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# OUTLOOK



**Battle of Nerves**





*Construction workers put the finishing touches on the new Library and Biomedical Communications Center. Readers will get a closer look at the new library in a future issue.*

# OUTLOOK

Volume XXVI, Number 3 Fall 1989

**Executive Director,  
Medical Public Affairs**  
Glenda King Wiman

**Executive Editor**  
Don Clayton

**Editor**  
Kathy Heine

**Design**  
Jean Lopez

**Photography**  
Tom Heine

**Circulation**  
Barbara Hebrank

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School of Medicine



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### **On the Cover:**

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Studies of nerve cell competition yield new insights into the formation of connections with muscle and processes like memory.

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## Institute of Medicine elects two medical school faculty members

**T**wo faculty members have been elected members of the prestigious Institute of Medicine of the National Academy of Sciences.

Drs. Harvey R. Colten and C. Robert Cloninger are two of 40 new members of the institute, which was created in 1970 to examine public health policy matters. New members are chosen by currently active members for major contributions to health and medicine or to related fields, among them social and behavioral sciences, law, administration, and engineering.



*C. Robert Cloninger, M.D.*



*Harvey Colten, M.D.*

Terms for new members began this past July, bringing the organization's total membership to 332, 16 of whom are active faculty from the School of Medicine. Election to the institute is both an honor and an obligation to work on behalf of the organization, its governance and its studies. Members make a commitment to devote a significant amount

of volunteer time on committees engaged in a broad range of studies on health policy issues. Current projects include a consortium approach to the development of drugs and vaccines against AIDS and an investigation of how the Medicare program—the nation's biggest payer for health services—can determine the quality of care received by Medicare patients.

Colten is Harriet B. Spoehrer Professor and head of the Department of Pediatrics. His research focuses on understanding the biochemistry, genetics and cell biology of inflammation in such disorders as cystic fibrosis, arthritis, asthma, juvenile diabetes, autoimmune diseases and inflammatory disorders of the intestinal tract. Using that knowledge, he attempts to find basic causes and define more specific forms of treatment for these disorders.

Colten has been head of the pediatrics department since

1986. He also serves as pediatrician-in-chief at Barnes, Children's and Jewish hospitals.

He came to St. Louis from Harvard Medical School, where he was professor of pediatrics as well as chief of the Division of Cell Biology and Director of the Cystic Fibrosis Program at Children's Hospital Medical Center in Boston.

Cloninger is professor of psychiatry and genetics, and head of the Department of Psychiatry. He is recognized worldwide for his work on the clinical assessment of personality and his adoption studies in Sweden.

Cloninger also has studied the classification and inheritance of many other psychiatric disorders, including schizophrenia, anxiety disorders, mood disorders and personality disorders. He is currently continuing his work on personality and several family and adoption studies. Also he is working with colleagues on molecular genetic research to locate linkage markers for specific genes related to susceptibility to alcoholism and schizophrenia. Cloninger joined the Washington University faculty in 1973, after serving a residency in psychiatry at the School of Medicine. ■

## Kao is named new director of gynecologic oncology division

**M**ing-Shian Kao, M.D., has been named director of the Division of Gynecologic Oncology in the Department of Obstetrics and Gynecology.

Kao succeeds H. Marvin Camel, M.D., who has stepped down as division director but will continue in his position as professor of obstetrics and gynecology.

Kao, professor of obstetrics and gynecology, has twice been named Teacher of the Year by former residents, and was given the First Annual Chief Residents' Award in 1983.

He joined Washington University in 1971 as an instructor in obstetrics and gynecology, after serving a four-year residency at Barnes Hospital, and was named professor in 1986. He also is on staff at

Barnes, Jewish and Children's hospitals.

Before joining Washington University, Kao served an internship and residency in general surgery at the National Taiwan University Hospital, and an internship at Methodist Hospital of Central Illinois in Peoria. He also served as a clinical fellow in gynecology at Queen's University in Kingston, Ontario.

Kao received his medical degree from the National Taiwan University Faculty of Medicine in 1961. He is a fellow of both the Royal College of Surgeons of Canada and the American College of Obstetricians and Gynecologists and a diplomate of the American Board of Obstetrics and Gynecology and its subspecialty of gynecologic oncology. ■



## “Old Age” could be Alzheimer’s

Even a slight decline in everyday functioning due to mental changes may be a sign of early Alzheimer’s disease, say researchers at the School of Medicine. Although occasional memory lapses often are perfectly acceptable for elderly people, more widespread change—even when subtle—is not necessarily an inevitable result of the normal aging process.

Autopsy studies conducted at the School of Medicine have revealed evidence of fully developed Alzheimer’s in the brains of five elderly patients who had shown only mild or questionable symptoms of the disease. Before their deaths the patients, who ranged in age from 75 to 86 years old, had done so well on psychological tests measuring intellectual ability that doctors disagreed on the diagnoses: were the occasional memory lapses reported by close family members normal for their ages, or were they symptoms of early Alzheimer’s disease?

The results of these autopsies may mean that Alzheimer’s disease is present in the brain for years before clinically measurable symptoms show up, according to John C. Morris, M.D., assistant professor of neurology. “Therefore, minor mental deterioration that often is chalked up to old age actually may be a warning signal of Alzheimer’s disease,” he says. Morris is an investigator with the university’s Alzheimer’s Disease Research Center and the associate director of its Memory and Aging Project, a long-term study of intellectual function in older adults.

“These findings also underscore the need to refine the diagnostic tools that are used to detect Alzheimer’s—tools which, while extremely effective at detecting advanced stages of the disease, may be inadequate when it comes to pinpointing early dementia. And early detection is vital because, although there is no effective treatment for Alzheimer’s disease at the present time, theoretically treatment



John Morris, M.D., interviews an Alzheimer’s patient.

would be most beneficial during the initial stages of the disease.”

Until recently, it has been commonly accepted that the tangled nerve cell fibers and deposits of degenerated nerve cell endings found in the brains of Alzheimer’s patients could also occur in lesser amounts in healthy, non-demented individuals—in other words, that a certain amount of brain damage occurs during the course of normal aging. Thus, a certain amount of forgetfulness and disorientation has been tolerated as part of the aging process.

That may not be true, says Morris. “This latest evidence from our control subjects suggests that it’s possible to live to a very old age with no sign of Alzheimer’s disease and with correspondingly maintained levels of intellectual performance,” he says. “There are differences between the normal aging process and senile dementia of the Alzheimer’s type (SDAT), and we believe that Alzheimer’s disease is not an inevitable part of aging.”

It’s important to understand the differences between the

they are gathering information on Alzheimer’s disease but are actually observing another disease.”

Beyond problems with diagnosis, Morris says, it’s important that investigators learn where normal aging ends and SDAT begins. “What is it that causes some people to remain vital while others develop SDAT?” asks Morris. The answer to that question, he says, may be a key to preventing the disease. ■

## New PT degree

The Program in Physical Therapy at the School of Medicine is now offering a doctoral program.

Designed to prepare researchers in movement science, the doctoral program is directed by Shirley Sahrman, Ph.D., associate professor of physical therapy, neurology and neurological surgery, and instructor of cell biology and physiology.

It is anticipated that applicants will come from a variety of disciplines, including physical therapy, engineering, biology and medicine. Participants in the program will receive instruction from an interdisciplinary faculty with research expertise in motor systems, vestibular systems, exercise physiology, aging and psychology.

The curriculum consists of coursework and laboratory experience in biocontrol, biomechanics and bioenergetics, and students will select one of these areas for their dissertation research. ■

normal aging process and Alzheimer’s disease, Morris comments. Many diseases or conditions can cause symptoms in older adults similar to those caused by SDAT, including Parkinson’s disease, Pick’s disease, stroke, depression and over-medication, and it is necessary to distinguish these illnesses from SDAT.

“SDAT may be overlooked or incorrectly diagnosed as much as 40 percent of the time,” says Morris. “Misdiagnosis may not only prevent people from getting the treatment they need for other conditions, but also frustrates the efforts of researchers who think



## Two become fellows of American Academy of Arts and Sciences

Two faculty members have been elected 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 William H. Daughaday, M.D., lecturer in medicine and Irene and Michael Karl Professor of Medicine emeritus; and Emil R. Unanue, M.D., Edward Mallinckrodt Professor and head of the Department of Pathology.



*Emil Unanue, M.D.*

Daughaday, an internationally acclaimed endocrinologist who directed the metabolism division for 35 years, was elected in recognition of his research on basic hormonal action, specifically that of growth hormone. He discovered that the action of growth hormone in stimulating growth is regulated by plasma factors called somatomedins and developed methods for measuring very small amounts of somatomedin in plasma as an index of growth hormone activity. These methods proved useful

in diagnosing disorders of human growth, such as dwarfism and acromegaly, creating a new branch of endocrinology.

Also known for his research on adrenal steroid transport and diabetes mellitus, Daughaday joined the Washington University faculty in 1947 and directed the metabolism division from 1951 to 1986. He served as director of the Diabetes Research and Training Center at the medical school until 1988 and is on staff at Barnes and Jewish hospitals. He graduated from Harvard Medical School in 1943 and served his internship at Boston City Hospital in Massachusetts.

Unanue is an immunopathologist who has centered his research on the interactions among immune system cells. He has been instrumental in showing the critical role played by macrophages, cells that activate the body's immune response to foreign invaders. Macrophages ingest and destroy foreign substances and also stimulate the production of specific white blood cells that attack invaders. Macrophage interactions with other immune system cells are important in organ transplants and in the body's response to many disease states, especially infection and cancer. Unanue and his associates have identified how proteins are handled by the macrophages as well as the function of histocompatibility molecules.

Unanue has been head of the School of Medicine's pathology department since 1985. He also serves as pathologist-in-



*William Daughaday, M.D.*

chief at Barnes and Children's hospitals. He came to St. Louis from Harvard Medical School, where he had been a faculty member since 1970 and Mallinckrodt Professor of Immunopathology since 1974. He received the doctor of medicine degree in 1960 from the University of Havana School of Medicine and served an internship in pathology at Presbyterian University Hospital in Pittsburgh. ■

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## NAS chooses medical school neurobiologist

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Dale Purves, M.D., professor of neurobiology, has been elected to the National Academy of Sciences.

Purves is among 60 new members selected for distinguished and continuing achievements in original research. Election to the academy, which now has 1,601 members, is one of the scientific community's most prestigious honors.

Purves is being recognized for his studies of the autonomic nervous system, nerve cells outside the brain or spinal cord that control such vital functions as breathing, heart rate and intestinal contractions. His work focuses on the formation and maintenance of synapses, the connections between nerve cells that transmit signals from one nerve cell to another. More recently, he and his colleagues have used digital-imaging techniques to map connections in mice, both in the autonomic nervous system and the brain, to study synaptic changes over time. The ultimate goal of this work is to learn more about memory—how the human nervous system stores information.

Their work may help answer one of the most important questions in modern neurobiology: how the formation and malleability of synapses is related to the nervous system's remarkable adaptive abilities. The work also could increase understanding of diseases in which synaptic connections fail to form properly or degenerate prematurely.

Purves joined the Washington University faculty in 1973 as an assistant professor of physiology and biophysics. He was named a full professor in 1979. He is co-director of the School of Medicine's Senator Jacob Javits Center of Excellence in Neuroscience, created in 1985 with a \$3.4 million award from the National Institutes of Neurological Diseases and Stroke.

Last year Purves published his second book, "Body and Brain: A Trophic Theory of Neural Connections." The book, well received by the neuroscience community, explains interactions between the



nervous system and the changing bodies of developing and evolving animals. Purves also is co-author of a textbook on neural development and has published numerous articles on his research.

Since 1977, he has served as an instructor and organizer of several Cold Spring Harbor summer courses on developmental neurobiology and on structure and function of the synapse. He is a member of numerous professional organizations, including the American Association for the Advancement of Science, Society for Neuroscience and Society for General Physiologists, and



**Dale Purves, M.D.**

is co-editor of several scientific journals. He is presently editor-in-chief of the *Journal of Neuroscience*.

Purves has received other honors for his work, including the Camillo Golgi Award of the Fidia Research Foundation, the Grass Foundation's Alexander Forbes Lectureship and the Mathilde Soloway Award in Neuroscience. He has twice been named Teacher of the Year by Washington University medical students. ■

## Labs teach local science teachers

**W**hile their students were vacationing this past summer, five high school biology teachers were hard at work in laboratories at the School of Medicine, working on projects that ultimately should benefit their students and quite possibly could improve the future of biomedical research.

The teachers, all from St. Louis, participated in a pilot research project designed to introduce and attract students to the biomedical sciences. For one month they worked as active partners in immunology labs at the School of Medicine and Jewish Hospital. Each then developed an instructional activity for their classrooms.

Carl Pierce, M.D., Ph.D., and Judith Kapp-Pierce, Ph.D., both professors of pathology and molecular microbiology, coordinated the project. Together they co-chair the education committee of the American Association of Immunologists (AAI), which sponsored the program along with the Biological Sciences Curriculum Study (BSCS), a national organization that researches and develops innovative instructional materials for science education.

Teachers shared their experiences and sent drafts of their lesson plans to BSCS for evaluation and review. Revisions will be made based on the response of students to the lesson, and, if successful, BSCS will make the final lesson plan available to high school biology teachers nationwide.

"The education committee of the AAI has been concerned

about the steady decrease in the number of people who are applying for graduate education in immunology and the biomedical sciences as a whole," says Pierce. "We thought one way to address the problem is to get people in high school interested in immunology."

Rather than bring high school students into the labs,

exciting field, but I think it is. There aren't many jobs that pay you to sit around and think, to solve puzzles and mysteries. That's where these teachers can help."

Barbara Herbst, a teacher from Ursuline Academy, worked in the Pierces' lab, one of five participating labs. Her project involved studying how different types of T-cells originate. T-cells play a major role in protecting the body from foreign agents and are the main



**Visiting teacher Barbara Herbst uses a flow cytometer to observe cell-surface markers on T-cells.**

where the impact is only on one person, the committee chose to bring in high school teachers because they can influence many students for years to come.

Outside of the family, school plays a major role in helping students decide on careers, points out Kapp-Pierce. She herself was influenced to choose biomedical science by two high school teachers.

"There are no real live role models of scientists for students to look at unless their parents are scientists. We're not visible," she says. "It certainly isn't thought of as an

target of the AIDS virus, which she says will be a point of interest for her students.

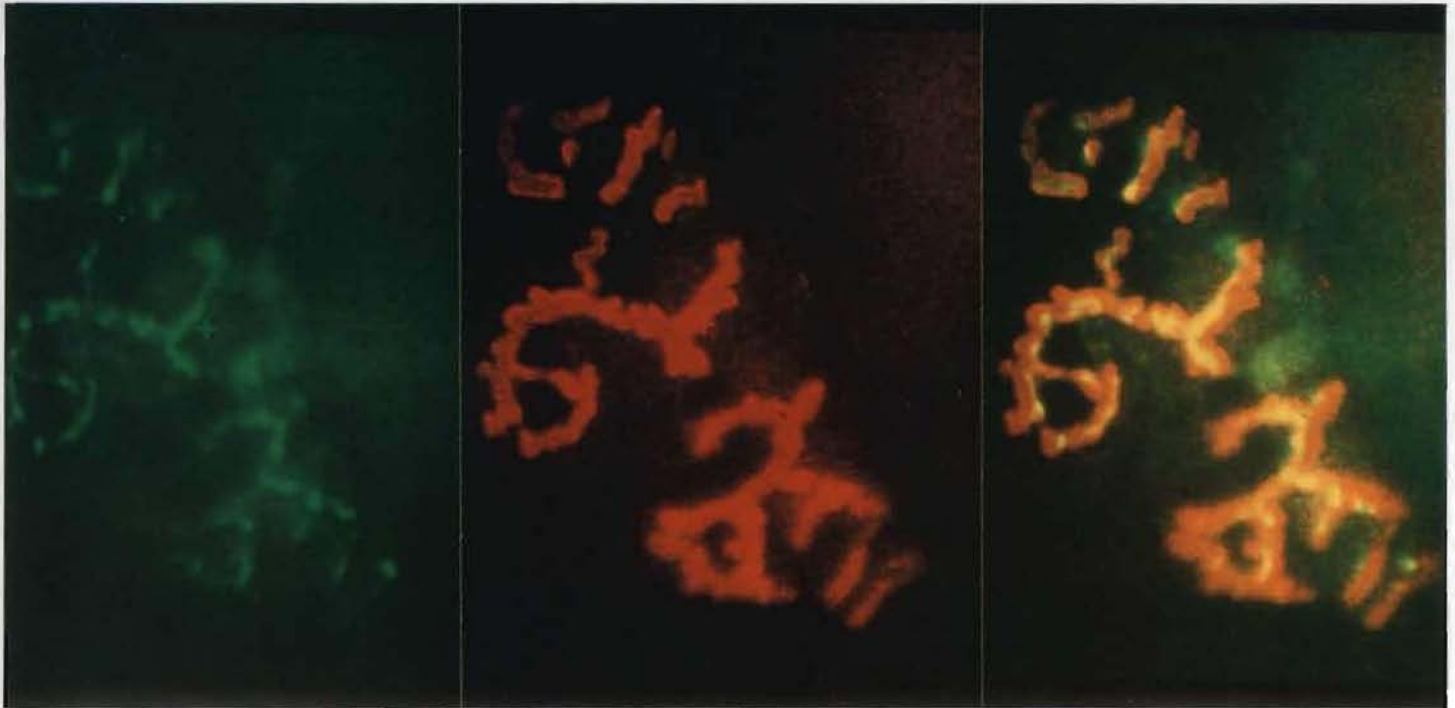
"My impression after the first day was, 'Wow! We're going to do all this. I'm going to learn all this.' By the end of the week, one of the professors told me I'd learned in four days what normally takes four years," Herbst said. "I took an immunology course, but now I'm actually doing things I read about. I think it's exciting, and I hope to go back to the classroom and get the students fired up about it." ■



# A BATTLE OF NERVES

*Competition between nerve  
cells yields clues  
about memory*

*By Steve Kohler*



*Receptors stained with bungarotoxin (red) and nerve stained with 4-Di-2-Asp (green) reveal how precisely nerve terminals align themselves with muscle. The yellow figure shows nerve terminals together with their receptors.*

**O**f all the mind's capabilities, memory may be the most remarkable. Somehow, each of us can recall thousands of details—from a social security number or the face of a favorite teacher to the quickest route home. Yet next to nothing is known about the biological process by which memory occurs.

However, neurobiologists at the School of Medicine have witnessed a process that displays characteristics tantalizingly similar to what we call memory. In studies with mice, they have been the first to observe a short-term reorganization in the nervous system that has life-long consequences, in much the same way that a short-term event like seeing a face just once can lead to lasting recognition.

The researchers have developed methods that enable them to study changes over time in nerve connections, called synapses. The work, reported in the May 1989 edition of the *Journal of Neuroscience*, provides surprising information about a basic nervous system process.

"In order to remember, the nervous system must somehow be able to change the structure and function of its connection," says principal investigator Jeff W. Lichtman, M.D., Ph.D., who conducts research on neuromuscular synapses in living mice. Though muscles are not involved in memory, the changes seen at junctions of nerve

and muscle "may be indicative of how nervous system changes occur more universally," Lichtman says. The neuromuscular synapse is both accessible and large enough to be studied.

For 20 years, neurobiologists have known that at a mammal's birth and for several weeks thereafter, some muscle fibers are innervated, or stimulated, by two or more nerve fibers. At maturity, however, all of the muscle fibers are innervated by only one nerve fiber. This change from multiple to single innervation—a process called synapse elimination—occurs, but there has been no way to see it happen.

Scientists have been restricted to viewing a synapse only once, since a laboratory animal has to be sacrificed in order to get a single, reliable look at the connection.

Lichtman, an associate professor of anatomy and neurobiology, offers an analogy: "Imagine trying to understand the rules and strategy of football but being allowed to see only one second-long bit of play from each game you watched. You might see the kick-off, a tackle and a penalty, but you could never understand the rules or even the objective of the game." Despite the difficulties, he says, synapse elimination has remained a particularly enticing process to learn about because, like memory, it occurs postnatally, changing neural connections while the environment is capable of having an effect.

To overcome logistical problems, Lichtman and his collaborators have devised methods for watching and recording the changes in the connection between nerve and muscle over time. They have been able to check the same synaptic junction as frequently as every day and as many as 18 times over the life of the same mouse. As a result, they have described an unexpected process.

### Surprise at the synapse

**T**he synapse consists of two major parts. On one side of the junction is the presynaptic cell, or neuron, with its long, tentacle-like axon reaching out to its target. On the other side is the postsynaptic target cell—in this case, a muscle fiber. (Target cells also can be other neurons or brain cells, depending upon where in the nervous system they lie and what their function is.)

When a neuron sends an electrical pulse down its axon, a chemical neurotransmitter is released at the nerve terminal. That chemical is sensed by receptors concentrated on the membrane of the target cell. Receptor activation instigates the appropriate action; in this case, it is muscle contraction. The area where the synapse lies and the receptors group on the muscle cell is called an endplate.



Traditionally, the nerve terminal has been considered the only dynamic part of the synapse, says Mark M. Rich, M.D., Ph.D., a member of the research team. And, he adds, the belief has been that multiple axons competed directly for limited territory on an endplate. "The thinking was that one nerve pushed the other away or somehow poisoned it and took over the receptors it had occupied, or that the loser pulled back and left the receptors vacant," Rich explains.

The latest investigations have revealed a different process. To temporarily denervate the sternomastoid muscle in the neck of a mouse, the nerve was surgically exposed, then crushed. The Washington University neurobiologists then watched as the nerves regrew. Sometimes, a muscle fiber was reached by more than one axon. The subsequent synapse elimination was the contest the scientists observed most closely.

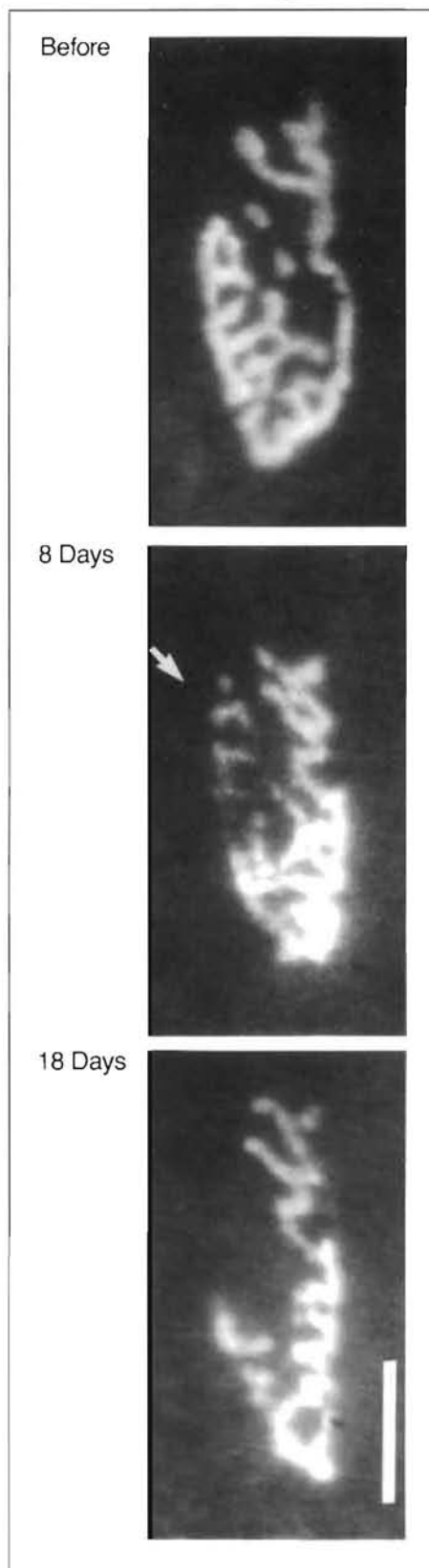
In one group of 107 mice, the nerves were exposed surgically and crushed twice. Nine days later, 22 percent of the muscle fibers showed more than one nerve connection. After six more days, only 4 percent still displayed double connections. Multiple synapses were forming, then being eliminated.

Photomicrographs showed graphically that the same endplates on the muscle were reoccupied by the nerves that regrew, whether that was one nerve or two. Patterns of receptors were observed on the muscle before the nerve crush and then during that period when no nerves reached them. As the nerves reconnected, they were seen to precisely reoccupy the same receptor areas.

But in cases of multiple reinnervation and subsequent synapse elimination, a strange thing occurred. As the competition between nerves went on and one nerve withdrew, not only areas of nerve were seen to be missing. Receptors from beneath the losing nerve also disappeared. "Something about reinnervation and competition caused permanent change in both receptors and nerves," says Rich. Only those receptors initially occupied by the winning nerve eventually remained; receptors beneath the losing nerve faded away.

A closer look revealed that the receptors on the target cells began to recede even before the losing nerve started to withdraw. "There is an elimination of receptors, apparently either a migrating or a pulling away, and it starts before the withdrawal of the nerve that will eventually lose," says Rich.

By returning to view the identical synapse in the same mouse many times, the investigators showed that once the receptors



*During synaptic competition of nerve cells for muscle, some receptors start to fade away (see arrow). By day 18, they have completely disappeared.*

leave a site from which a losing nerve retracts, that part of the endplate remains permanently denervated. Their photos depict clearly that after the initial competition is resolved, the form of the synapse then remains stable for several months.

"No one had anticipated such a major role for the postsynaptic cell," says Rich. Indeed, in commenting on the work, David Van Essen, Ph.D., a professor in the division of biology at California Institute of Technology, calls the findings "surprising." He says, "When one nerve is withdrawn, it's clear now that another doesn't move in and take over. That puts quite a different light on the subject. Years ago, I predicted that direct competition for space might be important in understanding synapse elimination. Now the mechanism appears to involve more indirect competition for something provided by the target cell." Van Essen adds that the work "is a major step in understanding the plasticity and changes in structure that will ultimately lead to an understanding of memory."

If presynaptic nerve cells are in competition for some product of the postsynaptic target cells, what might the substance be? No one knows, Rich says. He speculates that perhaps the nerve terminal releases not just its neurotransmitter, but another molecule as well, one that can somehow be split by the receptor. One fragment might then be returned to the presynaptic cell as a signal that its messages are getting through and that it is being effective. This scenario would make receptors vital in the maintenance of synaptic connections as well. But that is the subject for studies being planned and "pure speculation," Rich says.

More certain is that the reinnervation process in adults closely mimics the changes that normally occur in the developing nervous system of newborn mammals. Says Rita Balice-Gordon, Ph.D., a research associate in Lichtman's lab who has studied the "life-history" of a synapse using neonatal animals about one-tenth the size of the adults, "The similarities are striking."

### Creating a visible synapse

**T**hese repeated observations in living animals were made possible by three advances. Lichtman and co-investigators found fluorescent dyes that selectively stain nerve terminals and axons. Another compound marks receptors on the muscle fibers. Fluorescing in separate colors, the stains put colored jerseys on the players and allow them to be observed together. Balice-



Gordon has recently added to the scientific arsenal a stain that marks only the membrane of nerve endings, making it possible to see the outlines of axons and thereby eliminate any question of origin. Another type of stain allows several axons innervating the same muscle fiber to be labeled different colors, facilitating the study of how they intertwine even as synapse elimination occurs. The fluorescent quality of the dyes has also been important to the work because it allows illumination from above, critical when an entire living mouse is on the microscope's stage.

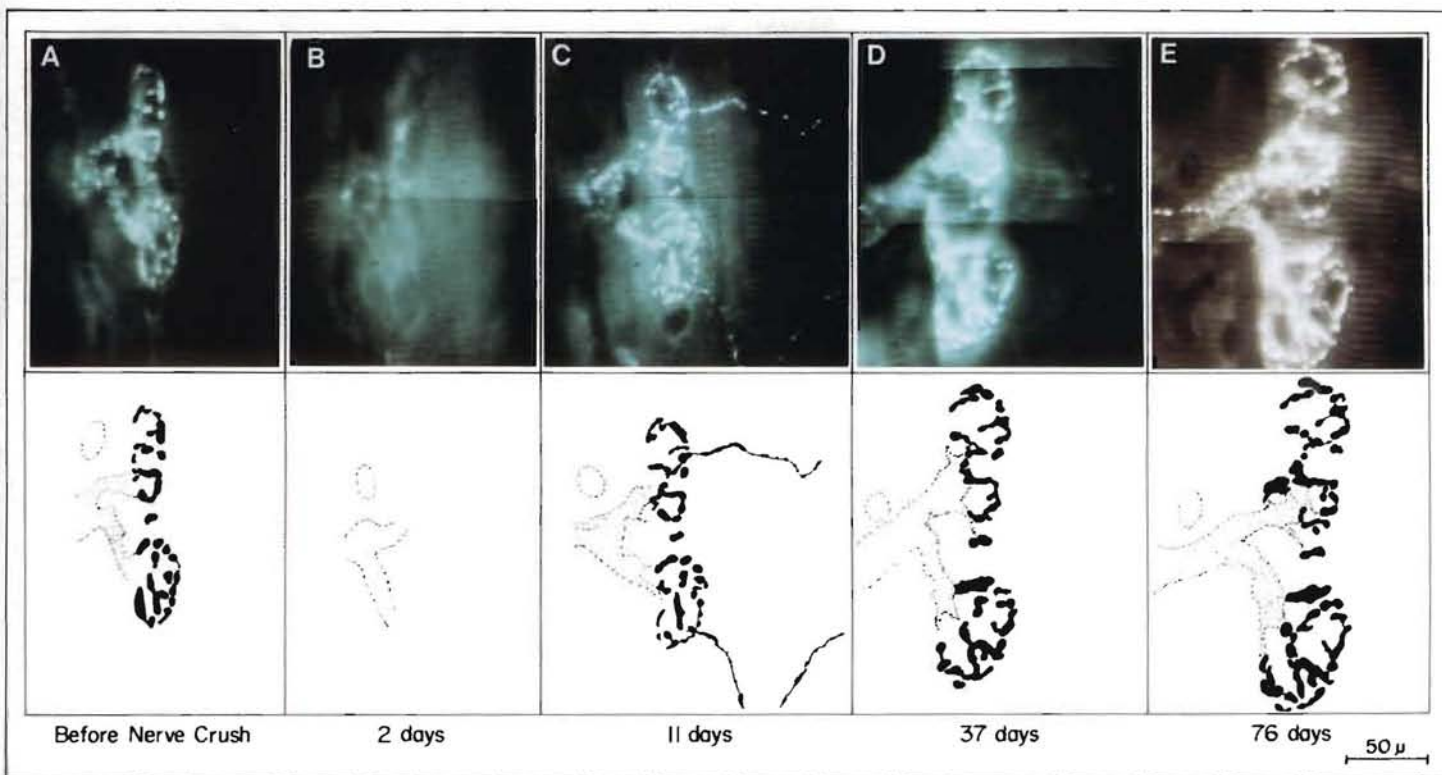
it. Learning to look at the synapse without changing it took a year."

To guarantee the validity of their experiments, the neurobiologists performed extraordinary controls. They showed first that if they operated on control animals without crushing the nerves, no changes in synapse configuration occurred.

In synapses that experienced only single reinnervations, no loss of receptors or nerves could be seen; reoccupation of the receptor sites was precise, complete and remained stable when re-examined over a period of weeks.

## Change and its role in the nervous system

**N**one of the members of the Washington University team is yet prepared to put forth the observation of a short-term nervous system reorganization with lasting consequences as a model for memory. Lichtman acknowledges that the neuromuscular synapse is uncomplicated compared to those of the central nervous system, where many axons reach each tar-



*During reinnervation of muscle in a living mouse, the nerve axon, after crushing, grows back in exactly the same spot.*

The second advance involves reducing the light required to a level low enough to avoid damaging delicate nerve tissues. To make visualization possible, the researchers employ a sensitive Silicon Intensified Target (SIT) camera. Complementing the SIT camera are digital image-enhancement techniques, products of the space program, to increase the clarity of the images.

Finally, Lichtman and his mentor, university neuroscientist Dale Purves, had to modify a microscope that accommodated a live mouse on its stage, complete with a provision for anesthesia to be administered to the animal. Describing the need for the special instrument, Rich says, "You may damage the living system just by observing

Further, the published studies show that permanently denervated muscles atrophy, but they do not lose receptor areas. In 11 endplates permanently deprived of their synapses, no receptor regions were lost, evidence that the nerve must be present for the changes to occur.

By re-examining the synapses not just twice but from five to 18 times, the researchers also controlled for subtle changes that might have been introduced by minor differences in technique, stretching of the tissue, or inconsistency in staining. "If receptors disappear or migrate and the nerve withdraws, then that change should be cumulative and progressive," says Rich. The team's serial photomicrographs reflect such a progression.

get cell and where temporal and spatial differences may have effects.

"Our knowledge is still too fundamental to say that with authority," adds Rich. "But whether the changes we've seen are descriptive of a memory system or not, researchers now must carefully consider the role of the receptor in any study of change in the nervous system."

Lichtman points out that although the team's example of synapse elimination identifies one process of change within the nervous system, and memory, too, requires change. "There is much to be done. The mystery of how memory works is what continues to drive most of neurobiology." ■



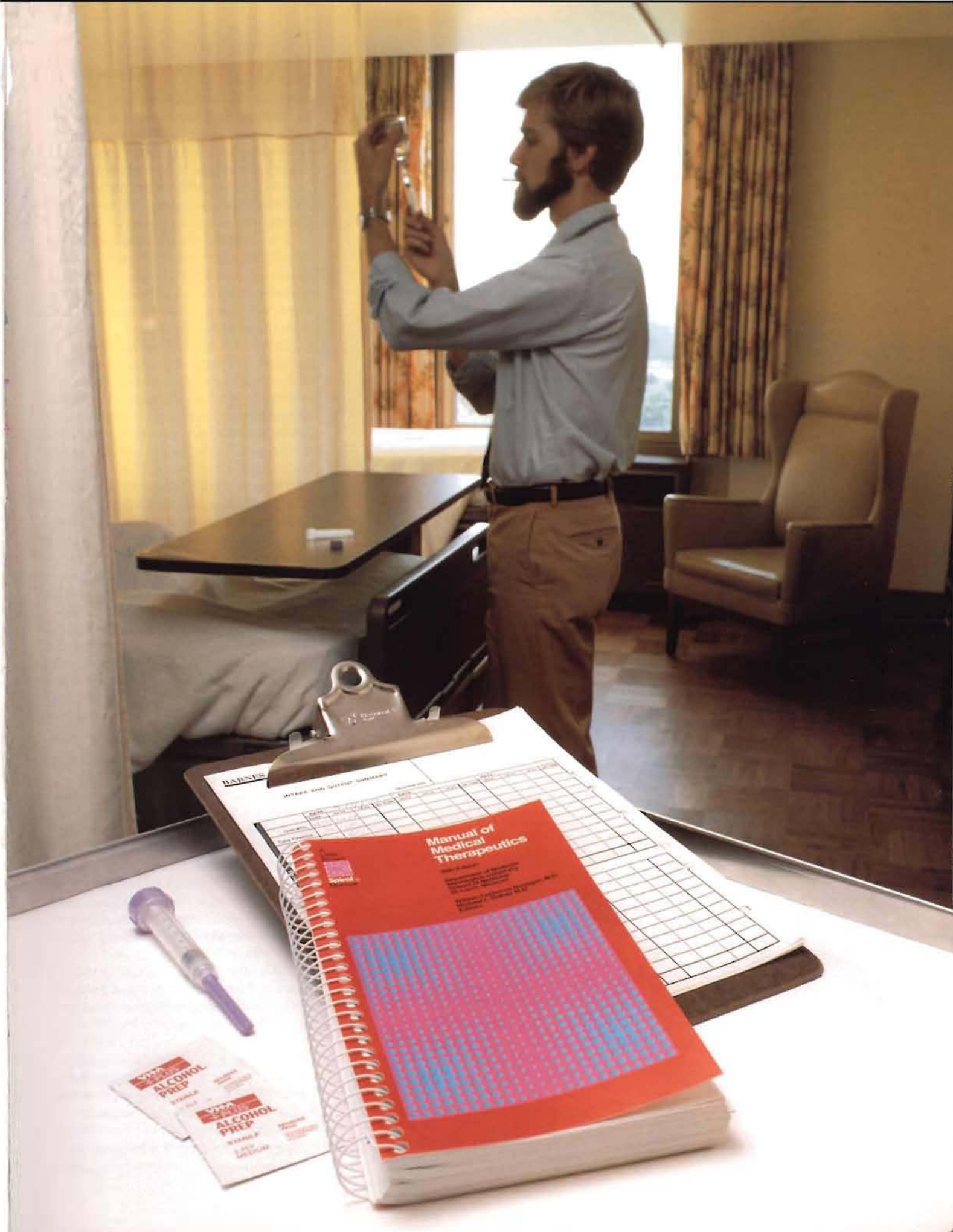
# M

# *edical Intern's Bible*

BY TONY DIMARTINO

*I*t was a quiet night in the Coronary Care Unit, and Michael Ridner hoped it would stay that way. This was his first week in the CCU. Most of the senior staff had gone off duty at 10 p.m., so he and the junior assistant resident were on their own.

No sooner had Ridner poured himself a cup of coffee than the calm was shattered by the urgent, drawn-out beep of a patient's heart monitor: The patient's heart rate had slowed to a dangerous degree, a condition called bradycardia.



BARNES

INTERIC DATA SYSTEM SUMMARY

### Manual of Medical Therapeutics

1981 Edition  
Authoritative and Comprehensive  
Reference for the Practitioner  
Authoritative and Comprehensive  
Reference for the Student  
Authoritative and Comprehensive  
Reference for the Researcher





"It was my first life-or-death emergency," Ridner recalls. "Four years of medical school training flashed before my eyes. I'd read about what to do, but I'd never had to actually do it! I knew what drug to give, but wasn't sure how much. That's when I reached for the Manual. I flipped to the section on arrhythmias and found dosage guidelines, delivery methods, possible toxicity—everything I needed to know. In seconds, the situation was under control."

**T**he Manual, as it's known at medical schools all over the world, is the Washington University Manual of Medical Therapeutics, a pocket-sized, spiral-bound review of the treatment of the most commonly encountered medical problems. Written by research fellows and junior faculty at

the School of Medicine, it's been published for 45 years, translated into 14 languages and is the most widely sold medical textbook in the world. The last edition sold more than a quarter of a million copies, and the new edition, published recently by Little, Brown and Company, is expected to do even better.

"It is, quite simply, the bible for interns and other health care practitioners," says Ridner, who served as co-editor of the new edition with William C. Dunagan, M.D., when the two were chief residents in the Department of Internal Medicine.

"Unlike conventional medical texts on the diagnosis and pathology of diseases, the Manual zeroes in on specific guidelines for medical therapy," says Dunagan. "Everything you need to know to make rational, safe treatment decisions is there, and you don't have to wade through an entire textbook to find it."

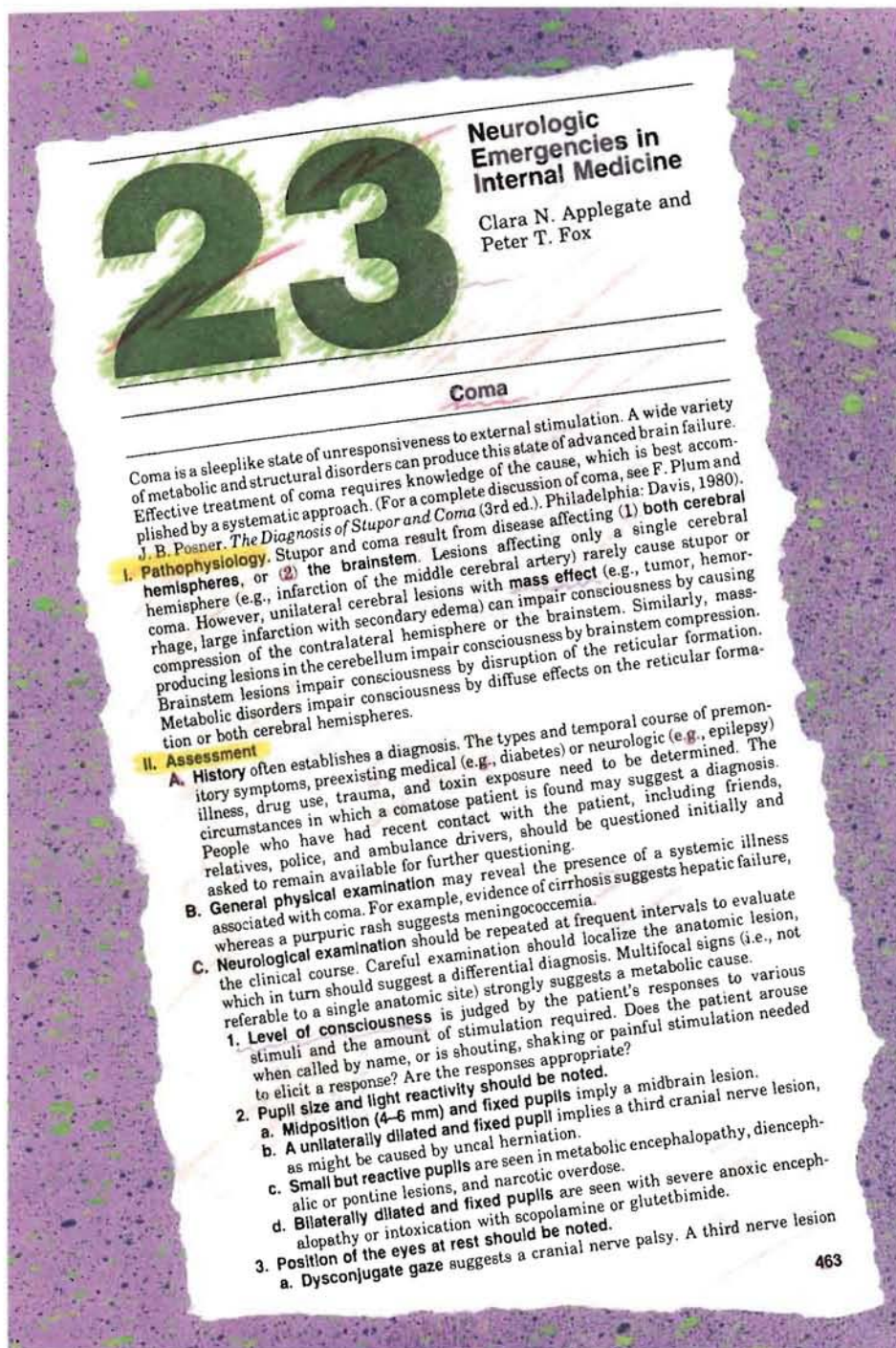
Written in outline format, the Manual's boldface headings, concise entries, and charts and tables are easy to find and read. Many of its 24 chapters focus on a specific area of internal medicine, such as hypertension, diabetes, and diseases of the heart, lungs, liver and kidneys. Other chapters, on general patient care and emergency medicine, deal with everything from fever and pain to drug overdoses and heat stroke.

**T**he Manual wasn't always as comprehensive as it is now.

"When I co-edited the first Manual back in 1943, it was just a sheaf of notes used by the residents during weekly teaching sessions for the house staff," says Lewellyn Sale Jr., M.D., now an associate professor of medicine at Washington University. "You couldn't even call it an outline. It was more like a list of topics, with minimal explanation—not very thorough, compared with today's Manual."

Another former editor agrees. "I co-edited the Manual in 1958, when it was 60 or 70 mimeographed pages that focused on maybe 16 diseases," says Charles W. Parker, M.D., professor of medicine and microbiology and immunology. "In those days, the whole thing was written by the incoming and outgoing residents. Some of the information was helpful, but overall it was sketchy, limited."

By Parker's day, the Manual had moved from the classroom to the ward floor. Third-





and fourth-year medical students consulted it frequently, often memorizing chapters, and brought it with them when they served residencies at other hospitals. Word got around. Other hospitals and teaching institutions started ordering the Manual from Washington University until the School of Medicine was distributing thousands of copies per year.

In the early 1960s, an enterprising manager from the medical textbooks division of Little, Brown persuaded School of Medicine officials to let his company take on the time-consuming task of publishing the Manual.

Robert Packman, M.D., was a co-editor of the first two Little, Brown editions of the Manual. "Even before we signed up with Little, Brown, we'd reduced the Manual's size, rewritten existing chapters, and added several chapters and an index," says Packman, who is now a professor of medicine at Washington University. "We took what was basically an 8½-by-11-inch annotated bibliography and turned it into a pocket-sized primer on the treatment of disease."

With national distribution came record-breaking sales. "The first Little, Brown edition in 1964 sold 10,000 copies right off the bat," says Packman. "The next edition sold 25,000 copies as soon as it hit the shelves, and went into reprintings. Since then, a revised edition has come out every three years, each one outselling its predecessor. The Manual had become an institution."

**T**he new edition is packed with information that had yet to be discovered 10 years ago, when Dunagan and Ridner were medical students, or even three years ago, when the last Manual was published. "Today, there are new diseases and new drugs, technologies and methods for treating both old and new diseases," says Dunagan.

These changes have been especially dramatic in the areas in which Dunagan and Ridner specialize, infectious and cardiovascular diseases.

"There's a whole new wave of antimicrobial drugs to treat infections," says Dunagan, who helped write the chapter on infectious diseases in the current edition. "Furthermore, we know much more about AIDS than we did three years ago. We have a better grasp on how to recognize and

manage complications that result from HIV infections."

Ridner wrote a new chapter on ischemic heart disease for the latest edition and says that other chapters about the heart had to be rewritten from scratch. "The diagnosis and management of heart disease has changed phenomenally. When I was in med school, there wasn't much we could do if somebody had a heart attack but send them to bed and hope for the best. Today, we can intervene with treatment ranging from

"It was my first  
life-or-death emergency,"  
Ridner recalls. "Four  
years of medical school  
training flashed before  
my eyes. I'd read about  
what to do, but I'd never  
had to actually do it! I  
knew what drug to give,  
but wasn't sure how  
much. That's when I  
reached for the Manual."

thrombolytic therapy to angioplasty to transplantation."

Dunagan, Ridner and their contemporaries have made every effort to ensure that the Manual keeps pace with rapidly expanding medical knowledge. But recent editions of the Manual may be too informative, some previous editors say.

"It's a bit unwieldy these days," comments Sale. "With so many facts cramming the pages, it's hard to find what you need in a hurry."

Packman agrees. "The type keeps getting smaller, and the Manual keeps getting thicker—the new edition is more than 500 pages. What's the point of a pocket manual if it no longer fits into your pocket?"

**A**nother former editor, Mark Frisse, M.D., may have the solution. Frisse, recently chosen as permanent managing editor of the Manual, is also on Little, Brown's editorial board for electronic publications.

"As medicine becomes more complex, it's our task to reflect that complexity and still retain the Manual's straightforward simplicity," says Frisse. With that goal in mind, Frisse and his colleagues in Washington University's Medical Informatics Group are working on a computer version of the Manual.

"Within a couple of years, health care practitioners will be able to call up the information they need on bedside computers," Frisse predicts. "Eventually, they'll be able to access not only the Manual, but also information from their notes and other textbooks."

Until then, the spiral-bound Manual will continue to be seen in coat pockets at medical schools and teaching hospitals throughout the world.

"I relied on the Manual throughout my internship," says Marc Goldberg, M.D., who attended Duke University School of Medicine. "I used it countless times on a day-to-day basis, especially when I was trying to figure out the right dosage for medications."

Packman recalls a trip he took to Israel in 1969. "I visited a field hospital in the middle of the Sinai desert, just a little Quonset hut with a dirt floor. I introduced myself to an Israeli who worked there, a young man who could barely speak English. He ran into the hut, and came out with a big smile on his face, waving a copy of the Manual."

The Manual gets fan mail from rural physicians who are isolated from major medical centers and up-to-date medical libraries. "We also hear from medical personnel in Third World and Iron Curtain countries," adds Ridner.

"In one form or another, the Manual will be around for a long time," says Ridner. "It's been honed and refined throughout the years to meet the needs of interns who are wondering, 'What the heck do I do now?' If you're looking for an in-depth analysis of the pathology of a disease, go to a conventional textbook. But for taking care of patients at 3 a.m. when there's nobody else around, the Manual can't be beat." ■







# Free Breathing

BY STEVE KOHLER

*F*or 17 years — two-thirds of her life — Cathy Goforth thought of herself as sickly and frail. Her physical limitations were so severe she knew, before trying, that she would fail at the simplest activity. Often, she lacked the breath to cross a room; her heart sometimes pounded wildly; occasionally she fainted without apparent cause.

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*Cathy Goforth works in her vegetable garden with her daughter, Kelly. Before radiologists corrected a dangerous abnormality in her lungs, Goforth was too weak to garden or do other ordinary physical activities.*



After informed diagnosis and treatment with an intricate interventional radiology procedure available at only a few medical centers nationwide, Cathy now knows she is not a weakling. She possesses more energy than she's had since she was nine. Instead of worrying that she lacks the strength to lift her daughter, she often exhausts other family members by day's end. A habit of failure and inability is becoming a pattern of success.

The drastic changes in Cathy Goforth's capabilities are the result of doctors having found and corrected an "abnormality in the development of the blood vessels serving her lungs," explains Daniel Picus, M.D., assistant professor of radiology at Mallinckrodt Institute of Radiology. Using tiny balloons and coils placed inside the vessels with a catheter, Picus and members of his team embolized, or closed off, seven dangerous, direct communications between an artery and a vein in Cathy's lungs. No surgery was necessary, and Cathy Goforth—awake throughout the procedures—went home two days later.

The malformations of the vessels, known as PAVMs, for pulmonary arteriovenous malformations, that caused Cathy's biggest problems are only one manifestation of the genetically transmitted Osler-Weber-Rendu disease that is named for the three turn-of-the-century physicians who first identified

its symptoms. Those include small red spots on the skin from dilated vessels (telangiectasia), persistent nosebleeds, aneurysms in the vessels anywhere in the body, gastrointestinal bleeding and the PAVMs that often lead to more serious complications, such as brain abscess and even stroke.

A rare condition, Osler-Weber-Rendu affects perhaps 5,000 people in the United States, though its diagnosis is difficult, and many patients may go undetected. Others, like Cathy Goforth, may not be fully aware of its implications in their lives. Several members of Cathy's family have the disease, but it has taken different courses for them and does not include PAVMs. So while she was growing up, Cathy's shortness of breath and fainting spells were never explored for their cause.

Meanwhile, the malformations allowed blood to bypass her lungs. Without benefit of the re-oxygenation that is the lungs' job, Cathy was chronically low in blood oxygen. She gulped for air, but to no effect.

"People 20 feet away said they could hear me breathe. Sometimes strangers asked 'Do you always pant like that?'" Cathy says.

Worse, the growing communications between vein and artery also short-circuited the lungs' function as a filter. Blood clots that formed in other parts of her body and entered the bloodstream—an occurrence

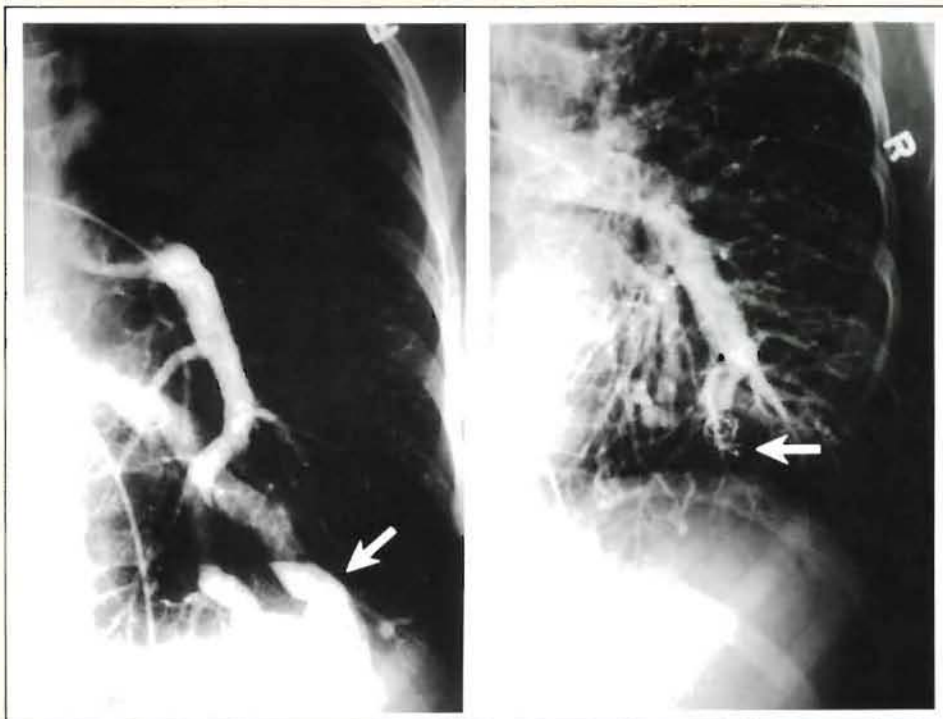
probably common in all of us—were free to bypass the lungs and travel until they lodged elsewhere. Most frightening was the possibility that such an embolus, or particle in the bloodstream, could block vital flow to the brain, resulting in a stroke. According to work done by Robert I. White, M.D., chairman of radiology at Yale University and pioneer of the technique to block the malformations, 36 percent of patients with PAVMs have already suffered one or more strokes at the time of their Osler-Weber-Rendu diagnosis.

Cathy's CT scan is happily free of any evidence of stroke. With her large malformations closed off and smaller ones now under close observation, the chance for future brain involvement approaches zero. She must be careful, however, to follow a strict regimen of antibiotics when having dental work done so bacteria that might enter her bloodstream don't escape the lung's filter, via the small malformations that remain, and cause a brain abscess.

Though it is unusual for Osler-Weber-Rendu's symptoms to appear before the age of 20, the disease is unpredictable; Cathy Goforth first began to have the characteristic recurrent nosebleeds when she was nine. The youngest of four children, she had seen similar bleeding in her father and two brothers.

That's a higher frequency than might be expected for a genetically transmitted disease that is classed as autosomal dominant, meaning that the genetic code for it is not on a sex-linked chromosome, and only one parent must contribute the gene in order for the disease to be expressed in offspring. Fifty percent of children born to couples in which one person has the disease can be expected to inherit. About 25 percent of the time, Osler-Weber-Rendu involves the life-threatening PAVMs that occur when a genetic defect somehow allows the body's veins and arteries to meet and communicate. Just one such malformation creates a risk of stroke and should be treated if possible, Picus says.

During her school days, Cathy could not participate in physical education classes and was soon labeled as "puny," she admits. Not until she married and became pregnant did the real basis for her infirmity become known. A bout with leg pains during her fourth month of pregnancy led her to the doctor and the eventual discovery of the PAVMs. Her Belleville, Illinois cardiologist first heard the rushing noise in her breathing. Later, through referrals, she found her way to Robert G. Kopitsky, M.D., an assistant professor of medicine in the cardiology division at Washington University.



*The X-ray on the left reveals a large pulmonary arteriovenous malformation connecting an artery and vein in Goforth's lung. Radiologists closed off this dangerous connection by placing tiny coils inside the vessels with a catheter, as seen in the X-ray on the right.*





**Daniel Picus, M.D., uses the screen pictured above to watch where he places the coils and balloons during a corrective procedure for PAVMs.**

Despite complications to the pregnancy that included pneumonia and an increasing strain on her heart, Cathy delivered a healthy daughter. Born six weeks prematurely, infant Kelly and her mother spent two weeks together in the hospital. Shortly thereafter, Cathy turned to Kopitsky, who diagnosed high output congestive heart failure, probably attributable to years of added burden on the heart as it pumped blood through abnormal connections. For assessment of the underlying problem, Kopitsky sought out Picus.

A practitioner of the burgeoning field of interventional radiology, in which physicians increasingly make delicate repairs inside the body without the need for surgery, Picus began with a test of blood gases. Results showed an arterial oxygen pressure of 71 millimeters of mercury. According to Daniel M. Goodenberger, M.D., assistant professor of medicine at the School of Medicine, the lowest normal level for a woman Cathy's age would be 82, and nearer 100 would be more common.

Chest X-rays and pulmonary arteriograms provided a detailed look at the vessels serving Cathy's lungs. Among the discoveries was one blood vessel that had enlarged from its normal 1.5 millimeter diameter (smaller than a pencil lead) to 14 or 15 millimeters (nearly the size of a grown man's thumb). Eight other PAVMs were also identified. "It's a wonder," says Picus, "that she avoided more serious complications, particularly stroke."

Using their radiologic map as a guide, physicians set out to shut off the PAVMs they'd found and let other, normal vessels carry blood to and from the lungs. Team

member M. Victoria Marx, M.D., describes the approach:

*We enter through the femoral vein in the patient's groin. The catheter goes up inside the large vein that returns blood to the heart, the inferior vena cava. Then right through the heart and into the pulmonary artery. We manipulate the tip of the catheter into the malformation, which can be difficult because it moves as the heart beats. It's good to have a team—not something I'd do alone.*

The radiologists then disconnect the catheter and leave behind either a balloon that they inflate just upstream of the offending junction between artery and vein or, alternatively, a coil of plastic that causes the target vessel to shrink around it. Picus says the balloons are his preference because they lock in place immediately, but they work only on vessels up to about eight millimeters in diameter. The slight risk in either case is that the implanted obstruction might float loose and travel. Care must be taken to place the payloads precisely and choose their sizes well.

In any event, the radiologists administer only a mild relaxant and local anesthesia for the small incision into the vessel. Cathy Goforth talked with her doctors throughout the procedures, reporting her sensations and asking questions.

Over three days, Picus closed seven of the nine PAVMs he had identified in Cathy's lungs. The biggest was embolized first, and her blood oxygen level jumped to 89 almost immediately. Two more sessions were necessary to embolize the other six.

But when they all were closed off successfully, her blood oxygen reached 98, close to ideal. Very little blood circulated without passing through her lungs.

Two remaining PAVMs were too small to embolize, Marx says, because they simply could not be approached. A third tiny malformation was discovered later. Monitoring of Cathy's condition will continue because PAVMs are known to grow slowly, approximately doubling in size over 20 years.

Two days after the therapy, Cathy Goforth went home with some lung pain and a stable blood oxygen level. Though she developed the pleurisy, an inflammation of the membrane around the lungs, that is a complication of the procedure for about 10 percent of its patients, this discomfort was far more bearable than what she would have experienced following chest surgery.

In fact, Goodenberger and Marx agree, she was not a candidate for surgery. "Too much of her lungs would have been cut away; she would have been made a permanent pulmonary cripple," says Marx. Without the interventional procedure, Cathy's only choice would have been the continued gamble of living with short-circuits of the lung. Goodenberger, who screens family members of newly identified Osler-Weber-Rendu patients, highly recommends the embolization therapy: "Compared to the morbidity and mortality of major surgery, it's clearly the right thing to do."

And he believes it should be offered only at a few major centers where the expertise is available and experience can be built upon. Right now, only Yale, Johns Hopkins and Washington University School of Medicine are known to be providing embolization for patients with PAVMs.

Cathy Goforth will require biannual checks of her blood oxygen level; should it ever drop by 10 percent, further therapy may be required. Otherwise, a patient in her position can be active to her ability, says White, who has reported the successful treatment of 276 PAVMs in 76 patients.

For Cathy, having found the breath to match her ambitions has been a godsend. Since her January treatment she's gained 12 pounds, and her vegetable garden, which she says "always used to get ahead of me," was productive and weed-free for the first time this past summer. Two-year-old Kelly, who'll be screened when the time comes, rides comfortably on her mom's hip. With cautious optimism, Cathy Goforth is energetically entering a new epoch, free of the debilitating effects and silent threat of her disease. ■



## Debt of gratitude

### *Alumni scholarships take the pressure off debt-laden medical students*

by Robert Lowes

**T**oday, fourth-year medical student Tom Vendegna isn't thinking about the \$61,500 in student loans he must start paying back when he earns an M.D. in 1990. He's worried about his patient in Room 9424.

The 86-year-old woman there is struggling with heart disease, high blood pressure and a host of other ailments. Plus, she has a history of stroke and breast cancer. Vendegna, working on the internal medicine service at Washington University Medical Center, realizes that the long-term outlook for his patient isn't promising.

"Hang in there," says the rugged-looking Vendegna, patting the woman's arm.

Her plight furrows the brow of the normally chipper medical student.

"If I can make her more comfortable," he says later, "I've done something."

The need for primary-care physicians who heal and comfort on the front line of medicine is great. Vendegna plans to meet that need, but observers in the medical profession wonder how many other students will follow in his footsteps, given the pressures of whopping educational debt. To retire their loans as soon as possible, some medical students reportedly choose specialties that earn them higher income. For that matter, the prospect of \$50,000, \$70,000 or \$100,000 of undergraduate and medical school debt may discourage all but the wealthy

from pursuing a career in medicine.

Fortunately, alumni of medical schools across the country are helping to ease the debt crisis. Grateful for the education they received, they're providing their alma maters with

student scholarships that knock down debt levels. At the School of Medicine, for instance, alumni have helped establish four full-tuition scholarships, and they hope to create 12 more over the next three years.



*Medical student Tom Vendegna always keeps his patients first in mind. Yet it's difficult not to think of the \$61,500 in student loans he must start paying back when he graduates this coming spring.*

The debt crisis in medical education stems in part from rising tuition. In 1939, tuition and fees for a first-year student at the School of Medicine were \$523. By 1969, this figure had almost quadrupled to \$1,910. Tuition and fees tripled in the inflationary 1970s, increasing to \$5,975 in 1979.

The rate of growth slowed down in the 1980s. Tuition and fees this fall will amount to \$14,100, a little more than double the figure in 1979.

Tuition hikes at the School of Medicine have reflected a nationwide trend. Average tuition and fees for first-year students at private U.S. medical schools increased 1,500 percent from \$1,050 in 1960 to \$16,864 in 1988, according to the Association of American Medical Colleges. In roughly the same period, from 1960 to 1987, the Consumer Price Index for all items rose only 284 percent.

Tuition and fees have clearly outstripped the cost of living, but they aren't the only expenses incurred by a medical student. In 1939, School of Medicine students could expect to spend \$50 to \$100 on books and instruments (head mirrors were *de rigueur*) and about \$355 for room and board. Their total medical school expense, tuition included, came to approximately \$950. Compare that to \$22,500 this year.

Medical schools have had to increase tuition to keep pace with physical plant and equipment costs as well as salaries. These costs have skyrocketed partly because medical schools expanded dramatically in the 1960s and 1970s at the prompting of the federal government.

"There was a perception in the early 1960s that there



were'n't enough doctors." says John C. Herweg, M.D., associate dean of student affairs. "So the government encouraged us to enlarge our entering classes."

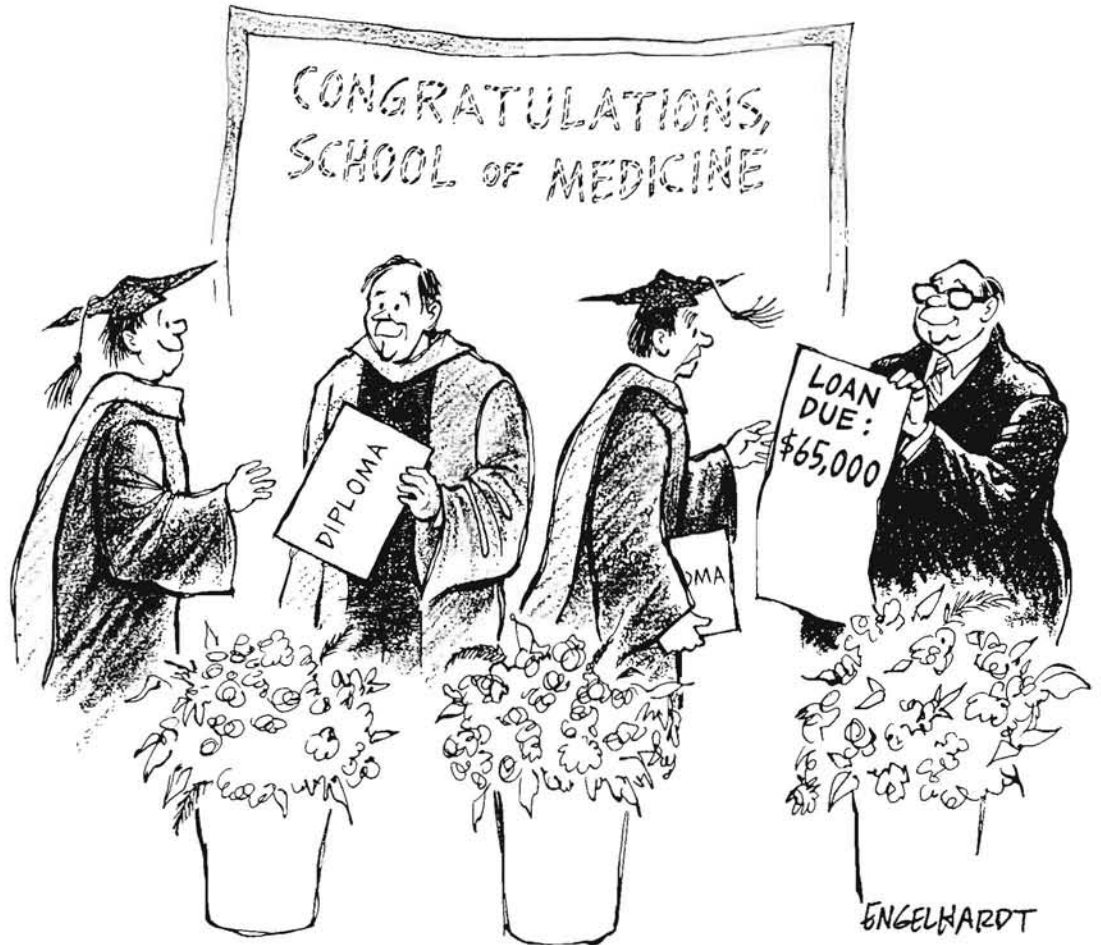
Besides offering schools a so-called capitation grant for each student, the federal government provided health profession scholarships and loans. With that support, first-year enrollment at the School of Medicine increased from 86 in 1962 to 120 in 1972.

But by 1976, federal capitation grants and scholarship money had dried up. The country had too many physicians, government officials said.

Medical school enrollments didn't decline appreciably, however, as the federal government reduced its support. What did decline was the role of scholarships in financial-aid packages. In the 1982-1983 school year, the last period for which national figures are available, 69.5 percent of financial aid for the nation's medical school students took the form of loans, according to the Association of American Medical Colleges. Scholarships amounted to 30.2 percent of financial aid, with work-study at .3 percent.

In 1987-1988, however, loans constituted 76.9 percent of all financial aid. Scholarships shrank to 22.6 percent. Work study increased to .5 percent.

Little wonder then that new M.D.'s have educational debts the size of home mortgages. In 1988, the average debt load for graduates of private medical schools was \$48,068, an amount that includes loans for undergraduate education. At the School of Medicine, it was \$45,626—almost double the amount in 1984.



"To take on this debt is a really frightening, awesome thing," says Joan Hartman Moore, director of public relations for the Association of American Medical Colleges. "So alumni scholarships are incredibly important."

From what Moore has heard from the field, some debt-laden medical students are saying they have no choice but to pursue a career as a specialist in a big city. The line of reasoning, she says, goes like this: "I'm never going to pay off my student loans if I practice primary-care medicine in a rural, under-served community."

The students most inclined to practice family medicine or pediatrics in either a rural area or an urban ghetto grew up in those areas, says Moore. Ironically, they also tend to be the heaviest borrowers.

There's the question of whether the farmer's daughter or the cab driver's son, however gifted intellectually, will be able to afford medical school in the first place. "As a society, we want to provide equal opportunity," says William A. Peck, M.D., vice chancellor for medical affairs at Washington University and dean of the School of Medicine. "As an institution, we want to provide equal oppor-

tunity to highly qualified individuals."

Peck says he's also concerned that heavy debt may deter some medical students from a career in research or delay a young physician's professional development as he takes temporary jobs to pay off his loans.

A 1988 survey of applicants who turned down a berth at the School of Medicine confirms that money weighs heavily on the minds of students. The second most frequently cited reason for choosing another school was lower tuition. The number-one reason was location, as in "I want to be closer



to my girlfriend" or "I prefer to live on the East Coast."

Tom Vendegna of River Grove, Ill., says he considered going to a state-supported medical school in light of his family's financial resources. His late father was a warehouse laborer who never earned more than \$4 an hour. His mother is a secretary.

"I remember thinking long and hard about picking Washington University or any private school," says Vendegna. "I was real close to going to UCLA, which would have been a lot cheaper. But Washington University covered me with loans.

"If they had required more money from my mother, I would not have attended Washington University."

By the time he graduates next May, Vendegna will have received \$38,000 in scholarships and \$61,500 in loans during undergraduate and medical school training. He estimates that his monthly loan repayments will eventually exceed \$600.

Vendegna says his father's long bout with diabetes helped motivate him to become a physician. Because he wants to stay close to patients' bedsides, he intends to practice internal medicine. "We need more primary-care physicians," Vendegna says.

His student loans, he says, haven't influenced him to consider specialties or subspecialties with potentially greater income.

"I think it has factored in some of my classmates' choices. I won't say everybody is doing what they want to do or that money isn't a factor."

Alumni of medical schools nationwide are trying to take the financial pressures off stu-

dents like Vendegna. Alumni of Yale University School of Medicine have increased their annual scholarship contributions from approximately \$50,000 10 years ago to approximately \$250,000 in the 1988-1989 school year, says financial aid director Pamela J. Nyiri. Plus, some alumni have converted the revolving loan funds they support into scholarship funds.

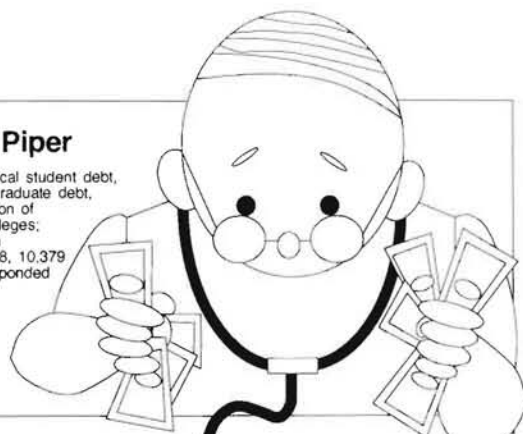
Both Yale alumni and educators worry about the consequences of gigantic loans, according to Nyiri. "The biggest problem is not having the freedom to choose," she says. "You can't choose pediatrics over ophthalmology if you walk out of school with over \$90,000 in debt." The Yale University School of Medicine held down student debt to an average of \$34,000 in 1988-1989.

Alumni scholarships have figured prominently in the financial-aid strategy of Johns Hopkins University School of Medicine. Of the \$2.3 million in scholarships awarded in 1988-1989, \$489,000 came from alumni, says financial aid administrator Sandra Morse. According to Morse, what motivates Johns Hopkins alumni is that they graduated with manageable debts and therefore bear the responsibility "to make it possible for future students."

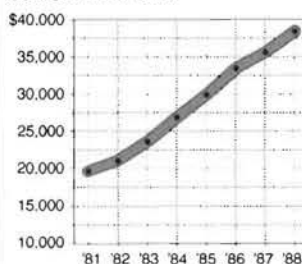
Over the past two years, Washington University, which spent \$1.1 million on needs-based scholarships this year, has set aside \$170,000 from unrestricted alumni contributions to fund approximately 71 percent of a new Distinguished Alumni Scholarship Program (the School of Medicine will provide the remainder). The first four full-tuition scholarships, to be awarded in the

## Paying The Piper

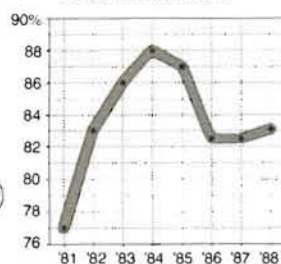
These graphs of medical student debt, which includes undergraduate debt, are from the Association of American Medical Colleges, LCME and Graduation questionnaires. In 1988, 10,379 graduating seniors responded to the questionnaire. Of those, 8,625 had debt; of those, 7 percent, or 573, had debt of \$100,000 or more.



### Average Indebtedness for graduating seniors with debt



### Percent of graduating seniors with debt



1989-1990 school year, are named after alumni who also taught at the School of Medicine. The four honorees are Eugene M. Bricker, M.D., '38, surgery; Mildred Trotter, Ph.D., '24, anatomy; the late Alexis F. Hartmann, M.D., '21, pediatrics; and the late Carl V. Moore, M.D., '32, internal medicine.

These four individuals were honored with named scholarships because they were held in high esteem by students, according to Kellie Burke, director of medical alumni programs.

Roger L. Mell, M.D., '65, president of the alumni association, says the new scholarship program is the alumni association's way of thanking the university for a superb education.

"There is a continuing need for strong financial support, so that the university can continue its excellent level of medical education," adds Mell. "The alumni association is committed to helping this endeavor."

That's good news for the future. ■

## Medicine and the way of the fish

by Barbara Yount

Whether he's practicing medicine or fly-fishing, Gordon W. Philpott, M.D. '61, stands out among the crowd. It is his enjoyment of almost everything he does that sets him apart.

If you ask Philpott what he likes best about his jobs as the Edison Professor of Surgery at the School of Medicine and associate director of the Department of Surgery at Jewish Hospital, he will tell you he likes it all.

Likewise, if you ask him what he likes best about fly-fishing, he will tell you he enjoys spending the day outdoors, learning about the water and observing the way of the fish.

Philpott says that since he began his medical career, it has become more challenging for those who want to teach, do research and practice clinical medicine. "Because of economics, malpractice situations and clinical problems, it is much more difficult today for someone to learn it all," he says. "My generation was lucky. In the 1950s and 1960s it was much more open."

It is the mix of academic medicine that is most appealing to Philpott. He says he enjoys "teaching residents who you know will one day be better than you are." He also finds fulfillment as a breast cancer specialist through helping patients arrive at good outcomes.

A native St. Louisan, Philpott has left his hometown only twice—to attend undergraduate



*Gordon Philpott, M.D., designs his own fish lures at his home in University City, Mo.*



school at Yale University and to do research at NIH in the middle of his surgical residency at Barnes Hospital.

It was Philpott's mentor, Carl Moyer, M.D., former Bixby Professor of Surgery, who encouraged Philpott to take a two-year research fellowship, without clinical duties, at the National Institutes of Health.

Embryology research conducted in the laboratory of A. J. Coulombre, M.D., at the National Institutes of Neurological Diseases and Blindness in Bethesda, Md., proved invaluable. "I'm still using that experience," Philpott says.

That experience provided background when Philpott and his small research staff characterized monoclonal antibodies that bind strongly to colon cancer cells but weakly, or not at all, to normal colon tissue. This discovery, which may result in a faster, more sensitive method of detecting colon cancer, led to a \$1.2 million NIH grant.

Along with Judith M. Connett, Ph.D., research assistant professor, Philpott currently is working with nuclear medicine specialists at the Mallinckrodt Institute of Radiology to identify the best imaging reagents for tumor detection. Imaging reagents attach to the antibodies and make them observable.

Philpott's devotion to the School of Medicine and its medical center spans more than two decades and is reflected through accomplishments he has made in various leadership roles. When he was asked to serve on the steering committee to raise funds for the School of Medicine's Library and Biomedical Communications

Center, Philpott successfully received contributions from all the full-time surgical faculty of Jewish Hospital.

Another achievement, one that has taken more than 10 years, is the consolidation of Barnes and Jewish hospitals' residency programs in general surgery. For the first time this year, a combined residency program will be administered

likely to be fly-fishing or preparing for a fly-fishing trip. It was from colleagues William Newton, M.D., former chief of staff of Cochran Veterans Hospital, and C. Alan McAfee, former director of surgery at St. Luke's Hospital, that Philpott developed a passion for fishing.

"They were my teachers and professors who became my

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"Because of economics, malpractice situations and clinical problems, it is much more difficult today for someone to learn it all."

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through the School of Medicine.

Although many of the surgical subspecialties already had combined programs, opposition among some faculty members at both hospitals kept the general surgery programs separate.

To Philpott, combining programs will not only make one overall program, but also will help him accomplish the task assigned to him in 1976, when he was named the Edison Professor. The job was to mainstream Jewish Hospital surgery programs with those at the School of Medicine. The combined program, says Philpott, was "the only logical and natural way to do it."

When he's not busy with academic pursuits, Philpott is

friends," Philpott says. "They constantly fueled my interest in fishing. I learned a lot from them." For many years the three fishermen made annual trips to Wyoming to fly-fish for trout.

Philpott continues to make annual trips to Wyoming as well as trips in recent years to more faraway places like the Bow River in Canada and to Alaska.

In March Philpott made his second trip to Christmas Island in the central Pacific Ocean to fish for one of the most challenging species known to fly-fishermen, the ghostly bone fish. "They are fast," Philpott says of the salt-water fish. "They're ugly. They look gray green in the water but are like white salmon when they're out."

When Philpott fished Christmas Island for the first time, he found an exotic coral island. Bone fish darted through its tropical waters feeding on crabs and shrimp, while barracudas and sharks lurked behind. Uninhabited in 1777 when Captain James Cook discovered it, Christmas Island today is home to a friendly tribe of Micronesians.

While Christmas Island provides a scenic backdrop for fishing, its remoteness makes it strictly a place for die-hard fishermen. Once a week a plane brings a new group of fishermen and picks up those returning. A single motel provides basic lodging and meals.

Philpott is not only a fly-fisherman, but also a fly-tier. A time-consuming craft, fly-tying is the art of constructing lures by wrapping hooks with bits of fur and feather to resemble insects and other natural fish prey. Philpott ties nearly all of his own flies. "It's fun to do," he says.

Philpott's fly-tying desk sits in a corner of a converted bedroom loaded with cellophane bags of feathers and skins, spools of thread and hooks of varying sizes. There are more materials than any one person would use in a lifetime.

Aside from fly-fishing, Philpott looks forward to spending more time doing what he enjoys: teaching, research and practicing clinical medicine. ■



# The Alumni Report

## Mell named new alumni president

**R**oger L. Mell, M.D., has been named president of the Washington University Medical Center Alumni Association.

Mell, an orthopedic surgeon at St. Luke's Hospital, is president of the Southern Medical Association as well as the St. Louis Orthopedic Society. He graduated from the School of Medicine in 1965.

Before joining the staff at St. Luke's Hospital in 1971,

Mell was chief resident in orthopedic surgery at Barnes Hospital. He completed his surgical internship and assistant residency in orthopedic surgery at Barnes.

Mell's training also includes assistant residencies in general surgery at St. Luke's Hospital and in orthopedic surgery at the Shriner's Hospital for Crippled Children in St. Louis. In addition, he served as chief resident in orthopedic surgery

at John Cochran Veterans Administration Hospital.

At St. Luke's, Mell is president of the Hospital Staff Association. He also serves on the board of trustees of the Southern Orthopedic Association and is a member of the American Academy of Orthopedic Surgery.

Mell is convinced that the best way for alumni to strengthen the medical school is to assist current students, so that the school will continue to graduate physicians who are extraordinarily competent and sensitive to the health needs of their communities.

Mell says that the alumni association should play a larger role in supporting medical students with scholarship funds. And he is particularly hopeful that the alumni association will be able to assist students who otherwise might not be able to afford a medical education.

"By assisting students, we can insure that the medical school will continue to be the outstanding institution it is today," he says. "We all owe a great deal for the training we received. Now it's our job to make that opportunity available to others." ■

## CLASS NOTES

### '30s and '40s

**Frank G. Zingale, M.D. '33**, has become involved in the establishment of nursing school scholarships.

Last year, **William C. MacDonald, M.D. '40**, spent the month of November at Sacre Coeur Medical Center in Milot, Haiti, teaching a Haitian

physician techniques in gastroenterology. He also spent 10 days there this past January and writes that he saw many grateful and appreciative patients.

**Eugene P. Johnson, M.D. '46**, is the new president of the Illinois State Medical Society.

### '50s and '60s

Two former fraternity brothers, **James McCaffrey, M.D. '52**, and **Gerald A. Goodhue, M.D. '49**, were pleasantly surprised when they met unexpectedly while circumnavigating South America aboard the S.S. Britannia.

**Gabriel S. Zatlín, M.D. '60**, was named chairman of the department of family medicine and director of the family practice residency program at St. Mary's Hospital in Hoboken, N.J.

**Elliot M. Finkelstein, M.D. '61**, is still practicing ophthalmology. He is now in solo practice after nine years of association. He writes that Beth is working for a medical computer company, Marie will start ophthalmology residency in July, Andy is in the business world, and Happy is a computer specialist in the Boston schools.

**Ronald E. Rosenthal, M.D. '61**, is chairman of the Committee on Emergency Medical Services for the American Academy of Orthopaedic Surgeons (AAOS). Rosenthal is vice-chairman, director of residency education and chief of the division of trauma in the department of orthopedic surgery at the Long Island Jewish Medical Center in Hyde Park, N.Y. He is also the AAOS delegate to the



Roger Mell, M.D.



American Medical Association's Commission on Emergency Medical Services, a member of the Emergency Medical Services Committee of the Medical Society of the State of New York and a former manager of the American Association for the Surgery of Trauma.

**Lewis H. Koplik, M.D.** '65, recently took a trip to Antarctica with the Washington University alumni association. He was also elected to the national board of the Association of Reproductive Health Professionals.

## '70s and '80s

**Robert Vance Rouse, M.D.** '74, is on sabbatical in Paris. He is trying to learn some neurobiology, he writes, and wishes he had paid more attention to Cowan, Bunge, etcetera.

**Glenn T. Hammons, M.D.** '76, writes that his work for the Physician Payment Review Commission to reform Medicare is very rewarding.

**Larysa Melnyk Dyrszka, M.D.** '78, is a pediatrician in private practice. She lives in New Jersey with her husband and three children and enjoys oil painting and sailing.

**Howard Jay Silverman, M.D.** '79, is attending Boston College Law School.

**Carl W. Ludvigsen Jr., M.D.** '80, Ph.D., J.D., became senior vice president and chief pathologist of Home Office Reference Laboratory, Inc., a leading provider of laboratory testing services for the insurance industry.

**Ray Lannom Watts, M.D.** '80, was recently awarded the George Cotzias Memorial

Research Fellowship by the American Parkinson Disease Association. The award provides \$150,000 for three years.

**Theodore Tsaltas, M.D.** '83, married Kim Davis, a fashion designer. He is assistant professor of obstetrics and gynecology at the University of Pennsylvania and director of the obstetrics and gynecology clinic at Pennsylvania Hospital.

**Ruth Susan Eisen, M.D.** '84, and her husband, Scott Eveloff, recently celebrated the first birthday of their son, Daniel, and the second birthday of their daughter, Emily.

**Steve Weinman, M.D.** '84, is assistant professor in the departments of medicine and physiology at the University of Texas Medical Branch at Galveston.

## FORMER HOUSE STAFF NOTES

**Philip E. Cryer, M.D., F.H.S. in internal medicine,** has been elected to the board of the American Diabetes Association. He is also the recipient of the Juvenile Diabetes Foundation International's David Rumbough Award. Cryer is a professor of medicine at Washington University, where he directs the Division of Endocrinology and Metabolism and the General Clinical Research Center.

**J. Joseph Marr, M.D., F.H.S. in internal medicine,** has been named senior vice president of product discovery research for Searle Research and Development. In his new position, Marr reports to Joseph M. Davie, M.D., Ph.D., president of Searle Research and Development and former

## Alumni Reunion 1990

May 3,4,5

Class of 35, 40, 45, 50, 55, 60, 65,  
70, 75, 80

head of microbiology at the School of Medicine. Marr was most recently professor of medicine and biochemistry and head of the division of infectious diseases at the University of Colorado Health Sciences Center in Denver.

**William R. Platt, M.D., F.H.S. in pathology,** is working on his third edition of "Color Atlas and Textbook of Hematology."

**William B. Wadlington, M.D., F.H.S. in pediatrics,** received a Practitioner Research Award from the American Academy of Pediatrics for outstanding contributions in research. He was also named "Pediatrician of the Year" by the Tennessee chapter of the American Academy of Pediatrics and Tennessee Pediatric Society for distinguished service in the care of children.

**Debra Collins, O.T.** '80, is still working as an employee at BOCES in Albany, N.Y. She also works privately. She married in 1986 and gave birth to a boy in July 1988. She and her family live in Schenectady, N.Y.

**Jeannette Conrad Dansberry, O.T.** '59, joined Wisconsin's Director of Vocational Rehabilitation to assist in developing supported employment programs for people with severe disabilities.

**Sandra H. Phipps, P.T.** '85, and her husband live in Hiram, Ohio. Their daughter, Helen Elizabeth, was born this past February.

**Ruth Rose-Jacobs, P.T.** '73, received her doctorate from Boston University this past May. She is married and the mother of three children.

## IN MEMORIAM

## O T H E R

**Michelle Michaelis Aylor, P.T.** '87, was married last year. After their honeymoon in Isla Mujeres, Mexico, she and her husband, Mark, moved to Las Cruces, New Mexico. Michelle is working at a hospital in El Paso, Texas, and Mark works at White Sands Missile Range. They have a one-year-old black Labrador retriever and own a three-bedroom home. Visitors, she writes, are welcome.

**Harvey R. Butcher, M.D.,** emeritus professor of surgery, died April 25, 1989.

**Charles L. Eckert, M.D.** '39, died July 1, 1989.

**Joseph Gallagher, M.D.** '44, died June 9, 1989.

**Lillian M. Hall, M.D.** '41, died November 26, 1988.

**Patrick R. Kelly, M.D.** '49, died December 18, 1988.

**F. Eugene Pennington, M.D.** '44, died April 25, 1989.

**Henry F. Scott, M.D.** '31, died March 19, 1989.

**Nelson W. Sheley, M.D.** '17, died February 10, 1989.





*Researchers in the lab of Jeff Lichtman, M.D., Ph.D., use glass microelectrodes to record events within neonatal mouse muscle cells. Such recordings complement live animal studies featured on page 6.*



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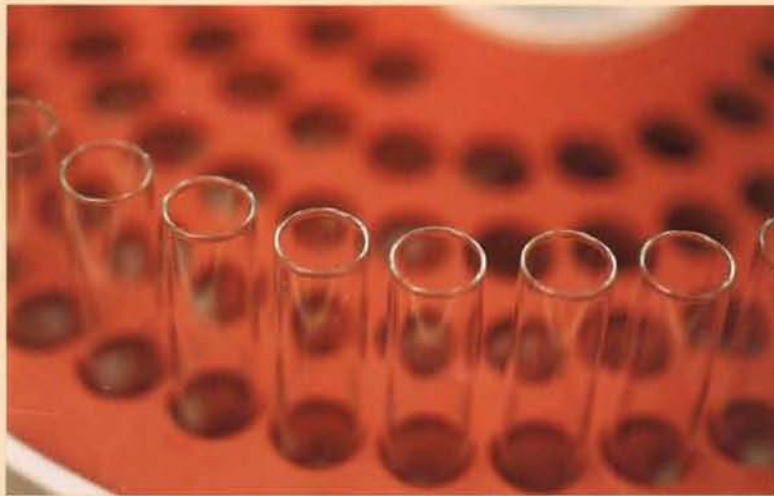
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