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People of average complexion should use a sunscreen with a sun protection factor of no less than 15 when they're out in the sun, according to dermatologist Ann Martin, M.D. See story on page 20.
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After years of dispute about the diagnostic features of schizophrenia, psychiatrists are uniting in an effort to understand and conquer it.

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Ed Dodson prods the bureaucracy to put an end to child abuse.

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David Russell, Ph.D., uses snake-like lampreys to study the brain’s control of respiration.

On the Cover:
“Family Portrait” was painted by Washington University psychiatrist Carol North, M.D., when she was schizophrenic. See story on page 10.
National Academy of Sciences Honors Frieden As One of 61 Distinguished New Members

Carl Frieden, Ph.D., professor and interim head of biological chemistry at Washington University School of Medicine in St. Louis, has been elected to the National Academy of Sciences.

Frieden is among 61 new members honored for their distinguished and continuing achievements in original research. Election to the academy is one of the scientific community’s most prestigious honors. The society, which now has 1,541 members, was chartered by an act of Congress signed by President Lincoln in 1863. The academy promotes research beneficial to human welfare and officially advises the federal government on science and technology.

Frieden is director of the Medical Scientist Training Program at the School of Medicine and was recently appointed interim head of the Department of Biological Chemistry. He is best known for his research on the relationship between the three-dimensional structure of proteins and their function. Specifically, he is attempting to describe the kinetic properties of proteins that act as catalysts, and the strategy they use for speeding a reaction. He is also studying actin—an important protein found in all cells of the body—and its relation to certain cellular functions.

In 1986, Frieden was honored for his scientific contributions by receiving MERIT status for a $1.2 million grant from the National Institutes of Health. MERIT (Method to Extend Research in Time) Awards provide long-term, uninterrupted financial support to investigators who have demonstrated superior achievement during previous research projects.

Frieden came to Washington University in 1955 as a postdoctoral fellow, and joined the faculty in 1957 as an instructor in biological chemistry. He was named a professor in 1967, and interim department head earlier this year.

He has served as a council member of the American Society of Biological Chemists and as an alternate council member of the American Chemical Society’s Division of Biological Chemistry. He is also a member of the American Society of Cell Biology and the American Association for the Advancement of Science, and serves on the editorial board of Biochemistry. He has served on the editorial board of the Journal of Biological Chemistry and Archives of Biochemistry and Biophysics. He received the St. Louis Award of the American Chemical Society in 1976. Frieden is co-author of more than 100 publications on his research.

Fear Strikes Elderly After the Fall

The tranquility that we often associate with aging may well be a myth, according to Barry Hong, Ph.D., a medical psychologist at the School of Medicine. A closer look may show, he says, that the golden years are in fact tarnished by anxieties and fears, and that one of the greatest fears is falling.

Post-fall syndrome is a fear that older people can develop after falling, according to Hong. It may begin gradually, but sometimes grows to such an intensity that many of its victims become incapacitated—unable to walk alone or to function independently—even though they have no physical disability. As a result they become housebound, not because of physical injuries, but emotional ones.
It’s such a gradual process that most people—including physicians—shrug it off as behavior consistent with old age, he says. Actually, it’s a treatable condition.

Rapid increases in the elderly population could make post-fall syndrome a critical public health issue, says Hong, who has long been interested in the psychological aspects of chronic illness. The syndrome threatens the lifestyle of its elderly victims by robbing them of their independence and forcing them to rely on family and friends.

Patients who have the syndrome tend to clutch and are unable to walk unsupported, have an abnormal gait because of hesitant or irregular walking, and an extreme fear of falling. The signs are pronounced and clearly related to one or more recent falls.

“It’s a problem that is underreported and often unnoticed,” Hong comments, perhaps because it’s not adequately identified. Little has been added to the literature since British researchers first described the disorder in 1982 in the Journal of Geriatrics.

To determine the prevalence and clinical course of post-fall syndrome, Hong is studying elderly people who have fallen. His five-year study is believed to be the only one now being conducted on the disorder.

One of the key issues he would like to clarify is how to categorize it: Is post-fall syndrome a particular form of agoraphobia (fear of open spaces), or a phobia in its own right? He thinks it is a phobia, but one that defies traditional psychiatric beliefs by beginning in old age.

“The usual thought is that anxieties and phobias develop in the late teens, certainly no later than age 30, and have resolved themselves by old age,” he explains. “If we’re right about this, though, post-fall is a particular phobia that occurs in old age and in fact is related to the experience that elderly people may have. That’s unique.”

Hong’s work on fear of falling is part of a large National Institute on Aging-funded project on the causes and prevention of falls and hip fractures in the elderly. He is using a subset of elderly people who have fallen, enrolling 200 who have broken a hip and 150 who haven’t been seriously injured. They will receive a full physical and neurological examination, and a series of psychological and psychiatric evaluations over time to explore the emotional consequences of falling.

Hong’s hypothesis is that post-fall syndrome develops gradually, like most phobias. “If fear of falling is begun by a psychological mechanism, then it’s something that can be undone,” he says. “It’s not a natural result of aging, and people don’t have to compromise their lives. Our goal as a nation should be to help elderly people live independently for as long as possible—fear should not be a barrier.”

Neurologist Uses Games People Play to Detect Brain Damage from the AIDS Virus

The Washington University AIDS Clinical Study Group is now using psychometric tests to help detect brain damage caused by AIDS long before other symptoms have appeared.

“We aren’t sure when it [AIDS] strikes or how it works, but we do know that it attacks the brain and is capable of causing great damage to the central nervous system,” says David Clifford, M.D., assistant professor of neurology, who studies AIDS in the brain.

Autopsies show that more than 90 percent of those who die from AIDS have brain damage caused by the virus. The virus can spread to the spinal cord and peripheral nerves, causing impaired movement, loss of bladder control, loss of sensation in hands and feet and severe tremors. Nearly 60 to 70 percent of AIDS patients experience a major disability because of AIDS dementia complex, which is very similar to Alzheimer’s Disease.

“To treat AIDS dementia complex and other manifestations of brain infection, we need to know more about when the virus enters the brain,” Clifford says. “Does brain damage occur suddenly, after the immune system has crumbled? Or is the virus gradually eating away at the brain, unrecognized and untreated because traditional tests aren’t sensitive enough to detect it?”

To begin answering these questions, Clifford will guide a small group of recently diagnosed, asymptomatic AIDS patients through a battery of tests designed to detect and evaluate early neurologic signs of AIDS infection.

Testing will consist of a traditional neurologic exam, a lumbar puncture to analyze spinal fluid for antigen and antibody response, a magnetic resonance imaging (MRI) brain scan that might show changes caused by viral presence and games to test attention span, memory and concentration. Results will be compared with those of patients who don’t have AIDS.

The games include tests of motor function and speed,
such as repetitive finger tapping and the peg board test; tests of language function, such as a verbal fluency task in which the patient is given 60 seconds to name as many words as possible beginning with a certain letter, and memory tests in which he is asked to recall facts from information presented.

Besides the games, early-stage brain scans may be another sensitive indicator of viral presence. Scans taken during advanced stages indicate that the virus causes little structural damage to the brain itself, even in patients with severe dementia.

Abnormalities caused by viral damage seem to occur in what Clifford calls "the brain's communication tracks"—the white matter, pale fibers that run from cell body to cell body.

What's encouraging from a therapeutic point of view is that, while the brain's supporting cells may be infected, actual structural damage to nerve cells appears to be slight. The nerve cells, which can't be replaced once destroyed, don't seem to be a major target for infection. "If we can reach the white matter while the viral infection is in an early stage, perhaps we can treat existing damage or prevent further damage.

"In the long run, though, what good will it do if we can fight off the infections and the cancerous tumors but the patient is demented, mute, unable to experience life?" Clifford asks. "That's what can happen when the brain is severely infected, and that may be the worst disaster of all." "

Joshua Sanes is Awarded $105,000 to Study the Formation of the Nervous System in Vertebrates

Joshua R. Sanes, Ph.D., associate professor of neurobiology, was among 14 scientists selected to receive a neuroscience development award from the McKnight Foundation, a group that presents awards to advance neuroscience research and to encourage experienced investigators to study the basic mechanisms of memory and diseases that affect memory.

Sanes's award, which totals $105,000, will provide three years of funding for his work on the formation of the nervous system in vertebrates.

His research addresses an issue that has become increasingly important in neurobiology: is formation of the nervous system in vertebrates due primarily to environmental influences or inherited ones? Recently, scientists have focused on environmental influences, Sanes says, but growing evidence supports his belief that cell lineage plays a crucial role, as it does with invertebrates.

Sanes's efforts are directed toward learning the genealogy of cells in the vertebrate neuromuscular system. His current studies in the chick embryo examine motorneurons and muscle fibers from formation to specialization, the point at which they acquire their ultimate function.

Eventually, Sanes hopes to use the information his studies generate to help form hypotheses about when, where, and how cells form and become linked to other nerve cells or to muscle cells.

Sanes came to Washington University in 1980. He served as a Sloan Fellow from 1980 to 1982, and is a member of the Senator Jacob Javits Center of Excellence in Neuroscience at the School of Medicine.

Fatty Acid-Free Diet Eliminates Organ Rejection in Rat-to-Rat Kidney Transplants

Researchers at the School of Medicine recently eliminated organ rejection in rat-to-rat kidney transplants by changing the diets of donor rats for two months prior to transplantation.

Reported in a May issue of the journal Science, their results mark the first time that dietary manipulation has been shown to eradicate specific cells within the donated kid- neys that trigger rejection in transplant recipients, according to James B. Lefkowith, M.D., and George F. Schreiner, M.D., Ph.D., who conducted the research.

"We have come upon something very fundamental, and though it may not have immediate clinical application it does have clinical relevance," Lefkowith says.

Schreiner and Lefkowith placed their donor rats on a diet that contained no essential fatty acids. After two months of this diet, the kidneys of the donor rats were depleted of white blood cells — the very cells that ordinarily trigger a recipient's immune system to reject a transplant.

Kidneys from 33 rats fed this essential fatty acid-deficient diet were not rejected when transplanted to another strain of rats, and no immunosuppressive drugs were required to sustain the transplants, according to Lefkowith.

Although the researchers don't now know how essential fatty acid deficiency short circuits rejection, they have postulated that fatty acid metabolites such as leukotrienes, which are known to play a key role in the immune response and in the stimulation and distribution of white blood cells, are a reasonable suspicion.

"We know that there must be some signal attracting the white blood cells into the kidney under normal circumstances," Lefkowith said. "No one yet understands why white blood cells go where they do—they're found in all tissue. Perhaps we're dealing with a way to intervene in that signal system."
Lefkowitz and Schreiner said they do not feel this research warrants placing human kidney donors on a fatty acid-deficient diet prior to surgery. "That would be foolish based on these findings alone," said Lefkowitz. "Much more would need to be done regarding the safety of such a diet in humans. However, this work does have clinical relevance. In other studies we have found that the diet also depletes the white blood cells in heart and pancreas tissue, and that that depletion can block some autoimmune diseases from occurring.

"With respect to transplantation," he added, "it is more reasonable to try to manipulate whatever systems are involved through a pharmaceutical that mimics the effect of the diet. We have to learn more about the role of essential fatty acids to reach that point."

**Correction**

The editors of *Outlook* would like to correct an error.

In the last issue's article on women in medicine, we did not correctly identify the first woman to enter the School of Medicine. Aphrodite M. Jannopoulos, M.D., '22, was the first woman to enter the school. Her husband, Armin C. Hofsommer, M.D., also graduated from the School of Medicine in 1922.

The editors express their deepest regrets for the error.

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**Japanese and American Scientists Meet to Discuss Research Collaborations in Gene Mapping**

Scientists from Japan visited the School of Medicine this past May to discuss prospects for Japanese and American collaboration in mapping the human genome.

The discussion was part of a formal symposium inaugurating a broad-based scientific exchange program between Washington University and RIKEN, Japan's preeminent government-sponsored research institution.

The symposium included presentations of highly regarded research conducted in more than 20 different laboratories at the two institutions from work on cancer-causing genes to the formation of communication links between nerve and muscle cells, the transport of messenger molecules within human cells and the nature of the diversity of the human immune system.

"This is the first case in which equivalent funds have been provided from both Japanese and American sources to support exchange visits for research purposes—by technicians and students as well as by professors—so we are especially eager to make it work," says David Schlessinger, Ph.D., professor of medicine and of microbiology and immunology. "We know it will work if we base the efforts on good science, which emphasizes the importance of the exchange of information at the symposium." Schlessinger and Fumio Imamoto, Ph.D., vice director of RIKEN's Tsukuba Center, planned and formalized the exchange program.

The exchange was inaugurated in Japan last spring, when nine faculty members from Washington University traveled to RIKEN to present their research. In addition to the symposia, the exchange will share their expertise in gene cloning with RIKEN scientists who will in turn proffer their own mastery of gene sequencing in a demonstration project, sequencing a complete yeast chromosome for which initial mapping and cloning have been done in the laboratory of Maynard Olson, Ph.D., professor of genetics at Washington University.

This particular spin-off from the general exchange agreement is RIKEN's first genetics collaboration in the United States. It is part of an extensive program which has placed Washington University's efforts at genome mapping among the most progressive and fruitful programs.

Visiting scientists from Japan enjoy an evening at the Missouri Botanical Gardens.
Residency programs at hospitals of the Washington University Medical Center claimed about a quarter of this year's graduating medical school class, according to Match Day results.

The remaining three-quarters of the class will be completing their residencies in 29 other states across the country, the most popular being California. Internal medicine was the residency of choice for the largest percentage of graduating seniors (44 percent), with pediatrics and surgery running close seconds both at 14 percent.

Only two members of the class will not be completing residencies next year. First-year appointments for the class of 1988 are as follows:

**Arizona**
Phoenix
Maricopa Medical Center
Lawrence P. Gassner, Internal Medicine Preliminary
Tucson
University of Arizona Affiliated Hospitals
William D. Rubin, Internal Medicine

**California**
Loma Linda
Loma Linda University Medical Center
Mark Turrill, Internal Medicine
Los Angeles
UCLA Medical Center
Steven J. Borowsky, Internal Medicine
Hubert S. Chou, Internal Medicine
San Diego
U.S. Naval Hospital
Thomas E. Hatley, Transitional
University of California
Audrey R. Talley, Internal Medicine Preliminary
San Francisco
Children's Hospital
Mitchell J. Wong, Internal Medicine
Kaiser Permanente Medical Center
Susan E. Minger, Pediatrics

**Left to right:** Jay Poorman, Peter Andersen and David Theodoro are none too disappointed in their matches.
Good news brings a hug from Sharon Moellenhoff.
Missouri
Columbia
University of Missouri School
of Medicine
Jeffrey R. Zohner, Internal
Medicine
St. Louis
(Washington University
Medical Center)
Barnes Hospital
Brian K. Dieckgraefe,
Internal Medicine
Emily K. Dohe, Internal
Medicine Preliminary
Marc E. Eichler, General
Surgery
Anne L. Fuhlbrigge,
Internal Medicine
C. Bruce Graves, Internal
Medicine
Timothy J. Henkel, Internal
Medicine
Perry D. Inhofe, General
Surgery
Robert G. Kaniecki, Internal
Medicine Preliminary
Andrew B. Landes,
Diagnostic Radiology
Lofton N. Misick, General
Surgery
Michael L. Moulton,
Internal Medicine
William A. Parks, Research
in Pathology
Stephen J. Pieper, Internal
Medicine
Karen L. Scharenberg,
Internal Medicine
Preliminary
Stephen J. Smart, Internal
Medicine
David A. Theodoro, General
Surgery
Mark J. Watson, General
Surgery
Gordon L. White,
Psychiatry
Children's Hospital
Kimberly S. Graves-Quayle,
Pediatrics
William C. Hollifield,
Pediatrics
Kathryn Lee Knutzen,
Pediatrics
Chihiro Morishima,
Pediatrics
Vida D. Sheen, Pediatrics
Catherine S. Tripp,
Pediatrics
Jewish Hospital
Richard M. DiValerio,
Internal Medicine
James R. Duncan, Internal
Medicine
Jeffrey L. Elliott, Internal
Medicine
James W. Forsen, General
Surgery
Neal A. Frenkel, Internal
Medicine
Samuel T. Shaikewitz,
Internal Medicine
Jason Shen, Internal
Medicine
David G. Standaert, Internal
Medicine
Emily Dohe (center) opens her match during this year's Match Day.
St. John's Mercy Medical
Center
Paula J. Chor, Pathology
Rosalie J. Hagge,
Transitional
Robert J. Optican,
Transitional
Glenn K. Shopper,
Transitional
St. Louis University Medical
Center
Janet L. Cranshaw-Mink,
Pediatrics
Janice J. Rha, Internal
Medicine Preliminary
Michael K. Thornton,
Obstetrics & Gynecology
St. Luke's Hospital
Yin Y. Lim, Internal
Medicine Preliminary
Gregory A. Smith, Internal
Medicine Preliminary
John R. Wilson, Internal
Medicine Preliminary
New Mexico
Albuquerque
University of New Mexico
School of Medicine
Joel R. Teicher, Obstetrics &
Gynecology
New York
Bronx
Albert Einstein College of
Medicine
John N. Constantino,
Pediatrics and Psychiatry
Brooklyn
Kings County Hospital Center
Claudia L. Corwin, General
Surgery
New York
St. Luke's Hospital Division
William G. Filmyer, Internal
Medicine Preliminary
Stonybrook
Stonybrook Teaching Hospital
David J. Parks, Internal
Medicine
Matthew F. Romanelli,
Psychiatry
Judy Rudnick and Glenn Shopper rejoice over their matches.

North Carolina
Durham
Duke University Medical Center
Brian A. Armstrong, Internal Medicine
Russell E. Hillsley, Internal Medicine
David S. Peterseim, Surgery Preliminary
Millicent M. Winfrey, Family Practice
Kenneth M. Zabel, Internal Medicine

Ohio
Cleveland
Case Western Reserve University Hospital
Brenda J. Kitchen, Pediatrics
Margaret L. McKenzie, Obstetrics & Gynecology
Cleveland Clinic Foundation
Howard M. Hack, Internal Medicine

Oregon
Portland
Oregon Health Sciences University
Peter E. Andersen, General Surgery
Jay C. Poorman, Internal Medicine

Pennsylvania
Philadelphia
Hospital of the University of Pennsylvania
Arthur J. Castelbaum, Obstetrics & Gynecology
Presbyterian University of Pennsylvania Medical Center
Eli F. Dweck, Transitional Medicine

Rhode Island
Providence
Rhode Island Hospital
George A. Kurose, Internal Medicine
Ronald R. Magee, Surgery Preliminary

South Carolina
Charleston
Medical University of South Carolina
Margaret L. McCarthy, Obstetrics & Gynecology
Alan D. Wilson, Diagnostic Radiology

Tennessee
Nashville
Vanderbilt University Hospital
Andrew H. Sonin, Diagnostic Radiology
Eleanor M. Walker, Internal Medicine

Texas
San Antonio
Wilford Hall Air Force Base
Charles L. Bane, Internal Medicine
Stacy K. Lewis, Internal Medicine
Daniel M. Ockner, Internal Medicine

Utah
Salt Lake City
University of Utah Affiliated Hospitals
John D. Kriesel, Internal Medicine

Virginia
Portsmouth
U.S. Naval Hospital
Robert E. Quast, General Surgery

Washington
Seattle
University of Washington Affiliated Hospitals
Mary E. Androff, Psychiatry
Geoffrey G. Thompson, Anesthesiology
David L. Watling, General Surgery

Washington, D.C.
Walter Reed Army Medical Center
Milton W. Anderson, Psychiatry
Jeffrey L. Jackson, Internal Medicine

Wisconsin
Madison
University of Wisconsin Hospitals & Clinics
Wayne R. Godfrey, Internal Medicine
Boyd D. Miller, Pediatrics
The first four paintings used to illustrate this story were painted by Carol North, M.D., research fellow and clinical instructor in psychiatry at the School of Medicine, while she was suffering from schizophrenia. The last painting, The Golden Hills of California, was painted by North after she was cured. Her recently published book, Welcome Silence, is a poignant account of her battle with schizophrenia and her miraculous recovery following dialysis.

Three years ago, John*, 31, faced a promising future. Fresh from graduate school, he had a new job as seed program administrator in the Florida Department of Agriculture, where he supervised a staff of 50 people. Then suddenly the voices began—whispers at first, growing more clamorous each day.

"I heard voices telling me to do things," says John, a 1976 Washington University graduate. "I thought that my telephone calls were being listened to. Finally I resigned, because I believed that people wanted to fire me."

Back home in St. Louis, John's mental state continued to deteriorate. He became convinced that the F.B.I. was grooming him to become a spy. If a car passed by, he knew the occupants were talking about him. In desperation, his mother took him to Barnes Hospital in the Washington University Medical Center, where doctors made a diagnosis.

Like 1.2 million other Americans, John was suffering from schizophrenia, a baffling disease that blights careers and ruins lives. Cruelly, it strikes at the threshold of adulthood, usually between the ages of 17 and 30. Its victims come from every social class, race and nation. And though the disease may hopscotch through several generations of one family, most patients have no family history at all.

It is also a disease with a harsh prognosis. In one 10 year study, only a quarter of the patients recovered completely; another quarter could function with some independence; a third quarter required an extensive support network; and a final quarter were either hospitalized or dead, mostly from suicide.

Tragically common and difficult to treat, schizophrenia cries out for scientific attention and public concern. Yet a mere $14 per patient is spent each year in the U.S. on schizophrenia research. And its victims may be neglected or stigmatized by a public that too often views schizophrenia as a moral failing, not the dread brain disease that it is.

"I think there's a growing consensus in psychiatry that schizophrenia represents a

*The name John has been used in place of the patient's real name.
very serious psychiatric disorder that has a variable course and outcome, but in general, has a poorer course and a poorer outcome than most other psychiatric disorders," says Samuel Guze, M.D., Spencer T. Olin Professor and head of psychiatry, and Vice Chancellor for Medical Affairs at Washington University School of Medicine.

But at long last, there are signs that things may be changing. After years of dispute about the diagnostic features of schizophrenia—indeed whether it is a discrete disease at all—psychiatrists seem to be uniting in an effort to understand and conquer it.

"There is a sense of hopefulness in schizophrenia research that has not been present until now," says Terrence Early, M.D., assistant professor of psychiatry. "After so many people have spent careers looking for it, we'll probably pinpoint the lesion causing this disorder in the next few years."

Washington University School of Medicine has led the field in its clinical approach to schizophrenia. Guided by Guze and Eli Robins, M.D., Wallace Renard Professor of psychiatry, the Department of Psychiatry has long advocated applying a medical model to psychiatric illness: diagnosing and treating it just like any other physical disorder. With funding from many grants, the department is engaged in promising biochemical and genetic research. Last year, a new research professorship in schizophrenia was endowed by the Couch family.

"I think we are one of the leading research departments of psychiatry in the country," says Guze. "We have probably had as great an effect as any in the last 20 years in re-orienting and re-shaping the way American psychiatry at the academic level is going about its work."

Yet much work remains to be done, he cautions. Science is closer than ever to discovering the cause of schizophrenia, but effective treatment—and possibly a cure—may still be years away. Meanwhile, much suffering continues among patients and their families.

"We can do better for our patients than we were able to 20 years ago," Guze says, "but we have a long, long way to go yet."

THE DIAGNOSTIC DILEMMA

In 1911, Swiss psychiatrist Eugen Bleuler introduced the term "schizophrenia" to describe the odd discrepancy he perceived between a patient's thought process and emotional response. Told of a friend's death, for example, a schizophrenic might laugh.

But Bleuler's term was soon popularized and widely misconstrued to mean split or multiple personality. Soon people were using "schizophrenic" whenever they had mixed feelings about something. "I don't think the average person understands anything about schizophrenia," says Guze.

Psychoanalytic explanations for schizophrenia proposed by followers of Sigmund Freud further confused people. In a theory now generally discredited, psychoanalysts blamed psychic trauma inflicted by parents on a child as the root cause of the disease.

In the midst of public misunderstanding, the psychiatric community has also been struggling to agree on the essential diagnostic features of the disease.

"If you have a very broad definition of schizophrenia, you're going to have a lot of patients with the disease," Guze says.

While the definition is narrower now, there is not yet complete agreement about all the symptoms essential to a diagnosis of schizophrenia. And some psychiatrists have wondered whether schizophrenia is a separate disease or merely one set of symptoms on a continuum of psychosis.

These questions arise from the lack of objective measures—blood tests or biopsies, for instance—to rely on in making a diagnosis.

"Diagnosis is based on the history of what has happened to the patient—the pattern of symptoms and signs—and the observations that a trained psychiatrist learns to make about a patient," says Guze.
Guze and Robins made a major contribution to this debate in 1970, with publication of a paper that used schizophrenia as an example in describing how to distinguish and categorize psychiatric disorders. Breaking new ground, they separated the clinical features of chronic cases from remitting ones. This paper, still influential, was used only recently as the organizing principle of a major psychiatric conference for the American Psychopathological Association.

At the same time, the Department of Psychiatry did what is now a widely known study of 500 psychiatric outpatients, including 60 schizophrenics. Years of follow-up confirmed that they could reliably diagnose schizophrenia as a discrete disease and predict which patients were likely to have a poor prognosis.

Then in 1973, the Robins-Guze approach was summarized in another important article the two co-authored with then-chief resident, John Feighner and other members of the psychiatry faculty. In it, they set specific diagnostic criteria for psychiatric research.

"For several years, that Feighner article was probably the most cited in American psychiatry," says Robert Cloninger, M.D., professor of psychiatry and genetics. "Its approach was officially adopted by the American Psychiatric Association. So this work set the stage for a revolution in clinical psychiatric practice."

SYMPTOMS AND TREATMENT

One patient wrote to scientists around the country frantically insisting that the government was implanting electrodes into the brains of unsuspecting citizens. Such delusions of persecution are common among schizophrenics, who may become convinced that neighbors, Communists or space aliens are trying to control them.

Hallucinations are another hallmark of the disease. Patients are often beset by voices that seem to be ridiculing them or encouraging them to do things they feel are wrong. They may see frightening images or startling colors, or feel horrifying sensations, such as insects crawling over their skin.

Disordered thinking is also typical. Unable to follow a logical line of thought, patients may become unintelligible. As one schizophrenic wrote: "No males, in my opinion, have ever gotten epidermis vibrations from organized crime bosses other than in a direct light encounter."

Late in the disease, blunted or flat affect often becomes an important symptom. The patient may say things without seeming to sense their emotional consequences. "You can talk to a patient who's depressed and understand what that person's feeling," says Guze. "You can talk to a patient who's schizophrenic and it's as if there were an emotional screen between you."

Contrary to popular myth, schizophrenics are not generally prone to violent outbursts. More often, their state of passivity and withdrawal makes them easy victims, readily preyed upon by those who are more aggressive.

Probing to find a cause for schizophrenia, scientists have sifted through medical histories of patients for common threads. Intriguing but inconclusive data has emerged. Children born in the late winter and early spring months may be more likely to develop the disease; some studies have revealed more prenatal and birth complications among babies who become schizophrenic.

In his work, Guze has classified patients according to "good" and "poor" prognosis cases. Among chronic schizophrenics, symptoms may develop insidiously in a child who is somehow "different": shy, awkward, unable to form close relationships. In more hopeful cases, the symptoms may appear abruptly and intensely in a previously well-adjusted adult.

Anti-psychotic medications or neuroleptics, first discovered in the 1950s, are widely used to help control delusions and hallucinations.

Generally safe, these drugs may cause unpleasant side effects, such as rigid neck, weight gain and photosensitivity. More serious still is tardive dyskinesia, involving involuntary movements of the tongue and mouth, possibly also legs and arms.

Even with these drugs, most chronic schizophrenics still require long-term therapy and substantial family or community support. "Our treatments for these patients are not optimal," says Early. "We have medications that suppress hallucinations and delusions, but most people do not lead happy lives with this disease. They still have a fair amount of disability."

GENETIC COMPONENTS

Along with its leadership role in the diagnostic issues surrounding schizophrenia, the Washington University Department of Psychiatry is now playing an important part in work involving the genetic and biochemical basis for this disease.

On the genetic side, investigators in the Clinical Research Center have recently started a "registry" of twins who have the disease and those who don't. Cloninger and Guze are also collaborating on a study in Norway, where excellent family records exist, to chart the occurrence of the disease through several generations of one family.

The question is no longer whether schizophrenia has a genetic component, at least in predisposing a person to the disease. Former Washington University psychiatric geneticist Irving Gottesman showed through his research that the risk of becoming schizophrenic can be 10 to 40 times greater than average if a person...
has one or more close relatives—especially a twin or two parents—with the disease.

“We’re not interested anymore in whether genes are important, but in which specific genes and what they do,” says Cloninger. “That way, we can understand the cause of schizophrenia and design rational treatments.”

The department has recently begun a St. Louis study headed by Keith Isenberg, M.D., assistant professor of psychiatry, to trace the molecular genetic causes of schizophrenia and develop a genetic marker which might be used to identify families with the disease. A team of investigators will also identify patients with at least one sibling who’s also schizophrenic, then hunt for other family members with the disease.

From blood samples of these patients, they hope to obtain DNA which, in the lab, may yield the genetic marker linked to susceptibility for the disease. New chromosomal tracking techniques being developed by Professor Maynard Olson, Ph.D., in the genetics department, should aid in this work.

What will they do with the offending gene? “If you can actually find the protein or enzyme that’s abnormal, there may be ways of repairing it or, a long way off, genetic therapy itself,” says Theodore Reich, M.D., professor of psychiatry and genetics, who is participating in this study.

This work may also provide a clue to the tantalizing question of penetrance: why some people apparently carry the gene, but never express it. “One of the exciting consequences of finding a genetic marker will be the ability to identify susceptible family members who have the schizophrenic genotype and who are therefore at very high risk of becoming ill,” Reich adds. “Then a very careful study will be devoted to what might have led to the disease.”

BIOCHEMICAL RESEARCH

Schizophrenia is an illness in which there are subtle changes in the structure of the brain. But they are mild in degree and we still don’t understand what abnormality in the brain’s physiological function causes the symptoms of this illness,” says Terrence Early.

He is trying to pinpoint that abnormality—and the precise brain structures involved—with the help of the powerful positive emission tomography (PET) system, which measures cerebral blood flow and oxygen metabolism. In his first study, published with Drs. Eric Reiman, Edward Spitznagel and Marcus Raichle, newly diagnosed, never-medicated schizophrenic patients were recruited for a study of regional cerebral blood flow.

The results surprised him. Patients had an abnormal increase in relative blood flow to the left globus pallidus, a structure located in the brain’s basal ganglia, long known to affect motor function and cognitive functions.

The left hemisphere link was further confirmed by a second study done in the neurology department’s cognitive neuropsychology lab, which tested the ability of schizophrenics to direct their visual attention. Patients were significantly slower to shift their attention to the right than to the left. In a separate test, they also demonstrated linguistic impairment. Both findings are consistent with left hemisphere injury.

Where precisely is this lesion? The clue may lie in the brain’s dopaminergic system. Dopamine is a neurotransmitter found in the brain, especially stimulating the dopamine system with certain drugs produces some of the symptoms of schizophrenia.

Anti-psychotic drugs, on the other hand, suppress hallucinations most likely by blocking the brain’s dopamine receptors. Current research seeks to identify which dopamine neurons are affected by those drugs and whether they show abnormalities that account for the symptoms of schizophrenia.

Another promising line of research in the Department of Psychiatry involves the common amino acid glutamate, which is found in high concentrations in the brain. Normally, it acts as an important neurotransmitter, briefly released from a brain cell in tiny quantities to excite nerve receptors and transmit a signal from one cell to another.

“But by the same mechanism it can also kill nerve cells,” says John W. Olney, M.D., professor of psychiatry and neuropathology, whose pioneering work over the past 20 years has established the growing field of excitotoxicology. “If allowed to accumulate outside those cells, glutamate can overexcite them and cause cell death.”

This accumulation may occur when there is a sudden breakdown in the brain’s delicate mechanism for holding glutamate in check and re-absorbing it after it has finished its excitatory work. Olney’s research shows that just such a damaging rush of glutamate may take place when there is a sudden deficiency in the brain’s supply of oxygen or glucose.

Not only does this explain brain damage from stroke or cardiac arrest, it also fits existing hypotheses about schizophrenia. Some scientists have speculated that the disease stems from subtle brain damage during fetal development. When the person grows to adulthood and needs full use of his damaged neural network, those systems break down and schizophrenic symptoms emerge.

That damage may be caused by a mild oxygen deficiency to the fetus. “If blood vessels from the placenta got compressed or twisted that could, tragically, cause reduction of the blood supply to the whole fetus,” Olney says. “But the most critical areas would be the brain, because a sudden outpouring of glutamate there would destroy some nerve cells.”

Using infant rat models, Olney’s team is now working to discover during which particular periods in fetal development in the brain are most susceptible to this damage. Eventually, they will relate these results to human gestation.
THE FUTURE

Some studies have shown that as many as a third of the homeless seen wandering our nation's streets are victims of schizophrenia. Society's neglect of these sick, often helpless, people has been called a national scandal.

Ironically, it is a scandal that grew out of good intentions. In 1963, Congress passed a bill providing funds for Community Mental Health Centers (CMHCs), which were supposed to radically improve the lot of schizophrenics. Hospital "warehousing" would cease; the CMHCs were to provide strong outpatient support for patients in their own communities.

But this brave new vision of deinstitutionalization failed. Today, most CMHCs specialize in providing psychotherapy for patients with "interpersonal problems." Chronic schizophrenics, discharged from state hospitals, have all too often gone without consistent care, rehabilitation services, even places to live.

"Nobody in his right mind could have opposed deinstitutionalization," says Guze. "But anyone who knew anything about patients in these hospitals knew that if you didn't provide the right kinds of programs, facilities and services, you were sooner or later going to have trouble. And we do have trouble."

Along with patients, schizophrenia research has suffered, too, from consistent underfunding. The $14 per schizophrenic spent each year on research compares to $300 per cancer patient and more than $9,000 per AIDS patient.

Some new hope has emerged lately, with a new national plan for research priorities in schizophrenia, developed this year by The National Institute of Mental Health (NIMH). Plans are also underway to set up a national gene bank, to facilitate large-scale molecular genetic studies.

The National Alliance for the Mentally Ill (NAMI), an organization composed of relatives and friends of the mentally ill, is also providing an eloquent new voice on their behalf. The group has taken a leadership role in demanding public recognition of the problems these people face and in providing support to families facing this tragedy.

Patients like John know too well the daily struggle required to live with schizophrenia. The same anti-psychotic drugs that keep his disease in check make him restless and cause involuntary finger-snapping. Unable to hold a full-time job, he does part-time volunteer work for a local church—hoping that eventually he will recover.

"The suffering of psychiatric patients and the devastating impact on their families is as great—and perhaps greater—than in any other group of illnesses," says Guze. "I want to be able to do a better job of taking care of people with schizophrenia and other disorders. And that, in the final analysis, is why our research is so important."
A little more than a decade ago, the children of Missouri—those both living and yet to be born—gained one of the best friends they’ll ever have.

It’s not that Ed Dodson suddenly developed an interest in the younger set. As a pediatric neurologist, Dodson, now 46, had chosen his life’s work in treating children’s diseases many years before. And, as the father of three children with another two to come, he shared firsthand a parent’s wishes that only the best might befall his offspring and others like them.

It was 11 years ago that William Edwin Dodson, M.D., professor of pediatrics and of neurology at Washington University School of Medicine, became so outraged that children were being neurologically destroyed through tragic occurrences of child abuse and neglect that he decided to do more than just treat their injuries. He decided to change the system that could have prevented such injuries from happening in the first place.

In 1977, Dodson—on staff at Children’s Hospital—treated an 18-month-old boy suffering from acute brain dysfunction. Through examination, Dodson determined the child had been asphyxiated during an incident of abuse.

“He was wrecked. He had to be institutionalized,” recalls Dodson, who says the final blow fell when the child’s male caretaker was tried for abuse but acquitted on all charges.

“I realized that area prosecutors didn’t know a lot about child abuse,” says Dodson. “We needed someone who knew what they were doing and had a special interest in these cases.”

So Dodson began a letter-writing campaign to local powers-that-be that resulted in the appointment of the first special prosecutor for child abuse and neglect in the City of St. Louis. It was a bureaucratic victory that whetted Dodson’s appetite for change in the state’s handling of child abuse cases, especially in the area of prevention.

“One case gets you started,” Dodson says. “People come in with a disease that’s preventable. Injuries inflicted on children should never happen. It offends the senses.”

Dodson became chairman of the Ad hoc Committee on Child Abuse Management at Children’s Hospital in 1977. In this capacity, he began to keep computerized records of children treated at the hospital for injuries and disease resulting from child abuse, and to chronicle similar patterns in cases.

Last year’s hospital child abuse statistics showed that 251 males and 376 females were treated for a variety of injuries resulting from both physical and sexual abuse and neglect. The average age of males treated was 4.2 years, and 5.3 years for females. Of those treated, 173 children were admitted to the hospital, producing an average hospitalization of 13 days.

Three children died.

The list of known perpetrators was led by mothers, followed by uncles, then fathers and live-in boyfriends.

While such statistics may shock the general public, Dodson finds them vital to targeting prevention programs. The need for such programs in the area became apparent about seven years ago, according to Dodson, when a young boy—one of eight children in a poor St. Louis family—died of pneumonia because his mother didn’t
provide proper medical care for a less serious illness.

Due to local media attention to the case, public outcry focused on the Missouri Division of Family Services (DFS), which is responsible for administering state child abuse treatment programs. But Dodson believed the solution lay in coordinating efforts of both public and private agencies.

He organized a series of informal breakfast meetings at Children's Hospital, inviting local law-enforcement officials, DFS staff, social service agency representatives and leaders from both Children's Hospital and Cardinal Glennon Children's Hospital in St. Louis. The result was increased communication.

"Ed made efforts in the St. Louis community to facilitate better coordination between programs," says William Siedhoff, deputy director of Jefferson City-based Missouri Department of Social Services and former director of the St. Louis City Office of Missouri DFS. "We had a fragmented effort in St. Louis. Everyone was doing his own thing."

Eds's is one of those all-important roles which are usually done by people who see the need. It requires someone with a lot of talent and willingness to deal with multiple groups of people. Ed recruited some of the local legal authorities as people who shared his commitment to attend the breakfast meetings at Children's Hospital."

Attendees of the informal group agreed that a private, non-profit agency needed to be established in St. Louis to address the problems of child abuse and neglect. "We needed an agency that wasn't partisan," Dodson says. "It had to be responsive to community needs."

The St. Louis Child Abuse Network was established in 1983, with Dodson serving as president of a board of directors made up of local professional and community leaders.

Through a grant funded by the Department of Health and Human Services, Human Development Services and the National Center for Child Abuse and Neglect, the Child Abuse Network convened a St. Louis Board of Inquiry to study "Fatal and Severe Child Abuse." The board studied 37 cases occurring in St. Louis between October 1983 and May 1985. Thirty-three of the cases were deemed to be caused by child abuse. Of the total cases, 11 children died; of 22 survivors, 10 were so severely injured they required institutionalized care.

Hospital costs incurred by survivors averaged $20,000. For survivors requiring lifelong custodial care, costs to society are expected to reach $2 million per child, including lost productivity time.

The study judged 18 of the 33 cases either preventable or displaying perinatal risk factors which indicated potential for abuse. "We couldn't identify any money being spent on prevention," Dodson says. "It was very clear we had something wrong."

Dodson explains. "We can look at families and know a family has a huge problem. Their kids have a three-fold higher mortality rate."

"First Step" received funding in 1987 to distribute donations from state income tax refunds earmarked for child abuse treatment and prevention programs.

Dodson became a governor-appointed trustee of The Children's Trust Fund in 1985.

"Up until this spring, the fund was only able to award $100,000 a year. This year, we'll award about $380,000," says Dodson with enthusiasm. "I'd like to see the trust fund spend $2 million a year. That's the cost of only one severely injured kid (for lifetime custodial care)."

The St. Louis Child Abuse Network joined with the St. Louis Regional Maternal and Child Health Council to create a targeted prevention program, titled "First Step." The program, created in 1985, links public health nurses with social service case workers to help families with high-risk factors for child abuse.

"We focus on the most difficult cases to prevent severe injuries and fatalities," Dodson explains. "We can look at families and know a family has a huge problem. Their kids have a three-fold higher mortality rate."

Dr. Dodson's war on child abuse occasionally takes him out of the hospital and into the courtroom. created in 1983 to distribute donations from state income tax refunds earmarked for child abuse treatment and prevention programs.

As co-chairman of The Missouri Department of Social Services Blue Ribbon Commission on the Future of Services to Children and Families, formed in 1987, Dodson has contributed heavily in suggesting changes to the state's current child abuse care system. The 40-member commission is scheduled to issue its 90-page final report this June.

Among other suggestions, the commission proposes a new governmental structure to administer child abuse treatment and prevention programs, including the addition of two key staff positions—a child abuse and neglect prevention coordinator reporting to the governor, and a
child abuse and neglect prevention specialist at DFS. The report also lists four detailed suggestions for more efficient operation of DFS in the area of child abuse program management.

"The commission said we need a government structure suitable for the task; child abuse prevention should be the highest priority; we should stop making (foster home) placements on availability instead of the child's needs; and we should spend money upfront on family preservation," says Dodson. "There's no single solution to this, but we've got to stop spending money only after kids are ruined."

Despite what may seem to be an adversarial relationship between Dodson and DFS, the state agency welcomes his remarks.

"DFS looks at Ed Dodson as a best friend in the sense that he's a constructive critic," says Michael Reagen, Ph.D., director of the Missouri Department of Social Services, who appointed Dodson to the Blue Ribbon Commission. "He's persistent and in the best sense an advocate. He cherishes children."

Dodson hopes publication of the commission's report will spur the community into action.

"The commission hopes the community will understand the problem and put pressure on the legislature to change it. . . . This is an election year. We hope politicians will read this and be motivated to do something about child abuse prevention," Dodson says. "Somebody needs to be in charge of developing an overall plan. We hope to get the governor's attention."

In addition to his work with the Blue Ribbon Commission, The Children's Trust Fund and the Children's Hospital Ad hoc Committee on Child Abuse Management, Dodson also serves on the board of directors of the Family Resource Center in St. Louis, as board chairman of Children's Welfare Services in the City of St. Louis and on the board of directors of the Missouri Chapter of the National Committee to Prevent Child Abuse.

When asked how much time he puts into the area of child abuse prevention advocacy, he answers rather modestly: "a lot." Fellow child abuse and neglect prevention advocates are more specific.

"If it wasn't for his time and energy, the St. Louis Child Abuse Network wouldn't be in existence," says Lee Ann Taylor, ACSW, Children's Hospital child abuse/neglect management coordinator. "He squeezes all these things in a busy neurological practice. He always finds the time. . . . I'm not exaggerating when I say he burns the candle at both ends."

Adds James Spanierower, Ph.D., president of Lindenwood College in St. Charles, Mo., and a member of the Blue Ribbon Commission: "I don't think I've met anyone who better combines a knowledge of what ought to be done about child abuse with an inspirational commitment to getting something done."

"He has a tremendous grasp of the issues, a strong commitment and the willingness to do everything that has to be done to further the cause, whether it be attending a board meeting or typing a letter," says Bill Franke of The Gannon Co. in St. Louis, another Blue Ribbon Commission member. "Ed Dodson has made many sacrifices to do this. He's been up until four in the morning many times working on aspects of a child abuse program because it had to get done."

Ironically, most of the time Dodson puts into the area of child abuse prevention does not produce the kind of output usually rewarded in an academic setting. As far as research goes, child abuse studies rarely meet quantifiable standards for publication. Dodson focuses on epilepsy treatment as his area of research expertise.

"It seems to me that doctors and others dedicated to helping people have two major tasks—to keep a problem from getting worse and making things better," says Michael Reagen. "Ed Dodson's dedication to child abuse advocacy talks about the character of the man and the value he places on his skills."

Adds William M. Landau, M.D., head of neurology at Washington University School of Medicine and Children's Hospital: "He's a very responsible physician because he saw a problem no one else would tackle. It's not an usual activity for a child neurologist. I'm very proud of his accomplishments. . . . We at Washington University and Children's Hospital think it's important."

Harvey R. Colten, M.D., Harriet B. Spoehter Professor and head of pediatrics at Children's Hospital, echoes Landau's words in describing university appreciation of Dodson's work in child abuse prevention.

"He's very committed to this area," says Colten. "It's one fraught with problems for busy people. Becoming embroiled in these legal and social issues can be time-consuming. I think it's just the importance of the issue. I'm delighted he is involved. The executive faculty, ad hoc committees and leadership of the pediatrics department do recognize his contribution."

Patty Wolfe, executive director of The Children's Trust Fund, who has worked in social services the past 12 years, describes Dodson as "an extraordinary example of a medical doctor being involved in this."

"I think a lot of physicians are willing to put their name on the dotted line or make a contribution," says Sue Stepleton, administrator of The Salvation Army Hope Center in St. Louis, and a Blue Ribbon Commission member. "I think Ed Dodson views his advocacy responsibility as important as his medical responsibility."

Dodson doesn't seem to separate the two areas.

"What we do in the hospital is only five percent of the issue . . . We patch them up and they leave our doors. But what are we sending them back to?"

Dodson describes the area of child abuse prevention as a real issue of government bureaucracy—an area in which he's become self-educated during the last 11 years.

"I know how to take care of a kid who's neurologically sick. I'm trained extensively for that," Dodson says. "But no one could tell me how to deal with these legislators."

As frustrating as it can be at times to try to change government systems, Dodson points to major victories such as the increase in funding to The Children's Trust Fund during the last few years. Those kinds of victories are what keep him involved in child abuse prevention issues.

"You've got to decide what you think is important. You can solve different problems within different means," Dodson says. "This is an important issue to clinical child neurology. If I can help prevent a number of head injuries from occurring, I've done something."

"Everybody thinks it's important, and somebody's got to do this. I just came to the conclusion that I wasn't the person to do this but neither was anyone else."
The Dark Side of Sunshine

BY ROBERT LOWES
In contrast with the era when "those things were never talked about," the entire subject of skin cancer is now undergoing microscopic scrutiny. And little wonder. The incidence among the three major varieties of skin cancer—basal cell carcinoma, squamous cell carcinoma and malignant melanoma—is increasing 3 to 5 percent a year, according to the American Academy of Dermatology in Evanston, Ill. Over 500,000 new cases are predicted for 1988, and the Skin Cancer Foundation in New York expects that figure to double in 25 years. Sometime during his life, one of every seven Americans will become another Richard Tibbs.

Malignant melanoma is the deadliest skin cancer, claiming some 5,800 lives annually. And it is on a rampage. In the 1930s, the incidence was one in 1,500 people, according to the Skin Cancer Foundation. It is now one in 127. The number of expected cases this year: 27,300. (While it is often called malignant melanoma, there is no such thing as a non-malignant melanoma.)

Skin cancer is the most common of cancers, yet it is the most curable. The National Institutes of Health reports that 95 percent of skin cancer patients are rid of their disease following medically approved treatment. At the same time, skin cancer is deceptive. Basal and squamous cell carcinomas can take 20 to 40 years to develop. Melanoma may appear 2 years after one blistering episode of sunburn in childhood.

Although skin cancer can arise from exposure to such diverse substances as coal, arsenic compounds and radium, sunlight is the number one culprit. Specifically, it is the ultraviolet rays of sunlight, the same rays that stimulate production of vitamin D in the skin. As is so often the case, moderate amounts help while excessive amounts harm.

Celebrity case studies are alerting the public to the dark side of sunshine. President Ronald Reagan, once enamored with deep tans, had basal cell carcinomas removed from his nose in 1985 and 1987. "I don't mind telling you all this because I know that medicine has been waging a great campaign to . . . convince people to stop broiling themselves in the sun," Reagan said after his first operation.

Solar broiling arises from a complicated interplay of society and environmental forces. Ann Martin, M.D., instructor in dermatology and clinical Director of the Dermatology Outpatient Center at Barnes Hospital says that our leisure-oriented lifestyle is putting us into the sun's spotlight. And suntans—cultivated on the beach and in tanning spas—have been equated with health and beauty.

"In the last century, women were looked at as lower society if their hands were tanned," says Martin. "That meant (they) worked in the fields. They wore large bonnets, gloves, long dresses and shunned the sun."

The population shift to the Sunbelt states has dramatically increased sun exposure for millions. To make matters worse, Martin says, the depletion of stratospheric ozone is allowing more ultraviolet radiation to reach the earth's surface and cook everybody.

At greatest risk are light-completed individuals who have difficulty tanning. A tan is nothing more than the skin's production of a dark pigment called melanin, which absorbs ultraviolet rays. Blacks have the most melanin and rarely suffer from skin cancer.

Gradual, cumulative exposure to ultraviolet rays appears to produce carcinomas of both basal and squamous cells, according to Martin. Basal cells are located near the bottom of the epidermis—the skin's outer layer—while squamous cells make up most of its surface. Martin says that ultraviolet rays trigger the carcinomas by inflicting wholesale damage to the dermis and epidermis and, in the process, damaging the DNA of the basal and squamous cells. Researchers suspect that ultraviolet rays promote skin cancer by also suppressing the body's immune system.

The basal cell carcinoma, which accounts for 80 percent of all skin cancers, resembles the work of a devilish jeweler. Martin described it as a translucent, pearl-like papule with a rolled border. At its center is an erosion, crust or ulcer that may be studded with various pigments. This type of skin cancer rarely metastasizes, or spreads to other organs.

Squamous cell carcinomas, which make up 15 percent of all skin cancers, are scaly, pinkish growths which, like basal cell carcinomas, may ulcerate in the center. Both skin cancers can become massive enough to damage surrounding tissues, leading either to disfigurement or death. Together they cost some 2,000 lives in 1987. But they are normally curable if detected and removed early.

A melanoma contains cancerous melanocytes, which are pigment-
producing cells. The cancer usually appears as an asymmetrical, brownish-black spot or bump that sometimes bleed. Typically, it measures more than one-fourth inch in diameter and develops ragged borders. The colors of Old Glory—red, white and blue—may appear. Melanomas sometimes arise in preexisting moles, particularly dysplastic nevi, a variety which resemble melanomas.

Dysplastic nevi often serve as harbingers of melanoma if the patient's relatives also have dysplastic nevi and have developed melanoma themselves. The growths, therefore, warrant either removal or careful monitoring.

The origins of melanoma are not clearly understood. Martin says the working hypothesis today is that short, intense exposure to ultraviolet rays—the formula for a bad sunburn—brings on this most dangerous of skin cancers. Again, societal trends explain the cancer's upswing.

"Malignant melanoma is a disease of the affluent," says Martin. "People are inside all the time. Their vacation is to get on a plane, fly south, bake for two weeks and come back."

With these brief binges of sun worship, she explains, the body does not have sufficient time for its melanocyte cells to produce enough protective melanin.

A study conducted in both Great Britain and the state of Washington showed that professional workers had the highest mortality rate owing to melanoma. Following them, in order, were clerks and salesmen, skilled craftsmen and unskilled labor. Another study found that office work correlated with primary melanomas on the trunk and extremities, suggesting these normally clothed parts of the body had been exposed during recreational activities as opposed to working hours.

The classic melanoma victim is a Caucasian of Celtic origin with light skin, light hair and blue eyes. Other factors implicated, but not firmly established, in the etiology of melanoma include oral contraceptives, fluorescent lighting and diets poor in certain vitamins.

The latency period for melanoma is shorter than that for basal and squamous cell carcinomas. Many victims are in their 30s and 40s. Their condition may have stemmed from severe childhood sunburns, says Martin.

"That's the message we're trying to get across," she says. "Keep your children protected. Do not let them get sunburned."

Like basal and squamous cell carcinomas, melanoma is almost 100 percent curable if treated early. To battle any of the three major skin cancers, physicians possess a number of weapons: simple surgical excision, electrical current destruction, radiation therapy, chemotherapy and freezing. A topically applied cream called 5-fluorouracil can eradicate superficial lesions as well as actinic keratoses, a precancerous skin condition characterized by rough, red patches.

In the case of melanoma, physicians sometimes employ experimental therapies such as the proteins interferon and interleukin-2 to bolster the body's immune system. But Martin says that the toxicity of these proteins has limited their usefulness. "They're really difficult to administer," she says. "People have become acutely ill." Researchers also are attempting to develop vaccines that would arrest the growth of melanoma.

Assessing the size of a tumor resembles judging an iceberg by its tip, says Zachary. There's more than meets the eye.

Mohs microscopic surgery, also called chemo surgery, consists of removing progressively deeper layers of skin and scrutinizing them under a microscope for cancer cells. Each layer of skin is cut into sections, color-coded for later identification, mapped into quadrants and frozen. The tissue is then sliced horizontally into four or five sections only six microns thick—about the thickness of two cells. These shavings are then mounted on slides and stained. If cancer cells are anywhere in the first set of slides, the surgeon removes a second tissue sample from the patient and repeats the process. Usually, it takes no more than three slices to ensure the removal of the entire tumor. The patient can rest in a waiting room between excisions and have his entire tumor removed within four or five hours.
What's more, Mohs surgery allows the surgeon to avoid unnecessary excisions. If Zachary finds a trace of cancer in a particular quadrant of his slice, his next slice will be limited basically to that section. Patients concerned about disfiguring facial surgery appreciate the precision of Mohs.

"The whole thing about Mohs surgery is that it is a tissue-sparing procedure," says Zachary. Dermatologic surgeons like Zachary prefer Mohs for tumors on delicate skin structures of the face. When patients have recurrent tumors in these areas, such as those around the eyelids, the success rate of ordinary surgical methods is about 50 percent. With Mohs microscopic surgery, he said, the success rate rises to about 99 percent.

Traditionally, specimens of excised tumor were examined by slicing vertically, like a loaf of bread, to search for residual cancer cells. Some cancer can escape notice, using this technique. Moh's surgery requires specimens to be sectioned horizontally, thereby examining 100 percent of the free margin of excision.

Most Mohs surgical centers treat only basal and squamous cell carcinomas. Zachary says that melanoma is hard to spot on frozen-tissue slides.

Hunched over a microscope, Zachary is a laboratory detective, hunting down suspicious-looking shapes in a bizarre cellular landscape.

"There's a hair follicle there—nothing to worry about," he said during one investigation, pointing to a circular shape in a tissue sample from a female patient. He then spotted an array of lymphocytes which looked like so much sprinkled rice.

"There's a lot of inflammation there. That's a tell-tale sign. Nine times out of 10, if you see inflammation, you'll find cancer if you cut deeper.

Zachary was initially pleased when he viewed slides from the first tissue layer taken from Tibbs, the retired postal worker.

"At first glance, this looks pretty good," he said about the slides. Then he spotted tumor budding off a hair follicle in one half of the tissue sample. And there was a large cluster of tumor in the other half. Zachary would have to go deeper.

A nurse summoned Tibbs back into an operating room, where he endured another shot of anesthetic. Zachary snipped off a second saucer of skin and said, "If I haven't got it all out, I'll eat my hat.

The second set of slides revealed yet more evidence of cancerous basal cells. Zachary told a frustrated Tibbs the news. "I don't know how far this extends, but we go until we get it all out, okay?" Tibbs lifted his hands in the air in agreement and resignation.

The third set of slides were the last. "He's looking good, very good," said Zachary, scanning the slide from top to bottom and side to side. Finally, he said the longed-for words: "He's clean."

Betty Byrd, the licensed practical nurse assisting Zachary, went out into the waiting room and told Tibbs, "We got all your cancer out." Tibbs leaned forward, smiled and said, "Good for you." His wife Marie—relieved, but still anxious—said nothing.

The good news did not signal the end of Tibbs' surgery. Now the wound had to be closed. About 25 percent of the wounds are allowed to heal naturally. Zachary uses skin grafts and flaps to close another 60 percent. He refers the remainder—the more problematic cases—to a plastic surgeon or an ear, nose and throat specialist.

When Zachary excises skin cancer, he is potentially saving a life. When he repairs the damage, he is striving to save the patient's self-image. After all, the patient must look at himself in the mirror. "They won't look good on day-one or a month later. But after six months, the majority looks very good. But they have to pass the shopping line test—whether anybody in the line recognizes they've had surgery. The majority do very well." Tibbs' wound covered most of his left nostril. After discussing his options with Zachary, Tibbs chose a skin graft. One more time, he submitted to a needle full of anesthetic—the worst part of the surgery for him. Zachary removed a patch of skin in front of Tibbs' right ear, trimmed it and sewed it on Tibbs' nose. The wound near Tibbs' ear was closed with a flap of loose facial skin. Tibbs, bandages and all, left the hospital with his wife about 5 p.m.—ready for supper.

Tibbs is careful to wear a hat outside these days when he's watering his begonias and impatiens, but not everyone learns the obvious lessons about sun and skin. A poster published by the Skin Cancer Foundation shows a young woman in a bathing suit holding up a reflector to brown her neck with sunlight. The poster reads: "When people find a better way to cure skin cancer, people find a better way to get it."

One commonsensical precaution is to avoid sunshine at its harshest. In the summer, that's between 11 a.m. and 3 p.m.

To save your skin, you also need to know its type. There are six. Type I, found in people of Celtic origin, always burns and never tans. Type VI, found in blacks, never burns because of its deep pigmentation. The average Caucasian has Type III skin, which burns moderately and tans to a light brown.

Understanding these skin types will help in choosing the right sunscreen for outdoor activities. Sunscreens protect skin by absorbing, reflecting and scattering ultraviolet light. They're rated according to their sun protection factor, or SPF. Multiply the SPF by the amount of time it normally takes to sunburn, and that's the amount of time that can safely be spent in the sun using that sunscreen.

"If you were to apply a sunscreen with an SPF factor of 12," says Martin, "you would have to sit in the sun 12 times longer to get a sunburn than if you had not applied any sunscreen at all."

"Individuals with normal skin types, like types two or three, can have up to five or six hours of unprotected exposure with application of SPF 15," says Martin. "But one needs to reapply sunscreens. Sunscreens dilute when you sweat and swim. Some advanced sunscreens, she says, are waterproof.

The American Academy of Dermatology advises the average person to use a sunscreen with an SPF of no less than 15, according to Martin. Patients with extremely sensitive skin may need higher SPF factors as advised by their dermatologists.

Martin also recommends rubbing in generous doses. "Most individuals don't apply the amount of sunscreen that was applied in the laboratory situation that created these SPF factors."

Of course, medical experts say that long pants, long-sleeved shirts and broad-brimmed hats provide the best solar protection. So does staying in the shade.

At least where skin cancer is concerned, it pays to be a "shady" character.

Christopher Zachary, M.D., recently accepted a new post as director of cutaneous surgery at the University of Minnesota in Minneapolis.
When they think of summer, most people think of baseball, barbecues, swimsuits and ice cream. David Russell, Ph.D., thinks of lampreys—those ferocious, bloodsucking eel-like creatures that hatch in the Great Lakes and rivers of the Midwest during June and July.

Why lampreys? Because they are ideal for studying how the brain controls respiration and how certain drugs and anesthetics affect this control, according to Russell, who has been studying lampreys for about six years. Such studies may not only help answer the basic question of how we breathe, but also provide new insights into apnea—a cessation of breathing related to Sudden Infant Death Syndrome—and other types of respiratory disorders.

A very primitive animal, the lamprey branched off relatively early from the ancestral stem vertebrate that later gave rise to all vertebrates, including man. It has since followed its own evolutionary course, remaining virtually unchanged for 300 million years.

By studying lampreys, Russell hopes to find remnants of the original primitive neural system for breathing. "It's reasonable to think that humans have that same system within our own brain, but that we've probably added a lot of sophisticated gear on top of it to handle the special requirements of breathing air and breathing in an upright position," he says.

While it may not be too appealing to consider these aquatic parasites as related to ourselves, there are enough resemblances to reasonably conclude that in studying lampreys, one may find out something about people, according to Russell, who is an instructor in anesthesiology at Washington University School of Medicine.

Lampreys have a series of seven openings, or gill sacs, along each side of the head that function much like human lungs, in that they are linked with capillaries through which gas is exchanged, and use muscles to change volume as water or air moves in and out. They are also one of the few aquatic animals to respire tidally. That is, they inspire and expire through the same hole, as do humans. Most fish and other aquatic animals draw water in through the mouth and expel it via the gills, which would be nearly impossible for the parasitic adult lamprey because its jawless mouth is so often sucking the side of a fish.

Yet there are substantial differences between lampreys and most mammals that make lampreys much easier to study. For one, the adults do not feed when they spawn and can be kept for up to a year just by chilling them down.

Even more important is the fact that lampreys do not both inspire and expire actively. Although they use muscles to push water out of their gill sacs, water is drawn in through passive relaxation. "If you compare it to a mammal, you've thrown away half the respiratory system," Russell says. "That straightaway simplifies things considerably."

Lamprey brains are also much more transparent, with large nerve cells that can be easily observed, according to Russell's mentor, Carl Rovainen, Ph.D., professor of cell biology and physiology, who is referred to by his colleagues at the School of Medicine as the "grandfather of lamprey neurobiology" because he was the first researcher to work with the lamprey nervous system.

The most important difference, however, is that the lamprey brain can be removed and studied apart from the rest of the body. Once removed, the lamprey brain will survive and continue to produce a spontaneous breathing rhythm. In contrast, the brains of most mammals would die within minutes from lack of oxygen, which is ordinarily supplied to the brain via the blood. The lamprey brain survives because it is highly resistant to this lack of oxygen, or hypoxia. "Some animals have just evolved special ways of running their cells that make them less susceptible to loss of oxygen, consistent with their life form of staying underwater or swimming in water that lacks oxygen," Russell says.

Once the lamprey brain has been isolated, its respiratory rhythm can be heard and recorded by attaching an electrode to the vagus nerve. "What you hear is the discharge of cells in the brain that control the respiratory muscles," Russell explains. "This is the respiratory rhythm. All we've got here is the isolated brain—there are no muscles or anything; the rest of the body is gone. So it's producing what's called a fictive rhythm. It's not really respiration, because there are no muscles to contract or expand. But it's the neural pattern that drives respiration and could be recorded in any animal if you went into the animal and recorded from its respiratory nerves."

Russell would like to know how this neural rhythm arises. By listening to the metronome-like clicking of the pattern which repeats itself once every second, Russell tries to locate and identify the nerve cells that are producing this pattern and to map the connections between them. To do this, he uses special dyes that kill nerve cells when exposed to light. Known as photoinactivation, this technique enables Russell to selectively get rid of nerve cells to determine whether or not they are necessary for the production of the respiratory rhythm. "If you have two types of neurons, for example, you can ask: Is neuron two required to produce this pattern? And you can answer that..."
The Misunderstood Lamprey

N otorious for the invasion of the Great Lakes and near destruction of the lake trout and whitefish, lampreys actually spend the majority of their lives as small, blind, toothless larva that burrow in streams and eat vegetable matter.

It is only in the last year of their seven-year life cycle that they develop teeth and eyes, begin to prey upon other fish and whales, and quadruple in size.

Lampreys attack fish by boring holes into the sides of the fish with rasp-like tongues. They then attach themselves with sucker-like mouths lined with teeth and proceed to suck the body juices out of their prey. Keeping the wounds open by secreting an anticoagulant, lampreys feed for several days before releasing their victims, which usually kills or fatally weakens most smaller fish.

In the spring, adult lampreys enter the rivers to spawn. Migrating upstream, they often traverse steep grades—even vertical walls and dams—to reach their final destination. Males and females scoop out their nests together in the sandy gravel, where the female lays many, tiny eggs. Then both parents die.

Lampreys first appeared on earth about 300 million years ago and have remained relatively unchanged throughout evolution. During the 20th Century, a very voracious variety entered the Great Lakes via the St. Lawrence Seaway, and became landlocked. By 1950, they had almost completely devastated the lakes’ populations of trout and whitefish. Since then, the U.S. Fish and Wildlife Service has established a number of biological stations around the Great Lakes to get rid of the lampreys with poisons called lamprecides.

In Europe, however, it is the lamprey that is endangered, due to construction of dams and excavations of gravel. There, the lamprey is considered a delicacy—especially in Finland and the Bordeaux area of France. Sold whole or in cans like tuna fish, lamprey is the only fish that should be consumed with red wine, as its flesh is dark and somewhat oily. A European lamprey aficionado might handle the popular marine animal this way:

**Lamprey Au Vin**

1. Bleed and skin lamprey, lightly frying to reduce fat.
2. Add precooked, fresh leeks, diced ham and a half bottle of red wine.
3. Bring to a boil with a pinch each of thyme, laurel and garlic.

*Bon appetit!*

question by staining neuron two, killing it by illumination and then asking: Does the rhythm continue? If it continues, then neuron two is obviously not necessary for the production of the rhythm.

Because Russell studies the lamprey brain separately from the rest of the animal, he can alter its ionic content to manipulate certain parameters of nerve cell activity. For example, nerve cells do not always communicate directly with one another, but often pass information along through a system of relays. Researchers have long struggled to distinguish such relays from direct connections between cells, but have not had much luck. "That’s really difficult inside an animal when you’re restricted to the ionic content of the blood," Russell says.

On the other hand, it is relatively easy to add a solution of elevated calcium to the isolated lamprey brain, which blocks the relay and allows only direct connections between cells. "You simply turn a valve, introduce a new solution, wait 10 minutes and collect your data," Russell says. "In 10 minutes, you’ve done an experiment that someone working within an animal could not do in a lifetime."

The isolated lamprey brain also allows for the bath application of drugs, which is highly useful in the search for drugs that enhance respiration. In an intact animal, it is hard to get drugs across the blood brain barrier—a mechanism that ordinarily keeps harmful substances from crossing through the lining of the blood vessels into the brain. "It’s also very complicated, because you have interactions of drugs with the rest of the body, not just with the part of the brain that controls respiration," Russell says. But in the isolated lamprey brain, "you can do a clean experiment and be sure that drugs are only acting on the brain and not on the muscles or some other peripheral mechanisms."

**Using the isolated lamprey brain as a model, Russell and a visiting faculty member from Osaka University in Japan, Makoto Takenoshita, M.D., have recently been successful in similarly isolating the brains of newborn rats—a preparation they are currently using to screen for drugs that may alleviate respiratory disorders.**

"Newborn rats seem to work because they’re small and especially resistant to hypoxia, a characteristic that aids them in their passage through the birth canal," according to Russell.

One common respiratory disorder among newborns, especially premature ones, is apnea, or the cessation of breathing. There are different types of apnea, Russell explains. One type is due to a blockage of the airway, while in others (central apnea) the brain simply stops producing the respiratory rhythm.

"The human brain responds paradoxically to hypoxia during birth," Russell says. "You’d think that when an infant experiences the lack of oxygen as it passes through the birth canal, it would try to compensate by bringing in more oxygen. Yet the exact opposite occurs. Respiration shuts down under hypoxic conditions."

One explanation for this is that the brain sedates itself by producing endogenous morphine-like compounds, or opioids. Clinical evidence for this is most striking in cases where newborns are treated with antagonists to opioids, and it relieves their apnea. Russell is currently using the newborn rat preparation to observe the action of the opioid antagonist naloxone, which entails dissolving the drug in saline and then letting it flow over the brain. "It’s simple and quick to do," Russell says. "We can screen a number of drugs in just one day."

Respiratory insufficiency can also be caused by anesthetics, which depress respiration. In some cases, respiration does not resume after the anesthetic has worn off, and in some hospitals it is standard practice to administer drugs that stimulate respiration as patients come out of anesthesia. Russell and Takenoshita are using the isolated rat brain to characterize the respiratory actions of anesthetics and drugs that counteract them. It was previously thought that anesthetics depress respiration by acting directly on the rhythmic respiratory neurons in the brain. Russell’s studies, however, show that volatile anesthetics depress respiration, in part, by blocking the spinal cord.

A better understanding of the respiratory rhythm may also impact two breathing disorders in which patients experience intermittent periods of apnea with rapid acceleration of breathing: Cheyne Stokes Breathing (which is fairly common among people exposed to high altitudes, patients with heart disease and sedated, elderly patients) and Biot’s Breathing (which is neurologic in origin).

The ultimate goal of Russell’s work with the lamprey, however, is much more basic. He would like to be able to answer the question: How do we breathe? “That’s a very important question,” he says, "because breathing is something we can’t do without.”
Alumni Achievement Awards:

Henry L. Barnett, M.D. ’38, founding chairman and Professor Emeritus of Pediatrics at Albert Einstein College of Medicine at Yeshiva University in New York, devoted his 50-year medical career to pediatric health care. The current medical director for the Children’s Aid Society in New York City, Barnett is a recipient of one of the most distinguished awards in pediatrics—the American Pediatric Society’s John Howlett Award—for his research on kidney and urinary disease in children.

Edwin G. Krebs, M.D. ’43D, Senior Investigator at the Howard Hughes Medical Institute in Seattle, has devoted most of his medical career to research, an interest that began while he was a medical student. Today Krebs is a noted biochemist whose research has helped the medical community better understand metabolism and hormonal actions, shedding new light on particular causes of metabolic disorders. As a leading educator, he helped start the University of Washington Medical School in Seattle.

Seymour Reichlin, M.D. ’48, Professor of Medicine and Chief of the Endocrine Division at Tufts University at New England Medical Center, has distinguished himself in neural science and endocrinology and is internationally recognized for his research. He has continuously directed training programs in endocrinology, assisting many students who have also achieved distinction in leading medical schools throughout the world. Reichlin was the first chairman of the department of medical and pediatric specialties at the newly founded University of Connecticut School of Medicine.

Alumni/Faculty Awards:

Samuel B. Guze, M.D. ’45, Spencer T. Olin Professor of Psychiatry and Vice Chancellor for Medical Affairs, helped lead psychiatry into a new age. Board certified in both internal medicine and psychiatry, Dr. Guze expertly combines research, administrative and clinical skills. As a teacher, Guze has trained numerous students who have also distinguished themselves throughout the country. He has been extremely active in research and treatment for alcohol abuse and is currently the principal investigator at the Alcohol Research Center at Washington University, the only continuously-funded research center on alcoholism in the United States.

Mary L. Parker, M.D. ’53, associate professor of medicine and director of the student health service, has demonstrated great concern for the university student by organizing and upgrading the student health service. She is recognized by her colleagues for her investigative work in studies of growth retardation in children and for developing methodology for measuring growth hormones. Parker is extremely active in community health through a community outreach program that surpasses the boundaries of the university and was the first woman president of the Washington University Medical Center Alumni Association.

Hyman R. Senturia, M.D. ’33, professor emeritus of clinical radiology, is recognized by his colleagues and students as an outstanding radiologist and physician who is dedicated to the education of students and house staff. Outspoken and friendly, he has won the admiration of students with his superb skills as a teacher, exemplified by the number of senior students who flock to his radiology elective. They have honored him by electing him Teacher of the Year on four separate occasions.

Distinguished Service Award:

Winfred A. Showman, M.D. ’21, devoted most of his medical career to his 50-year dermatologic practice in Tulsa, Oklahoma, where he was one of the first regional physicians to use cortisone treatment successfully for patients with pemphigus, a condition characterized by skin lesions. He and his wife established the Winfred A. and Emma R. Showman Professorship in Dermatology at the School of Medicine, a contribution of lasting impact.
Joshua Jensen, M.D. '38, welcomes the class of 1988, represented by Mary AndrofJ, to the Alumni Association.

Assistant Vice Chancellor and Director of Development Mark Bates gives John P. Roberts, M.D. '45, and his wife Tove a "walking tour" of the new library.

John Patton, M.D. '28, is welcomed to the banquet cocktail party.
Winfred A. Showman, M.D. '21

F. Dale Wilson, M.D. '38, (right) and James Cravens, M.D. '43D, at the Vice Chancellor's Recognition Breakfast.

Associate Dean John Herweg, M.D., reads a list of one student applicant's extra-curricular activities as part of Saturday evening's entertainment.

Howard Steiner, M.D. '38, and wife Eleanor
A legacy at their 50th and 20th reunions, the Drs. Larry Kotner.

Bill Seidler, M.D. '43M, and wife Mary dance to the music of the "Hot Docs."

Alumni and spouses at the St. Louis Art Museum.

Stanley Burris, M.D. '53
F. Dale Wilson, M.D. '38, and Mike Karl, M.D., professor of clinical medicine.

Dallas Anthony, M.D. '43M, receives an update from the new President of the Alumni Association, Ron Evens, M.D. '64.

"Where and When"

Second-year students provide the finale to the Saturday evening banquet.
Alumni learn about the latest research at scientific sessions.

Alumni Association President Thomas Richardson, M.D. '63, surprises Samuel Guze, M.D. '45, with an Alumni Faculty Award.

Drs. Ron and Elizabeth Sowa dance away their 25th reunion.
Russell Blattner, M.D. '33 (left) renews acquaintances at the Dean's Luncheon.

Henry Royal, M.D., associate professor of radiology, explains the PET process.

Charlotte Hagemann (center), Ella Mae Magness (left) and Marilyn Arneson

Dr. and Mrs. Michael Reif, Class of 1968, chat with Dean M. Kenton King.
Spouse's program fashion seminar at Plaza Frontenac.

Drs. Ray Charnas and Burte Guterman at the Class of 1943 March dinner.

Capturing the night.

Marv Levin, M.D. '51, presents Alumni Lifetime Membership Certificates to the Class of 1938.
John Wilson, M.D. '43D, and wife Helen

Mark Frisse, M.D. '78, (right) enjoys the welcoming cocktail party.

Harold Kent, M.D. '78, and Kathleen Kavanagh

C. Read Boles, M.D. '43D
Construction progress on the new School of Medicine Library and Biomedical Communications Center is symbolized by the July “topping out” ceremony. Library committee chairman Bernard Becker, M.D., (right) is joined by library director Susan Crawford, Ph.D., (left) and associate librarian Barbara Halbrook as the final bucket of concrete is hoisted to the seventh floor. The new $15 million library is expected to be ready for occupancy in May 1988.
This spring, the School of Medicine graduated 124 M.D. candidates, 26 health administrators and 21 occupational therapists. Physical therapy, which graduates most of its seniors in the fall, graduated 48.