning to talk as well as those in oral programs, and most are not learning to talk well enough to be understood.” Furthermore, Geers adds, they are not learn-
Students at CID are encouraged to use speech in public situations through outings to Baskin Robbins and other places of interest.

ing to sign English at any higher level than orally educated deaf children learning to speak English.

Both Geers and Moog agree that using signs and speech can be very helpful for a deaf person to communicate, but they maintain that learning spoken English before signing is crucial.

"There is no evidence that shows a profoundly deaf child can be taught simultaneously to sign and speak and do both well," Moog comments. "There is also no evidence that a child can first become a competent signer and then learn to speak well. However, there is evidence that if you become a competent talker, you might later acquire signs if you wanted to be able to use both systems. Everybody that we've ever studied who was competent with both modes, learned to speak first and sign later. Our philosophy is to start with an oral program, and become completely proficient orally before attempting signs," says Moog.

Only 10 Percent Taught in Oral Programs

Advocates of total communication have criticized CID's results, saying that reading levels were high because CID tested economically advantaged children whose parents had the money to get them the best education possible. However, according to the Office of Demographic Studies at Gallaudet, of the some 20,000 profoundly deaf children being taught in the United States, only 10 percent of them are taught in spoken language programs, Moog notes. "That in itself reduced the pool from which we had to draw," she says.

"We believe that at the time of the study there were fewer than 500 children nationwide in the 16- to 17-year-old age group who had been educated exclusively with the oral approach. We tappèd a sizeable proportion of the orally educated sample in that age range. There was no reason for our sample to be skewed socioeconomically because we paid all expenses for the testing."

Moog does attribute the small number of children in oral programs partly to financial reasons. "Speaking is extremely hard for a deaf person, and it's hard to do well. It is also expensive to do well. It takes very highly trained teachers to teach deaf children to talk, and I think there are probably not a lot of people who want to finance it."

On the other hand, Geers says, the expense is a concentrated one. The expense is probably equivalent in both methods of teaching. When children are very dependent on sign language, they are either required to stay in special education all the way through adulthood or have an interpreter accompany them in a normal-hearing setting.

Whereas for children who speak, it's very expensive on the front end, she says and adds, that after intensive instruction in an oral program over several years the children are then placed in regular classrooms with normal-hearing children.

"Children at CID are taught in small groups with a ratio of one teacher for every four children, and most teachers have master's degrees," says Geers. "So it's very expensive to teach these children, but it's also relatively short term."

Susan's parents began receiving training with her in CID's parent/infant program soon after she was deafened by meningitis at the age of two, and she began intensive instruction at the CID school starting at age 3. Like most CID students, she was placed in a regular school after finishing elementary education. In some cases, children are ready to be mainstreamed by the time they reach first grade, especially if they are diagnosed during infancy and are well-fitted with hearing aids.

Participating in a Hearing World

Most people are under the misimpression that deaf people cannot talk well enough to be understood, according to Moog. However, when the teens in the study were rated through an interview technique developed by Gallaudet, 90 percent of them were rated as being proficient at speaking English. "I think speaking proficiently improves their ability to interact and participate in the hearing world if they so choose," Moog says.

Susan is a prime example. She communicates confidently and rather easily with her hearing friends at Kirkwood High School and she interviewed without an interpreter for the modeling she has done at a local mall.

In order for deaf children to develop spoken language skills at Susan's level, the study results suggest they should have at least average nonverbal intelligence, early educational management, early amplification and auditory stimulation, instruction in spoken language from an early age and no sign language instruction until spoken language is firmly established.

As a reward for working hard during the testing, Susan and the other students spent much of their week sightseeing in the St. Louis area. They ordered their own food at restaurants, bought their own tickets to an amusement park, asked the tour guide questions at an underground cavern and spent one evening dancing and talking on a riverboat ride on the Mississippi River. "They went independently everywhere a normal-hearing person would, and they didn't need to be accompanied by an interpreter," Moog says.

"That's the point of teaching speech. If you can only communicate using sign language, and nobody can understand you when you speak, you probably won't have as many opportunities as those who can speak."

The Deiters family couldn't agree more.
This isn't the first time Dale Purves has put his career on the line. Twenty years ago, he tossed aside a surgical residency in favor of a postdoctoral fellowship. "The next two or three years were painful," he recalls, "because I vacillated a lot, wondering if I'd made the right decision. How could I tell my in-laws I was studying leeches, when they thought I was training to be a neurosurgeon?"

Purves, an M.D., is now professor of neurobiology at Washington University School of Medicine, where his research involves small mammals. White coats replace green scrubs these days, and mice take the place of patients.

In life, synaptic endings on neurons can be made visible by the uptake of a vital dye which fluoresces. The small bright spots pictured here are endings on autonomic ganglion cells in a living mouse.
The lights in the lab are low when Purves begins his daily stint of surgery. A white mouse sprawls over a microscope stage, nose-to-nose with the researcher. The animal’s brain is the size of a pea, and Purves aims for just one speck. Deftly he incises the skin and drills through the skull, the whir of the drill drowning out the steady dub, dub, dub of the respirator. Next he removes a minute part of the brain’s membranous covering. Through the microscope lens, the right olfactory bulb comes into view—the part of the brain that can distinguish the smell of cheese from that of a cat in hiding. Purves cares little for this bulb’s function, though; he seeks it for its baroque. ornate construction.

The brain research began last winter, a culmination of Purves’ earlier ventures. “The issue that has always interested me is: What is the basis of change in the nervous system?” he explains. “We grow up, we learn things, we become distinct personalities. Obviously that has a neurological basis. Something goes on in the brain that forms the embodiment of those changes. To a neurobiologist, the obvious way to look at that is to study the same nerve cells, the connections between them, and the way in which those connections change over time.”

Obvious but not easy. The brain is a tangled mass of cells, each with hundreds or thousands of interconnections. No one has viewed this intricate landscape and then looked again later to see if its microscopic contours have changed. But in the last five years, using a simpler part of the nervous system as a model, Purves and his collaborators have worked out techniques that may make such an enterprise possible. “Dale is studying the nervous system in a way that no one else has ever imagined,” says postdoctoral fellow Anthony LaMantia, Ph.D., who recently came from Yale to work with Purves.

Yet It Does Move

When Purves was a medical student, scientists thought of the nervous system as a static network of cells that became interconnected during development and then stayed forever wired in a rigid pattern. This viewpoint came largely from the work of Roger Sperry, Ph.D., a CalTech scientist who won the Nobel Prize in 1981 for his work on communication between the two hemispheres of the brain. Sperry proposed that the nervous system develops according to its genetic blueprint as nerve cells recognize their correct neighbors through the pairing of complementary labels. Thus each cell would fit into place and keep a fixed relationship with the cells around it, rather like a piece in a jigsaw puzzle.

“There’s a great deal of evidence for this lock-and-key method of recognition,” Purves says. “But what this hypothesis suppressed for 20 years or so is the idea that, in addition to specificity being important in nervous system development, there is also a great deal of malleability.”

The video screen behind Dr. Purves displays an image of the arrangement of nerve terminals in the olfactory region of a living mouse brain.

Some of the evidence for such malleability has come from Purves’ studies of the autonomic nervous system, which consists of nerve cells entirely outside the brain or spinal cord that control functions such as breathing, heart rate and intestinal contractions. “The advantage of working with the autonomic nervous system,” explains Purves, “is that it consists of honest-to-God nerve cells but is easy to get at because of its peripheral location. Also, autonomic ganglia [groups of nerve cells] are much easier to deal with than the central nervous system because their cells make fewer interconnections.”

Nerve cells have round bodies plus long arms that reach to or from other cells. Messages travel along nerve pathways in the form of electrical impulses, which move from a cell body to an outgoing arm called an axon. Branches of the axon then make contact with the next nerve cell in the pathway, not by fusing with it but by close contact at points called synapses. The two cells communicate across synapses with chemical signals that act very briefly—usually over a few thousandths of a second. The receiving end of the synapse is either the body of the next cell or an arm called a dendrite.

“There are two broad ways of thinking about how the nervous system operates in us and other sophisticated animals,” Purves explains, “although the two aren’t mutually exclusive. One is that the changes that occur in the course of our lives all have to do with biochemical and electrical changes among fixed sets of synaptic connections. The other is that the connections themselves change. So far, the first approach has prevailed.”

Purves’s findings point to the second interpretation, however. When he and colleagues Jeff Lichtman, M.D., Ph.D., David Johnson, M.D., Ph.D., and Rich Hume, Ph.D., studied nerve cells in autonomic ganglia, using electrodes small enough to fit into single cells, they found that connections which formed initially kept changing during embryonic life and for long periods postnatally.

“We believe the reason for these adjustments has to do with the establishment of the right numbers of normal synapses,” says Purves. “If you want each ganglion cell to be innervated by, say, five different nerve cells, that’s something that really has to be worked out in the course of development. It’s very hard to imagine how such numerical accuracy could be achieved with complementary labels.”

A more logical way, suggests Purves, would be through chemical dependencies between nerve cells. “Synapses need trophic support to stick around; otherwise they simply disappear,” he argues. “The result is an ongoing ability of the nervous system to adjust to circumstances.”

The concept of trophic interactions—the long-term dependence of nerve cells on substances from the cells they innervate—originated in the 1930s with the work of Viktor Hamburger, Ph.D., Edward Mallmeckrod Distinguished Professor Emeritus of Biology, and Rita Levi-Montalcini, M.D., professor emerita of biology. In 1986, Levi-Montalcini received a Nobel Prize for isolating the first trophic factor, nerve growth factor, at Washington University in 1951.

The original idea of trophic support, now generally accepted, is that embryonic nerve cells either acquire a fair share of the trophic agent they respond to or die.
Now Purves is suggesting that trophic substances also maintain synaptic connections, which may form initially and then disappear if they receive insufficient support. "Competition for trophic agents," he says, "appears to determine how many synapses each nerve cell makes, how many different nerve cells contact a target cell when the shouting is over."

In his new book, *Body and Brain: A Trophic Theory of Neural Connections*, to be published by Harvard University Press this fall, Purves develops this theme to explain interactions between the nervous system and the changing bodies of developing and evolving animals.

**Taking a Dim View**

The discovery that the embryonic nervous system isn't rigidly wired together led Purves to wonder if the nervous system of adult animals is also malleable. "Sperry would have said not," he says, "but the question is still open. The obvious way to answer it is to look at some cells and their connections in the adult nervous system and then examine those same cells at a later time. Lots of people must have thought about doing that but, until recently, the technology was unavailable."

Five years ago, Purves realized he could get images of living nerve cells by combining several newly developed technologies. First he acquired a video camera that can operate with 300-times less light than usual—such low-light-level cameras are normally used for security or military purposes. This allowed him to make images of nerve cells stained with fluorescent dyes without harming the cells, as would happen if they were exposed to sufficient light to make regular photographic images.

To the camera, Purves and his group linked a powerful computer with an image digitizer, a technology borrowed from the space program. The digitizer breaks a video image into a quarter of a million dots, called pixels, and then assigns a number to each pixel according to its brightness. White pixels are assigned the number 0 and black pixels the number 256, with the numbers 1 to 255 going to the various shades of gray in between. "The reason that's terrific," explains Purves, "is that, once an image has been digitized, the computer can play with it. So you can take a crummy image, whether of the surface of a planet or an autonomic ganglion, and make it very much better. You can enhance it by increasing the contrast, by averaging many images, or even by assigning colors if you want. You're limited only by your imagination."

In 1983, Purves began to use this procedure to make pictures of nerve cells while leaving them unharmed and thus able to be viewed again at a later date. Working with him were graduate student James Voyvodic (now a postdoctoral fellow at the University of London), who developed the large body of software needed to process the images, and postdoctoral fellow Robert Hadley, Ph.D. (now assistant professor of anatomy at the Medical University of South Carolina), who already had experience with non-toxic dyes and low-light-level cameras.

Looking at nerve cells in autonomic ganglia, the researchers first stained dendrites with a fluorescent dye and made images the computer could store and later enhance. Then they repeated the procedure several weeks or months later, imaging the same nerve cells, which they identified by size, shape and proximity to landmarks such as tiny blood vessels.

"What we found," says Purves, "was that the dendrites in a mature mouse's autonomic ganglia changed continuously. It was subtle, taking three to four weeks before we saw quite obvious changes. The dendrites look like branches of a tree, and the major branches stayed the same. But when we looked at the smaller branches, we found that some disappeared, others extended, and others were newly formed."

Not satisfied with imaging dendrites, Purves, Lichtman and medical student Lorenzo Magrassi turned their attention to the branches of axons, which end in blobs called synaptic boutons. "A bouton is the part of a synapse that represents an end of an axon," Purves explains, "whereas a dendrite is a branch from the next nerve cell in the pathway. So if you want to see how connections change, looking at boutons gives you a more direct assessment."

After a frustrating search, Magrassi, who is now continuing his studies in Italy, found a family of fluorescent dyes that would stain the synaptic boutons without harming the nerve cells or the mouse. The dyes were tested on nerve cells that innervate muscle. Purves and his co-workers then examined synaptic stability in autonomic ganglia related to salivary
glands. With the low-light-level camera they made images, first, of the surfaces of identifiable nerve cells and, second, of the stained synaptic boutons that sat directly on them. When the two types of images were enhanced and superimposed, the positions of the boutons showed quite clearly. And when the whole procedure was repeated over progressively longer times with the same cells it was clear that there were substantial changes in the arrangement and number of boutons.

"The significance of the work we report here is twofold," wrote Purves, when he described this research in Science last November. "First, these methods allow visualization of synaptic terminals on living nerve cells. This approach may be useful elsewhere in the nervous system. . . . Second, our results suggest an ongoing rearrangement of interneuronal synapses in maturity. . . . [They] indicate that connections between nerve cells in mature mammals may be considerably more dynamic than has generally been thought."

This conclusion has important implications. "If the connections between nerve cells are continually changing," says Purves, "then it's a whole different ballgame than if synapses are modified through biochemical changes in fixed sets of connections. The mechanisms are going to be very different, so the whole approach to studying the nervous system changes—how one approaches the research and also how one thinks about a whole variety of clinical disorders, from mental retardation to responses to injury."

Seeking the Right Connections

Instead of sticking with the autonomic nervous system, Purves decided this year to brave the gargantuan task of looking for changing connections in the brain. "The peripheral nervous system is a good place to start," he says, "but the brain is where the interest is because it's obvious that all the amazing things we do, from creating symphonies to scientific research, are by and large going on in that part of the nervous system."

There were, and still are, many practical problems to be solved, such as how to drill a hole in a mouse's skull and seal it without damaging the brain between one round of surgery and the next. One creative solution came from a tube of bathtub caulk, which can be squirted into thin sheets of plastic and then cut to plug the hole. "We struggle with such problems every day," says Purves. "It's good to have several people working on the project because when one person gets discouraged, the others can keep him going."

Finding a suitable part of the brain to study also wasn't easy. For several months, Purves and LaMantia searched for a region that was both accessible and rich enough in features for its cells to be individually identifiable. "There was a day back in March," LaMantia recalls, "when we were really frustrated. We'd been looking at the cerebral cortex for several weeks and hadn't been having much luck. Over lunch, we said, 'We'll give it one more push, and if nothing comes of it, we'll go back to autonomic ganglia.' So after lunch, I took a brain out, and so did Dale. We stained them and saw the glomeruli in the olfactory bulb and realized that here was something we could study."

Glomeruli are balls of dendrites and axons that adorn the olfactory bulb, and they offer the distinctive topography the scientists are seeking. For starters, Purves and LaMantia will look at the glomeruli themselves to see if their positions change over time. Later, using a new type of microscope that scans with a laser beam, they hope to study the structures in greater detail, looking for more subtle changes involving dendrites or synaptic boutons.

"The transition from the peripheral nervous system to the brain is proving to be very difficult, but I think we'll get somewhere," says Purves. "If we can stick with it for another 10 years, I think this will turn out as well as our work with the autonomic nervous system. Or maybe that's just whistling in the dark. One never knows."
Leonard Kent, M.D. '43, has his way lovers will give Vrieseas on Valentine's Day, red and green Guzmanias will adorn homes at Christmastime and thoughtful children will give Aechmeas on Mother's Day. These exotic names belong to equally exotic plants, bromeliads, and Kent is hoping they will capture some of the floral business from the growers of roses, poinsettias and chrysanthemums.

He unabashedly calls bromeliads "ideal house plants." They require little care, he says. They can do without water for up to two weeks and will survive in dimly lit homes. Generally, a colorful flower spike grows from the center of a rosette of waxy leaves. Each bloom lasts from three to six months.

Bromeliads are members of a large family of tropical plants that includes the pineapple and Spanish Moss. Except for one species that grows in Africa, bromeliads naturally occur only in Central America, South America, the southern United States and the Caribbean islands.

Kent's passion for plants in general and for bromeliads in particular is obvious when one visits his home in Vista, 55 miles north of San Diego, Calif. His acre and a half of property looks like a botanical garden. A maze of narrow paths winds amidst a jungle of palms, eucalyptus and tropical fruit trees. Exotic trees, shrubs and flowers from around the world cover every square foot of earth.

Kent walks along the path pushing away branches in his way like a jungle explorer in an old Tarzan movie and recites the Latin names of each plant. Amid the rampant greenery he spots something amiss. "Whoops, I've got a weed and it's gone to seed," he says as he yanks at it with both hands. "I'd better get rid of this while I can."

From the brass pineapple knocker on his front door to the paintings in his bathroom, Kent's love for bromeliads is apparent. A stained glass window depicting a bromeliad is set into his front wall. There are collections of pre-Columbian, African and Eskimo art. In every room prints and photographs of bromeliads hang on the walls.

"You've got to understand, it's a disease," says Kent with a smile. "With the inanimate objects like the pre-Columbian art it's easy to stop, but when it comes to living things they keep multiplying. It's hard to quit."

Kent caught the bromeliad "disease" 25 years ago when he went to a nursery and saw a beautiful flowering plant which the nurseryman couldn't identify. At that time bromeliads were little known in the United States. He became interested in these mystery plants and collected them at every opportunity. He traded specimens with members of the bromeliad society and got plants by mail from nurseries in Florida. "I tried to get one of every plant that existed," he says.

At one time, Kent says, he probably had the largest bromeliad collection in the world, numbering about 1,500 species. He started his collection in a six-foot-
wide greenhouse adjoining his Los Angeles home, hanging plants above one another to use every foot of available space.

His plant collection soon outstripped this space so Kent bought property with more greenhouses in Los Angeles. He built additional shadehouses on this property which he soon had jam-packed with bromeliads.

During this time Kent was busy selling bromeliads to other collectors on a mail-order basis. He supplied bromeliads to prestigious institutions such as the Missouri Botanical Garden, New York Botanical Garden and Denver Botanical Garden. More recently, a bromeliad garden at the San Diego Zoo has been named in Kent's honor.

Still, Kent had to divide his time between his burgeoning mail-order business and a successful practice as a doctor of internal medicine. "I had a huge practice, actually," he says. "I was busy because in my time we made a lot of house calls." During weekdays he practiced medicine, and at nights and on weekends he would ship plants with the help of his family.

Eventually, Kent's oldest son, Jeffrey, got the idea that bromeliad culture could be a successful full-time business. Jeffrey worked for a year at a commercial nursery to learn to grow plants on a massive scale.

In the meantime, Kent visited commercial growers in Europe where they have been mass producing bromeliads for about one hundred years. "I went to visit growers in Holland, Belgium and Germany and I saw that it could be done and that it was a profitable business. After a year we bought land in Vista and built a 10,000-square-foot commercial greenhouse. Crazy!" he says, as if not quite believing it himself.

As the business prospered, Kent's son Larry got involved as a sales manager. Using the Yellow Pages and a small truck, he took plants from florist to florist to sing the praises of bromeliads. Interior decorators and supermarket floral departments saw the value in these tough but colorful plants and began to supply the Kents with plenty of business.

Soon Kent's remaining son, Michael, jumped on board the family business as marketing director, producing slick, colorful catalogs and posters of Kent's bromeliads.

Not only has Kent founded a huge commercial bromeliad nursery, but he has also followed in the footsteps of the intrepid European plant collectors of the 1800s. His favorite historical collector is Edouard Francois André, a French aristocrat who explored the trackless jungles of South America before the turn of the century, searching for new species of bromeliads.

Kent likes to show a biography he has on André, depicting the Frenchman fighting off wild animals and being carried on a chair through the jungle by Indian servants.

A crew of 25 employees tends to acres of plants at Kent's nursery.

Kent's own collecting adventures, although more sedate, have taken him to many tropical locations such as Guatemala, El Salvador, Costa Rica, Panama and the Yucatan. He vividly remembers his first collecting trip to Jamaica in 1963. When he saw his first bromeliad growing in the wild, he got so excited he ran through the jungle. He brushed against a poisonous plant and got an itchy, blistering rash.

He also tells of some tense moments along the border of Colombia and Ecuador when he encountered a patrol of Colombian soldiers and was caught without a permit for his Ecuadoran rental car.

Then there are tales of collecting plants in drenching rain, in mud that "sucks your boots off." He tells about driving on narrow, winding mountain roads in Ecuador with precipitous cliffs just inches from one's tires. "Collecting is fun but very tiring," Kent says. "At times the jungle is quite spectacular, the waterfalls and rivers." He also recalls seeing jungle animals such as monkies, sloths and coatimundis.

But, adds Kent, the accommodations can be as horrible as the jungle is beautiful. "It's beyond belief the places we slept in," he says. "You can't imagine. The bathrooms are horrible. There are bugs running around. They're supposed to be hotels but they're wooden shacks with just a small bed and a bare, hanging light bulb."

Avoiding "Montezuma's revenge" in those areas is a major concern. "In those situations I usually eat hard-boiled eggs" Kent says. "I feel safer with that, although that can be trouble too these days."

Getting the bromeliads into the hands of the collector presents its own set of obstacles. Most bromeliads are epiphytes, or air plants. They cling to tree branches,
often high above the ground, and get their nourishment from the rain and forest litter that drops onto the plant.

Kent has used several different methods to gather bromeliads. He has used an extendable aluminum cutting pole to cut the plant free. Sometimes he uses a rope saw. He has even used a rope with a rock tied to the end. He throws the rope across the tree limb near the bromeliad and pulls the rope against the plant until it falls free.

"None of these methods compares to a human hand," Kent says. "If you can find a native who will climb the tree for you, that is the best way. But sometimes you are frustrated. You can’t reach the plant."

When Kent picks a wild bromeliad the first thing he does is gives the plant a sharp snap. The leaves of bromeliads overlap at the base to form water retaining cups. These little pools are havens for small jungle creatures, including venomous snakes. Shaking the plant tosses away any unwelcome animals. "Never put your hand into a wild bromeliad," Kent admonishes.

When Kent can’t be in the jungles he uses another method of great European collectors of the 19th century to acquire new bromeliads. He has local collectors working for him in Central and South America who send back unusual specimens. "When I first began I tried to get people who were known to collect orchids to collect bromeliads," he says. "They wouldn’t always know what a particular plant was but they would collect it and send it to me anyway." Although Kent himself has never had any serious accidents in the jungle, one of his collectors entered the San Marta cocaine district of Colombia and was never heard from again, he says.

Back in Vista, Kent takes a visitor to see his greenhouses. He opens a sliding door into a carefully controlled tropical environment with a constant relative humidity between 60 and 80 percent and temperatures between 65 and 85 degrees. Bromeliads crowd wide benches as far as the eye can see. One bench is full of robust plants with mottled leaves, Aechmea fasciata, the "mystery plant" that first piqued Kent’s interest in bromeliads. Shelves suspended above the main benches are full of smaller seedlings.

"I wasn’t kidding," Kent says. "I told you it was big. As you can see there is not too much in bloom. We try to sell what is in bloom." The Kents use a mixture of water and ethylene gas poured into the cup of the plant to induce blooming 10 weeks later. In this way plants can be brought into flower when they are scheduled to be shipped to the customer.

Today Kent’s role at the nursery is mostly as an overseer. He is at the greenhouses early nearly every morning to be among the plants. What began as a hobby has turned into a sprawling, complex industry. The nursery employs 25 people. With the aid of a potting machine imported from Holland, a few workers can pot 3,000 plants per hour. Some employees use walkie-talkies to communicate among the three widely spaced growing areas.

The Kent nursery was the first nursery in the United States to propagate bromeliads on a large scale by seed, rather than by vegetative offshoots from the mother plant called "pups." It takes about 2.5 years to bring these plants from grasslike seedlings to blooming plants, Kent says. The Kents have also used cross pollination to create some of their own unique hybrids. One is named "Irene" after Kent’s wife.

So what do Kent’s medical colleagues think of this physician turned bromeliad baron? "They’re amazed that this could happen and so am I," he says laughing. "I never anticipated this."

For Kent, his continuing interests in medicine and botany are not at odds. "I think there is a lot in common between plants and people," he says. "They don’t have arteries and veins but they do have a circulatory system, and hormones involved. There are similarities, perhaps more than we realize."
Two years ago Dan Bean bruised his ankle on his wife's rocking chair. Unlike any bruises he'd had before, this new black and blue mark did not just fade away, but erupted into an open sore that wouldn't heal.

Dan's doctor diagnosed the wound as an ulcer and prescribed some ointment, but the sore didn't get any better—it just got bigger.

Soon it was the size of a half-dollar, and the 81-year-old began to curtail his physical activity out of fear that the ulcer would get even larger. The inactivity caused him to stiffen up and become arthritic. And it took its toll on a man who worked four years past his retirement and always prided himself on being strong and active. "Before the sore—even after he retired—dad did things out in the yard and did push-ups every night to stay in shape," his daughter Linda Rollins recalls. "Once he got the sore, the doctor didn't want him to move around too much because he thought it would cause the ulcer to run. My father took this to mean he should stop everything and sit around.

At his age, sitting around made his arthritis 10-times worse."

Sitting around didn't even help the sore, nor did the home visits by nurses who cleaned and dressed the wound three times a week. Dan's doctor consulted other physicians about Dan's ulcer and experimented with different treatments, but nothing worked.

Finally, after Dan had suffered for almost two years, his doctor received a brochure about a new wound-healing center at Washington University. There, under the care of Thomas A. Mustoe, M.D., assistant professor of surgery in the Division of Plastic and Reconstructive Surgery, and nurse specialist Laurel Wiersema, Dan's ulcer began to heal at last.

Dan was not alone in his situation before coming to the wound-healing center, according to Mustoe. Some of the patients he treats come to the center with ulcers that have not healed for 10 years. "There are clearly patients out there who are not being successfully treated in the sense that they have ulcers for years, and the cost to them both in terms of time off from work, chronic dressings and cleansings and limitation of activity is really significant," he says. By some estimates, chronic leg ulcers are a $4 billion a year problem, and the cost of physician ser-
Shown here are cross sections of wounds made through the epidermis (E) and the dermis (D) in experimental tissues. The growth factor PDGF was applied to the wounds pictured on the left while the wounds displayed on the right were untreated. The micrographs trace the healing process on day two after the wound was made, on day five and day 14.

**Day Two**

Arrow indicates increased number of cells migrating into the wound treated with PDGF compared to the untreated wound. PDGF attracts large amounts of white cells highly beneficial to healing in the early stages.

**Day Five**

The wound treated with PDGF shows an increased number of collagen-producing cells that accelerate the healing process.

**Day 14**

The increased amount of scar tissue formed in the wound treated with PDGF results in healing that is 70 percent stronger than in the untreated wound. The PDGF application advances healing by four to six days in the two weeks after wounding and produces a much stronger scar than in an untreated wound.

The most important prospect of PDGF treatment is substantially increased recovery for patients with diminished wound-healing powers caused by diabetes, peripheral vascular disease and radiation and chemotherapy.
cies, medication and hospitalization in persons who are trying to recover from bed sores tallies to $7 million.

These problem wounds are currently treated by physicians from a wide variety of specialty areas, none of whom care for wounds as their central interest. And despite impressive advances in dressings, topical antibiotics and debriding agents that help remove unhealthy tissue, few physicians really know what's available to them or have the time to research all of the new products on the market.

To make matters worse, there is such an overwhelming volume of literature on recommended treatments that it is difficult for the non-expert to sort out the good research from the bad.

As a result, there's a high level of ignorance on how to treat chronic wounds, and misconceptions and strange regimens abound. "It's remarkable how many otherwise very critical people use wound-healing regimens that are unproven," says Mustoe, who has seen patients who have used and have even been advised by doctors to use honey, sugar, antacids, heat lamps, even sour cream on their wounds. And one common, almost universal, misconception is that patients shouldn't get their wounds wet—the exact opposite of what needs to be done to keep the wound clean.

Even when the physician's advice is good, wounds often don't heal because patients misinterpret or fall short of carrying out their doctor's instructions. Patients tend to take what they're told very literally, according to Wiersema, sometimes exaggerating the doctor's orders past the point where they are beneficial. When told not to get their wounds wet, for example, patients may take this to mean that they shouldn't wash at all. Still others may literally put themselves to bed when advised to elevate their legs. Patients, especially elderly patients who don't have much money, may not use what's prescribed because they cannot afford it.

The new wound-healing center at Washington University addresses these problems by focusing completely on wound healing, thereby bringing expertise into an area where there essentially is none. The center takes a very scientific approach to wound healing by reviewing the scientific literature, assessing the effectiveness of treatments and testing new products.

Among the most exciting products to be tested are some of the body's own healing agents, which can be manufactured in large quantities through genetic engineering techniques. Animal studies by Mustoe in collaboration with Thomas Deuel, M.D., professor of medicine and biological chemistry, and Glenn F. Pierce, M.D., Ph.D., instructor in pathology, show that two genetically engineered growth factors—Platelet Derived Growth Factor (PDGF) and Transforming Growth Factor-beta (TGF-b)—can, in sufficiently large quantities, speed healing. Clinical trials of several growth factors should be underway soon, pending FDA approval.

In the meantime, the majority of chronic wounds can be healed, given an appropriate treatment strategy. Mustoe cites the example of a 69-year-old woman with arthritis, who came to the clinic with massive leg ulcers, and who had for 10 years. They were so big that she had been hospitalized at least twice for skin grafts and was in danger of losing her legs.

She had been applying a vinegar-like solution of acetic acid that was not only killing bacteria, but was also killing the living tissue. She also was not washing the wound or changing the dressings enough to keep the area clean.

Healing began when she stopped using the acetic acid and started to wash her wounds three times a day with a non-irritating detergent. In addition, Mustoe prescribed a topical antibiotic that doesn't harm normal tissue as well as an adherent bandage that would absorb pus and other debris from the wound. "Most wounds don't need our services," according to Mustoe. Those that do are chronic—that is, they have been present for at least two months. The majority of these chronic wounds fall into one of two categories: pressure sores and leg ulcers.

Pressure sores, which include bed sores, occur when someone lies, stands or sits on a pressure point for so long that circulation is cut off and the tissue dies. Leg ulcers, on the other hand, are sores that usually develop after some minor trauma, such as bumping one's ankle on a rocking chair. There's a break in the skin, bacteria get in and the sore enlarges.

"Normal skin is fairly resistant to bacteria," Mustoe explains, "but in skin where circulation is impaired—for whatever reason—the bacteria can get the upperhand very easily."

One of the most common circulatory problems predisposing people to ulcers is venous insufficiency, a condition in which the veins in the legs have trouble returning blood to the heart, according to Gregorio Sicard, M.D., a vascular surgeon who serves as a consultant to the wound healing clinic.

Ordinarily, blood is returned to the heart from the legs by muscular contraction. Sicard explains. As blood is forced up the veins via contraction, it is trapped by a series of valves that keep the blood from falling back down with gravity.

But if these valves are destroyed—by clots, for example—any blood that is squeezed up through muscular contraction will simply fall back again with gravity. When the legs swell with too much blood, the vessels that carry blood to the skin become separated from the skin. Deprived of an adequate supply of blood, the skin darkens in color, looks and feels like leather and eventually starts to break down. This makes the skin difficult to heal, because blood is so critical to healing, providing oxygen and nutrients that support living tissue and preventing infection by supplying white blood cells.

Sicard estimates that .5 percent of the population suffers from venous insufficiency, which is common among women because they are at high risk for blood clots during pregnancy. This condition accounts for a loss of 2 million working hours in the U.S. each year. "Unfortunately we, as humans, have to walk upright," Sicard says. "It's because of this that we are the only animal that faces varicose veins and other circulatory problems, because gravity is against us."

Diabetes, the use of steroids and arthritis may also interfere with circulation and wound healing, which is why the wound-healing center emphasizes a multidisciplinary approach. The center, which opened last May, also draws upon consultants in dermatology, orthopedics, dietetics and social work. As a surgeon, Mustoe is able to offer a surgical opinion, while at the same time trying to spare patients from surgery. "Our goal is number one to spare people from surgery and number two to help them get back to a normal life," Mustoe says. "If we can do that, we've really done something.
The Hazards of Self Diagnosis and Treatment

As humans, we are fortunate to have a variety of senses to help us appreciate our environment. As an ophthalmologist, my concern is the visual system.

Recently, I reported a small series of patients who lost vision due to inappropriate use of over-the-counter eye drops. Four of the patients suffered acute angle closure glaucoma, and one patient suffered a dislocated lens implant.

Obviously, the patients who suffer blindness after self diagnosis and self treatment are quite rare. In fact, I have heard of anecdotal reports of similar cases.

In my own practice, it is not unusual to find that patients have indulged in self diagnosis and self treatment. Many patients who are seen in my office for problems ranging from eye infections to injuries, tell me that they had tried over-the-counter eye drops for several days before making their appointment.

This raises concern because some over-the-counter eye drops contain medication that can dilate the pupil. While this may not harm individuals with normal vision, such dilation can cause blockage of the drainage channel in extremely far-sighted individuals, resulting in an elevation of pressure in the eye (acute narrow angle glaucoma). In individuals with iris supported lens implants, excessive dilation of the pupil may result in the lens moving out of position, with damage to the cornea if the condition persists.

As physicians, we must remind ourselves and our patients that any medication is a double-edged sword in that there are good and bad effects of its use. When a medication is developed, the Food and Drug Administration tries to select for approval those medications which have been thoroughly tested and are as free of side effects as possible. This process is lengthy and has been the subject of some controversy.

The Food and Drug Administration refers to over-the-counter drugs as medications that "are generally regarded as safe for the consumer to use by following required label directions and warnings."

Yet the problem of individuals harming themselves by inappropriate use of over-the-counter medications is not unique to ophthalmology. Reports of fatal cardiac arrhythmias as a result of over dosing with inhalers have also appeared.

It is important for us as health care practitioners to instill in our patients the notion that in any medical condition, delay in proper diagnosis or treatment may result in damage. It is this possibility that makes it impossible to generalize about a safe method of using over-the-counter eye medications. A patient with an eye problem must be examined by a physician to determine what is going on. If an eye problem is associated with pain, loss of vision, exudate, trauma, exposure to toxic substances, and persists, examination by an ophthalmologist is advisable.

In educating our patients about the dangers of self diagnosis and treatment, we must first be aware of the factors that encourage them to self diagnose and treat. One very important factor is media advertising, which inadvertently trivializes the consequences of errors in diagnosis and treatment. Other factors are a desire to avoid loss of time and money by not seeking medical attention. In some states, pharmacists are allowed to legally dispense medication. Many of the new health insurance plans impose barriers between the patient and the health care provider. It is also just plain human nature to give medical advice.

In summary, I have reported blindness that occurred after misuse of over-the-counter eye medications. Although this is a very rare situation, the consequences can be devastating. It is impossible to know how widespread this problem may be. With the influence of media advertising and a variety of factors imposing barriers between patients and health care, it is not unreasonable to expect the trend to self diagnose and self treat to increase. As physicians, we should be aware of this problem and advise our patients and the general public to seek medical attention if a health problem persists.

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This is the opinion of the author, not necessarily shared by Washington University, Washington University School of Medicine, Washington University Medical Center, or the policy of any of these entities. Outlook welcomes replies to this editorial and invites contributions from its readers on other subjects.
Many alumni are familiar with Marv Levin, M.D. '51, through his role as chairman of the William Greenleaf Eliot Society membership committee for The School of Medicine.

In the five years he served in this capacity, Levin has asked, urged, humored, explored, prodded and even twisted the arms of so many of his fellow graduates that some may even think Marv Levin is the Eliot Society.

But there's another side to Marv Levin—the side that his patients and their families see, the side that's valued so heavily by his colleagues and friends.

As a practicing endocrinologist, his skill and bedside manner have earned him an unequaled reputation, especially in the treatment of diabetes. The Marv Levin his patients know is best summed up in one of the many letters of appreciation he's received, like one from a patient's son who writes that "undoubtedly it was your care, professional skill and imagination, but more importantly the enormous trust that my father has built with you over the years that was probably in large part responsible for pulling him through."

Caring about his patients in this way is what Levin finds most satisfying in life. "Most of us went into medicine for the same reason," he says—"because we really wanted to do something for our patients. And the fact that we can help sometimes is what makes all
those years of medical school and residency worthwhile. People will talk about the prestige and the monetary rewards, but the real satisfaction is in the personal gratification you get from caring about your patients.”

Next to his patients, Levin, who is a professor of clinical medicine at the School of Medicine, finds his greatest joy in education. One long-held criticism of faculty and students at the School of Medicine is that they don’t share their expertise with people outside the medical center.

Levin, on the other hand, has helped sow his knowledge about diabetes of the foot on all four corners of the earth. Just this past year, for example, he served as a visiting professor at 32 conferences throughout the world and led congressional lobbying efforts for the funding of special therapeutic shoes that can help prevent amputation in patients with diabetes of the foot. He has also served as a medical expert on KMOX and other local radio shows, and is currently serving on the board of an international traveling university that brings medical knowledge to underdeveloped countries in South America.

In his many travels, Levin has amassed quite a few travel journals from exotic lands. Among them is a journal he kept during the month he spent in China (1982) as part of a 16-member United States Task Force on Endocrinology. There, he and six other physicians from the School of Medicine toured rural areas, made rounds with Chinese physicians, reviewed cases and lectured in their areas of expertise. On route to the Summer Palace in Beijing, he wrote: “Along the way we are passing many farms. There is no grass, every single square foot is under cultivation. There are no tractors, only some horses, but mostly peasants doing the physical work. We are passing streams where there are Chinese in the water clamming; along the banks there are fishermen. All the fields have intricate irrigation ditches and again all the farm work is being done by hand with relatively primitive tools. And everywhere you look there are bicycles, bicycles, bicycles. There are very few cars and a moderate number of horse-drawn carts.”

Upon a visit to the Convalescent Hospital in Wushi, he wrote: “We went into a room where they were treating a man for headaches by using an electric comb; another fellow was receiving ion therapy with some peculiar device hanging over his head which was emitting, so they said, special ions, and he simply sat there in the chair. I guess he was getting ionized while he waited for lunch. In the next room they were dunking people, at least to a degree in hot wax—couldn’t be too hot, they all looked very happy—for treatment of arthritis.”

It is because Levin values his own education at Washington University that he has been so willing to give back to his field both as an educator and as an alumni volunteer. The university’s orientation towards research has helped shape his career into what it is today, according to Levin, who was one of the first to show the decrease of bone mass in diabetics.

The co-editor of an authoritative text on the diabetic foot, he served as co-principal investigator for the University Group Diabetes Program and contributed to a landmark study by Washington University Medical Center physicians testing the theory that precise blood sugar control through the use of insulin can help prevent the complication of diabetes.

He received honorable mention in the Van Meter Prize for outstanding thyroid research with his co-author and mentor William H. Daughaday, M.D., Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism, in 1955, and the American Diabetes Association’s Pfizer Award for outstanding clinician of the year in 1979. He was also awarded honorary membership in the American Dietetic Association for promoting the role of dieticians in physicians’ offices.

“I feel that we all owe a debt of gratitude to Washington University for giving us such a fine education,” he says. “Most of us wouldn’t have some of the things we have if we hadn’t graduated from here.”

It is this feeling of commitment that has driven him to accomplish as much as he has for the Eliot Society, establishing three and laying the groundwork for a fourth Alumni Endowed Professorship.

In addition to his Eliot Society activities, Levin has helped organize numerous golf tournaments in support of the St. Louis American Diabetes Association, for which he is a former president, and current editor of the national group’s two journals: Clinical Diabetes and Diabetic Medicine. Although he’s been golfing since the age of 12, he regrets that “the only success I have not had in life is a hole in one.”
Ron Evens takes the reins as Alumni President

Ronald G. Evens, M.D. '64, became the new President of the Medical Alumni Association this past July.

He assumes the position from Thomas F. Richardson, M.D. '63, associate professor of clinical psychiatry, who last year led the effort to revitalize national alumni programming.

Evens is the Elizabeth E. Mallinckrodt Professor and Head of Radiology, Director of Mallinckrodt Institute of Radiology and Vice Chancellor of Finance for Washington University. With the exception of two years spent at the National Institutes of Health, Evens has devoted his entire career to the university and hospitals of its medical center.

Under his direction, the university's radiology department has evolved into one of the five largest and most modern radiology departments in the world. And his own contributions to the field have earned him the presidencies of two of the most prestigious radiologic associations: the American Roentgen Ray Society and the Association of University Radiologists.

Yet his demanding work schedule has not prevented him from becoming actively involved in the affairs of his university and alumni association. Having served as chairman of his class for every one of his five-year reunions, Evens says he is willing to work for the alumni association because "I believe in it and in its service to people."

Alumni provide essential financial support for quality education through Alumni Professorships and both clinical and pre-clinical Professor of the Year Awards, he points out. It also offers alumni the opportunity to further their education through alumni reunion scientific programs and other post-graduate education programs.

Evens is particularly sensitive to the increasing need for student scholarships in light of the spiraling cost of medical education and student indebtedness. "Debts of $100,000 and more are no longer a rarity, but almost the norm," he says. "Today's medical students are the bread and butter of our future. As alumni, we need to help our school allow individuals with need to come here without having to take on such serious debt."

In addition to his responsibilities as a radiologist and alum, Evens is an avid runner, having run marathons in St. Louis, New York City and Munich and "lived to tell." He and his son, Ron Jr., who ran with him in Munich, are planning to run another marathon together next year.

Evens' entire family has close ties to the university community and medical center. Evens' wife, Hannah, is a graduate of Barnes School of Nursing, Ron Jr. and his sister Christine are both Washington University graduates and their sister Amanda is completing her senior year there.

A family man, Evens is active in his church and in the Boy Scouts of America. He plans to stay in St. Louis, "doing whatever the university wants me to do."
Graduating Students Choose Needleman and Schwartz as "Teachers of the Year"

This past spring the Class of 1988 named Alan L. Schwartz, M.D., and Philip Needleman, Ph.D., "Teachers of the Year" in their respective areas of clinical and basic science. As such, their departments have received $10,000 each from the School of Medicine's Medical Teaching Fund.

This year's graduating class was the fifth class to choose Needleman, the Alumni Professor and Head of Pharmacology, as its "Teacher of the Year." He plans to use his award money to continue a special program for medical students in which they are trying to design a computer research model that can serve as an alternative to research on animals. While Needleman doubts that the computer will ever be a satisfactory substitute for animal research, he believes that it can be developed into a sophisticated supplement to "take teaching beyond the lab."

When asked what he likes most about teaching, he describes a certain point during the dog blood pressure experiment, when the students fall into a certain pattern of logic, but obtain results that are totally different from what they expected. "I love to watch the students and see the lights turn on in their heads as they grasp an area of understanding that will be important to them for the rest of their lives," he says.

"My biggest worry at graduation is that it's one thing for students to be responsive to what you teach them, but that those same students will be about 25-years-old when they graduate and still have eight or more years of training to go. What we teach them here is only 10 percent of their education. Ninety percent is on their own. What we really need to do is teach them to be responsible for their own education."

Schwartz, who is the Alumni Professor of Pediatrics, was chosen as teacher of the year for the first time this year. He plans to use his award money to buy new instructional texts for the pediatric ward.

"Teaching is the single most important thing you can do in a university," according to Schwartz, who views his role as one of "trying to prepare the next group of people to ask the questions we aren't clever enough to ask and answer the questions we can't answer."

Donald Eggleston, M.D. '30, is retired and living with his two daughters. His wife, Mary Ethyl, passed away.

Henry V. Kirby, M.D. '33, is still in solo family practice in Harrison, Arizona. He also directs two nursing homes and has been coroner for the past 25 years. His wife, Elva, of 47 years died in 1983. He remarried Marilyn, a nurse, in 1984.

Eleanor Steindorf, M.D. '38, now retired, is active in the Camera Club of Laguna Hills and is interested in environmental causes. Before retiring, she was an assistant professor of obstetrics and gynecology at the University of Southern California School of Medicine and Director of Maternity and Child Health.
for the Long Beach Health Department. She writes that, until his death about two years ago, she frequently saw Jim Nolan, M.D. '38. "He really made a name for himself internationally in the field of gynecological cancer," she writes. She would like to be remembered to the "girls"—Marion Dakin, Margaret Carter and Dorothy Gill.

Alexander Ling, M.D. '44, recently retired as senior partner of Neurosurgical Associates of Northeastern Ohio after 34 years of practice. He was also chief of neurosurgery at Fairview General and St. Alexis hospitals in Cleveland.

Patricia F. Lanier, M.D. '46, is medical director of the oncology program at Pomona Valley Community Hospital in Pomona, California—a 399-bed hospital that serves the entire Pomona Valley area. She is also chairman of the hospital's department of medicine.

Robert E. Nelson, M.D. '46, continues to work in general, vascular, thoracic and pediatric surgery. He serves on the board of directors at Central Plains Clinic and the Sioux Falls Surgical Center in Sioux Falls, South Dakota. He was widowed in 1983 and remarried a surgical nurse named Ann.


Paul E. Siebert, M.D. '52, writes that his son John has finished his residency and has followed his father's footsteps into the field of cardiology. Paul now has five granddaughters and one grandson. He is still practicing part-time.

William D. Sawyer, M.D. '54, received the honorary degree of Doctor of Science from Mahidol University in Bangkok, Thailand. The award cited Sawyer's participation in the development of the university while serving as Visiting Professor and Chairman of the Department of Microbiology of the Faculty of Science. The citation singled out his efforts in advancing the graduate program to the doctoral level and his work in building the institution's research capabilities. Sawyer is President of the China Medical Board of New York, Inc.

On a recent 18-day trip to the Antarctic Peninsula, Havner H. Parish Jr., M.D. '56, surgically implanted cardiac monitors into two penguin chicks. "Not bad for a retired urologist!" he writes. "The patients did very well."

William J. Crowley Jr., M.D. '61, has become chairman of neurology at the University of Missouri-Columbia School of Medicine. Crowley is the founder and first president of the Missouri State Neurological Association. He has held academic posts at the University of Texas in San Antonio, the University of Virginia and the University of Oklahoma.

Ronald E. Rosenthal, M.D. '61, is currently chairman of the Committee on Emergency Medical Services for the American Academy of Orthopaedic Surgeons. The chief of orthopedic surgery at Queens Hospital Center in Jamaica, New York, Rosenthal also serves as associate professor of clinical orthopedic surgery at the State University of New York at Stony Brook.

Kenneth L. Sims, M.D. '69, has transferred from the Naval Hospital in San Diego, where he was head of anatomic pathology and director of the blood bank, to Oakland, where he is chief of laboratory service and director of the pathology residency program.

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**Jackson Johnson Scholars 60th Anniversary**

Are you a Jackson Johnson Alumnus of the School of Medicine? Nearly sixty years have passed since the first scholar was named, and we're thinking of having a reunion. In order to include everybody and to verify our records we'd like to hear from you. We need especially to hear from you if you were a Jackson Johnson Scholar between 1949 and 1954. Please send your current address with your name and year of graduation to:

Mrs. Madeleine Kraus
Medical Alumni & Development Programs
Box 8049
St. Louis, Missouri 63110
314-362-8272
Thomas W. Woodrow, M.D. '74, is a board-certified cardiologist with a private practice in Tampa, Florida. He is also a clinical professor in cardiology at the University of Southern Florida at Tampa. He and his wife, Katherine Seymour, have three children: Andrew, 7, Jane, 4, and Emily, 1.

Linda Loney, M.D. '76, has been named Clinical Chief of Pediatrics at the Massachusetts Hospital School, a residential school and hospital for physically handicapped children and adolescents in suburban Boston.

Stephen G. Young, M.D. '78, has been selected as one of two 1988 Syntex Scholars by the Syntex Corporation of Palo Alto. The award recognizes outstanding potential for contributions to cardiovascular research, and is made to scientists who are in the formative stages of their careers. As a Syntex Scholar, Young will continue his research with the University of California at San Francisco-affiliated Gladstone Foundation, examining mutations associated with familial hypercholesterolemia, a syndrome which renders affected families free of atherosclerotic disease.

Lanyard K. Dial, M.D. '81, has been appointed director of the family practice residency program at Ventura County Medical Center. Dial is an assistant clinical professor of family medicine at the University of California at Los Angeles and coordinator of geriatric services for the Ventura County Medical Center and for the County’s Health Care Agency. He and his wife, Mary, a family physician in private practice, live in Ojai, California.

Anthony Griffin, M.D. '87, was elected to the resident position of the American Medical Association’s Council on Constitutions and Bylaws. Griffin is a resident in general surgery at Barnes Hospital.

John Hinderliter, M.D. '81, has accepted a position as assistant professor of cardiology at the University of North Carolina-Chapel Hill.

Alice Ann Gricoski, M.D. '81, has been elected vice president of the Gallia County Medical Society. Gricoski practices general surgery at the Holzer Clinic in Gallipolis, Ohio, and is the co-editor of the Mont Reid University of Cincinnati Surgical Handbook.

Robert J. Glaser, M.D., FHS in internal medicine, received an honorary doctor of science degree from Washington University this past spring. Glaser is a trustee of the university and the Director for Medical Science at the Lucille P. Markey Charitable Trust.

Robert A. Ratcheson, M.D., FHS in neurosurgery, has been elected a new Director of the American Board of Neurological Surgery.

William R. Platt, M.D., FHS in pathology, has been appointed a lecturer in pathology at Johns Hopkins University School of Medicine. He is working on the third edition of Color Atlas and Textbook of Hematology, published by Williams and Wilkens.

IN MEMORIAM

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Joseph C. Jaudon, M.D. '33, clinical professor emeritus of pediatrics at Washington University School of Medicine, died April 15, 1988.
Julius K. Neils, M.D. '43D
Daniel F. Sullivan, M.D. '43D
Image processing produced this image of the endings (yellow spots) on a nerve cell. See story on page 12.
Tree-clinging bromeliads collect water from jungle showers in a cup formed from overlapping leaves. See story on page 16 to see how Leonard Kent, M.D. '43, is promoting bromeliads as "ideal house plants."