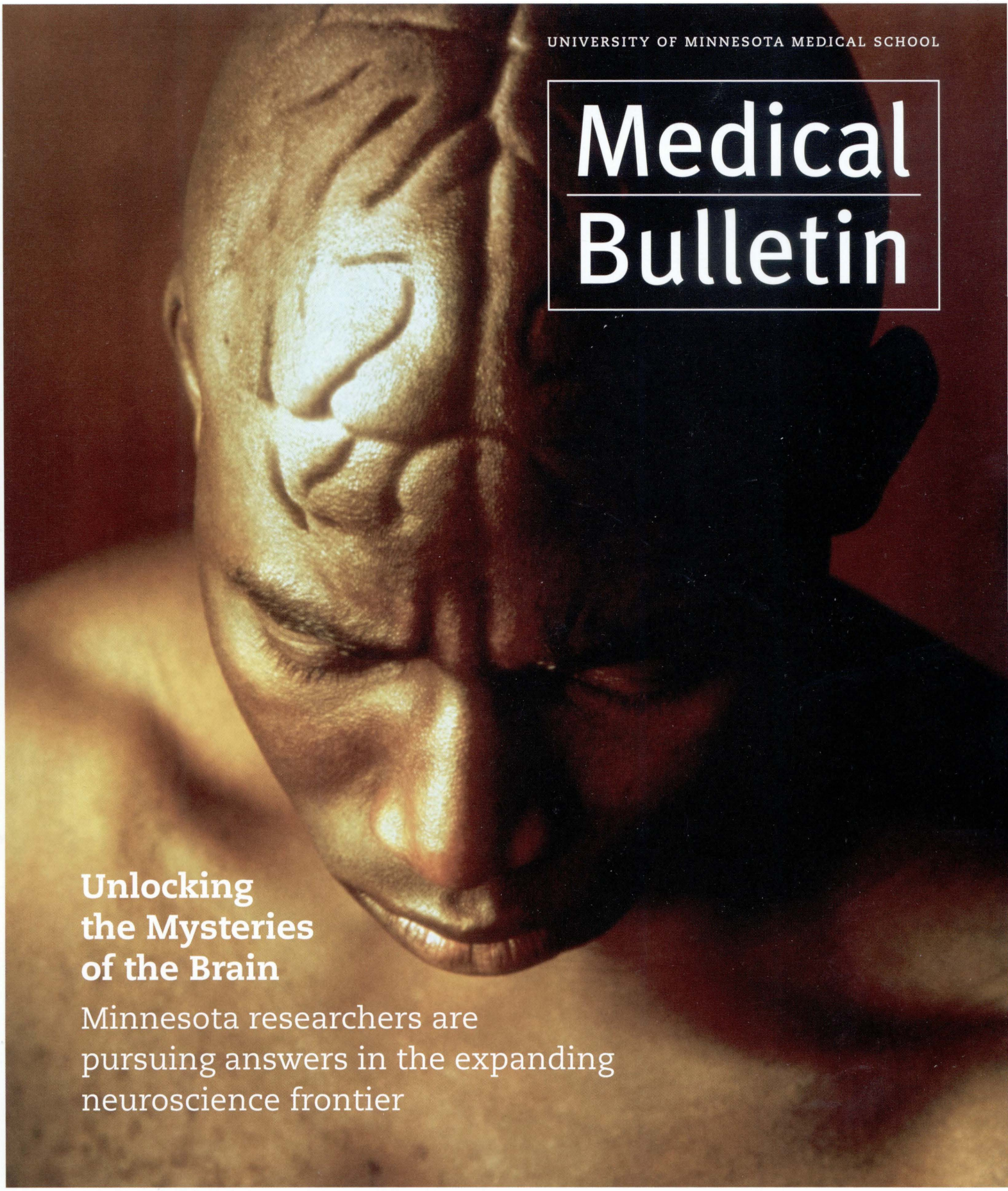
A PUBLICATION OF THE MINNESOTA MEDICAL FOUNDATION

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL

# Medical Bulletin



## Unlocking the Mysteries of the Brain

Minnesota researchers are pursuing answers in the expanding neuroscience frontier

**WINTER 2005** Bringing light to mental illness ☐ The aging brain and Alzheimer's ☐ Regaining control of Parkinson's disease ☐ Exploring the link between a sleep disorder and neurodegenerative diseases

## DEAR FRIENDS,

The human brain is an endlessly fascinating organ. During the earliest days and years of development, our brains generate a set of neural circuits more powerful than a supercomputer. As we grow, learn, and age, our brains adapt in ways we're still trying to fully comprehend. When our brains show signs of disease or disorder, the questions multiply.

The answers may be elusive, but our need to find them is tremendous. Neurological disorders currently affect one of every five Americans. That translates into approximately $400 billion a year in direct costs and lost productivity. Of course, the human toll is unmeasurable. For these reasons and more, many believe that understanding the scientific underpinnings of the human brain is one of the great challenges facing us in the 21st century.

In 2003, University President Robert Bruininks announced eight academic initiatives designed to push the boundaries of knowledge by harnessing the University's power to cultivate work across disciplines. One of those initiatives focuses on Brain Function across the Lifespan.

In this issue of the *Medical Bulletin*, you'll read about how researchers at our Medical School are working with colleagues across disciplines and extending their work into the larger community to grapple with some of neuroscience's most complex issues: schizophrenia, Alzheimer's, and Parkinson's disease.

This is certainly not the sum total of our scientific quest, but rather a picture in time of some of the fascinating and far-ranging research being generated at the University of Minnesota. With the support of our alumni and benefactors, we look forward to continuing our groundbreaking work for years to come.

**Deborah E. Powell, M.D.**
Dean, University of Minnesota Medical School

MINNESOTA MEDICAL FOUNDATION
*at the University of Minnesota*

The mission of the Minnesota Medical Foundation is to improve the quality of life for the people of Minnesota, the nation, and the world by supporting the advancement of health-related education, research, and service at the University of Minnesota.

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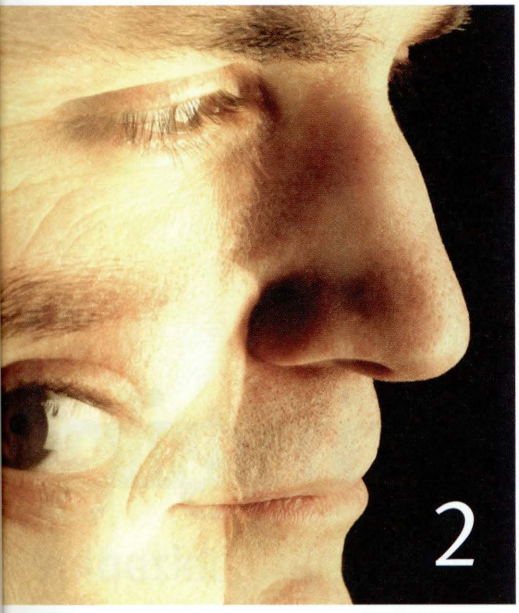



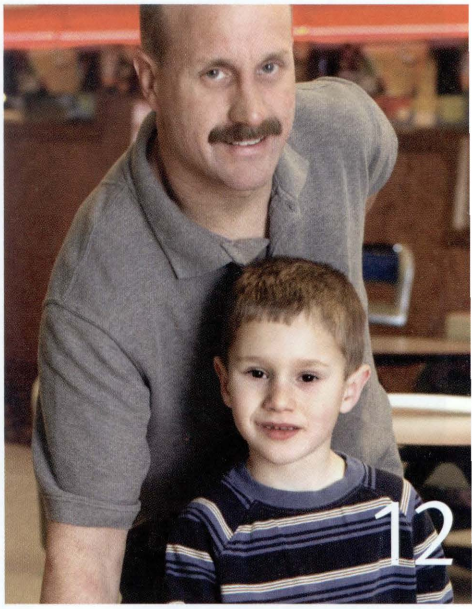


## Features



### DEPARTMENTS



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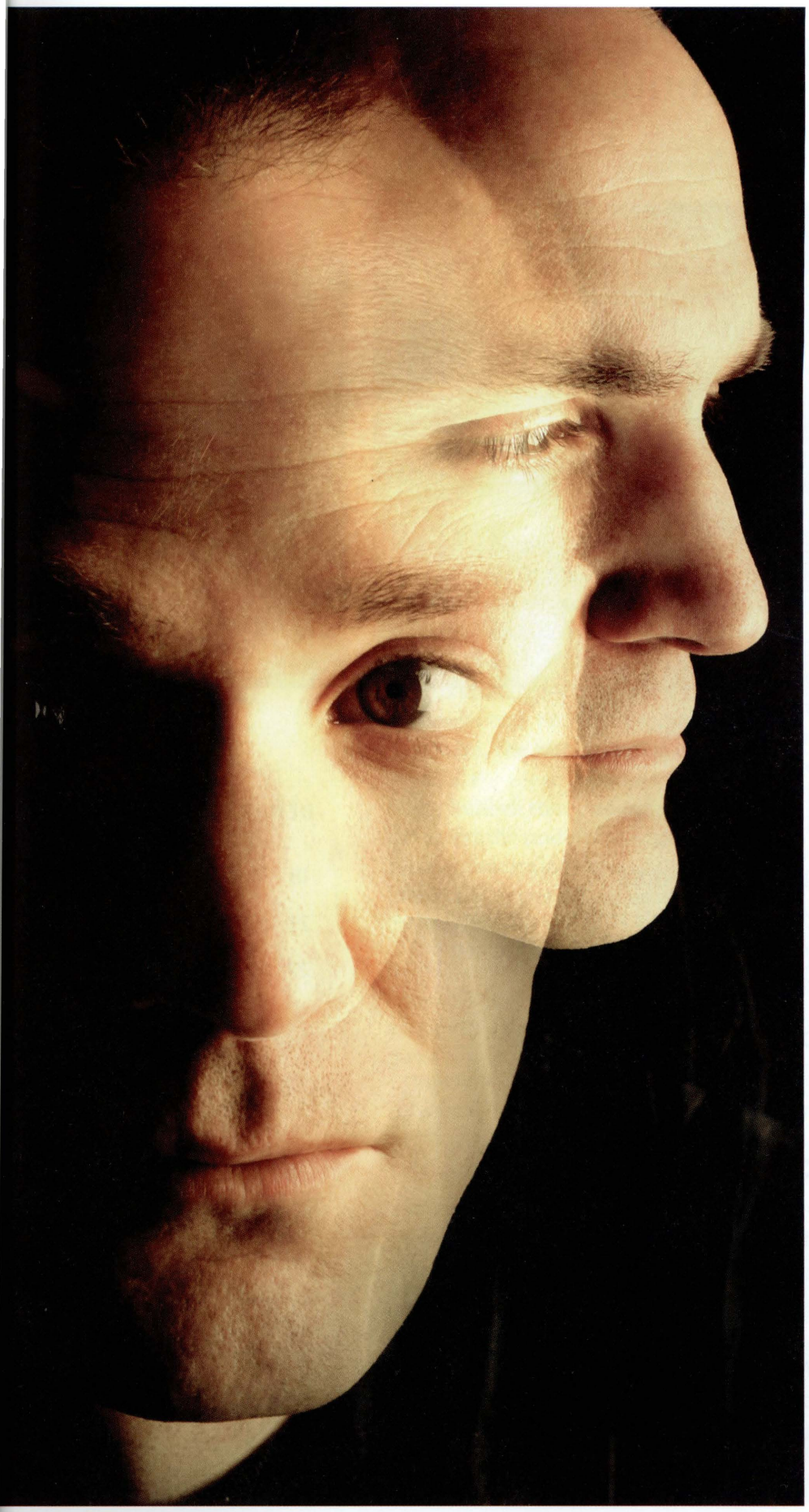


PHOTOS: TIM RUMMELHOFF

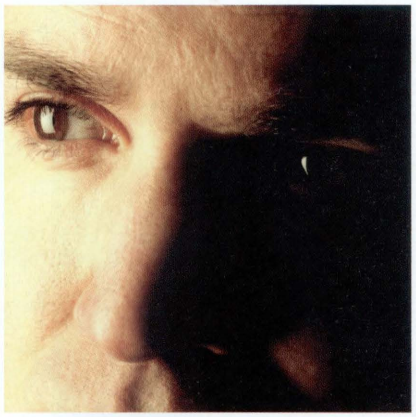
# Bringing

## Pictures of schizophrenia

UNDERSTANDING THE HUMAN BRAIN is like putting together a jigsaw puzzle with an unknown number of pieces to create a picture that has never been seen before—in the dark. The University of Minnesota is among the best places in the world to work on this puzzle.

In line with the goals of President Bruininks' initiative on Brain Function across the Lifespan, important parts of the puzzle are coming together to form a coherent picture. The University's broad program, focusing on the neurosciences across departments, campuses, and colleges, is bringing fantastic new "flashlights" to bear on problems in the neurosciences. Current research into schizophrenia—perennially one of the most serious, baffling, and tragic disorders of the mind—is especially exciting.

Researchers in the Departments of Psychiatry and Psychology are currently exploring the brain's structure



# light to mental illness

## and other disorders of the new plastic mind

and connectivity by applying high-field magnetic resonance imaging (MRI) techniques developed at the University's Center for Magnetic Resonance Research (CMRR), then applying what they are learning to those suffering from schizophrenia.

### Building a better flashlight

"Magnetic resonance has proven to be a dynamic field," says CMRR director Kamil Ugurbil, Ph.D., who holds the McKnight Presidential Endowed Chair of Radiology. This fall, the center brought its new 9.4 Tesla MRI online and began to generate its first images of human subjects.

Instruments used in magnetic resonance imaging and spectroscopy manipulate the nuclear spins of a subject's body using a magnetic field and radio-wave pulses to generate data that reveal the inner workings of the body. MRI uses magnetic resonance to create pictures, a routine exam used at hospitals to diagnose back injuries or head trauma. Magnetic resonance spectroscopy, or MRS, reveals the chemical makeup of the body. Both are important tools used to develop a better understanding of the body, including brain structure, chemistry, and function.

Typical hospital MR scanners use a magnetic field strength of 1.5 Tesla. The CMRR began pushing the limits of the technology back in 1991, when the laboratory acquired a state-of-the-art 4 Tesla human magnet. Ugurbil has long been an advocate of high-field (3 Tesla and above) and ultrahigh-field (7 Tesla and above) MR. While the technical challenges of achieving optimal performance increase at higher fields, so too does the possible resolution and sensitivity.

In 1999, the CMRR again raised the bar when researchers acquired the first 7 Tesla magnet that could be used for

**The most amazing thing about the brain is how dynamic it is. The question now becomes, 'How can we harness this plasticity to treat mental disorders? How can we redirect the brain's inherently dynamic abilities to intervene therapeutically in mental illness, stroke, and brain disorders of all kinds?'** – Kelvin Lim, M.D.

PHOTOS: TIM RUMMELHOFF


Kamil Ugurbil, Ph.D., will be researching the brain and schizophrenia using this state-of-the-art 9.4 Tesla magnet. Typical hospital magnetic resonance scanners use a field strength of 1.5 Tesla.

human studies. Ugurbil predicted at the time that other laboratories would be watching carefully and would try to replicate the CMRR's studies. His prediction proved true: Many institutions, including Harvard's medical school, the NIH Intramural Research Program, Stanford, and the University of California at San Francisco, to name a few, are establishing similar capabilities. The 9.4 Tesla instrument, made possible through critical support from the W. M. Keck Foundation, is the next step in the technology's evolution. Going forward, Ugurbil expects "significant gains in the sensitivity of spectroscopy" as well as better understanding of biological functional organization on a smaller (molecular) scale.

"I am an optimist," Ugurbil says, "and this is the principle that drives this entire lab—that we can always do something better: improve *x* here or *y* there, always pushing the limits of the amount of information we can get. I find this superbly exciting." As the lab looks to the future, he notes, "We are becoming more and more disease-oriented," with researchers conducting work into cancer, stroke, schizophrenia, substance abuse, and across the neurosciences.

## A vital, collaborative atmosphere

Ugurbil and other researchers at the University of Minnesota are collaborating with organizations across the country to better understand and treat schizophrenia and other mental disorders. For example, the Mental Illness and Neurosciences Discovery Institute (MIND Institute) supports several interlinked projects focused on schizophrenia at the Center for Magnetic Resonance Research and the Department of Psychiatry as well as the Minneapolis Veterans Administration Medical Center. Support from the National Institutes of Health (NIH) is fundamental to this research at the University.

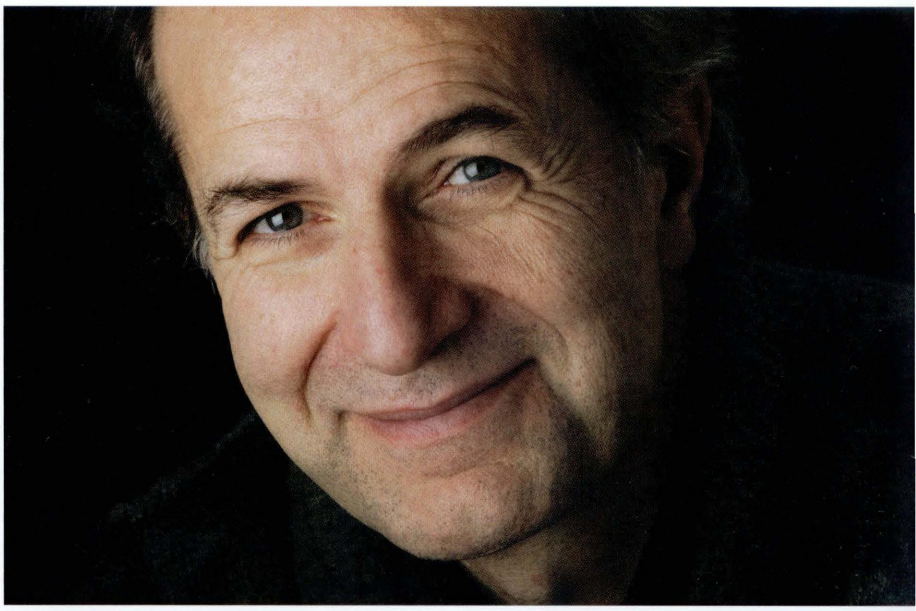
The University of Minnesota is also one of eleven sites taking part in the Biomedical Informatics Research Network (BIRN) studies at the NIH's National Center for Research Resources. BIRN is an effort to build a nationwide high-speed computer network to share brain images and integrate data across institutions. Tremendous energy and talent are being brought to bear on these projects.

Kelvin Lim, M.D., site coordinator for the BIRN project at the University of Minnesota, worked in some of the most prestigious research centers in the world before joining the University, including Johns Hopkins, Stanford, and New York University. Currently he holds the Drs. T. J. and Ella M. Arneson Endowed Chair of Psychiatry.

He radiates enthusiasm about both his work and the research environment at the University of Minnesota, saying, "What is so impressive about the U is both its breadth and depth. We have been able to establish collaborations across departments and schools, and this is enabling tremendous

TOP TO BOTTOM

Kamil Ugurbil, Ph.D.
Kelvin Lim, M.D.
Angus MacDonald III, Ph.D.



interdisciplinary and translational work to take place."

## The importance of neuroplasticity

Lim is interested in understanding the brain's ability to adapt. His work challenges the classic view of higher cognitive function. This view is based on the belief that single regions of the brain are responsible for specialized functions and that these functions are static and rigidly defined. The view of the brain he and other investigators are advocating is one where higher cognitive function is a process involving interactions between functionally specialized, anatomically separate brain regions. This view is supported by fMRI data that can measure the brain activity associated with a cognitive task.

One technique that Lim finds especially useful is diffusion tensor imaging, or DTI. Using DTI, researchers can examine the physical connections within the brain by measuring the magnitude and direction of the diffusion of water molecules. This work is revealing the living brain's organization and other features that haven't been measurable until now. DTI has applications across a range of neuropsychiatric disorders, including alcoholism, cocaine dependence, geriatric depression, schizophrenia, and the effects of HIV-1 infection on the brain.

"The most amazing thing about the brain is how dynamic it is," says Lim. "The question now becomes,

I am an optimist, and this is the principle that drives this entire lab — that we can always do something better: improve *x* here or *y* there, always pushing the limits of the amount of information we can get. I find this superbly exciting.

– Kamil Ugurbil, Ph.D.

'How can we harness this plasticity to treat mental disorders? How can we redirect the brain's inherently dynamic abilities to intervene therapeutically in mental illness, stroke, and brain disorders of all kinds?'"

### Neuroplasticity and schizophrenia: bringing basic research to patients

Lim is furthering his research with colleague Angus MacDonald III, Ph.D., of the Department of Psychology. Together, they are working on a study aimed at harnessing the brain's natural plasticity to improve the lives of patients suffering from schizophrenia. The study is supported by the University's NIH-funded General Clinical Research Center (GCRC).

Schizophrenia has been difficult to define over the years, given that three different patients suffering from the disease might not share a single symptom. According to MacDonald, the current literature argues for a "three-factor model": A patient might manifest symptoms such as delusions or hallucinations; disorganization (such as muttering or ordering and reordering the contents of a shopping cart); or stopping communication in mid-sentence. "What would be tremendously interesting," says MacDonald, "is if these symptoms turned out to be neurobiologically distinct."

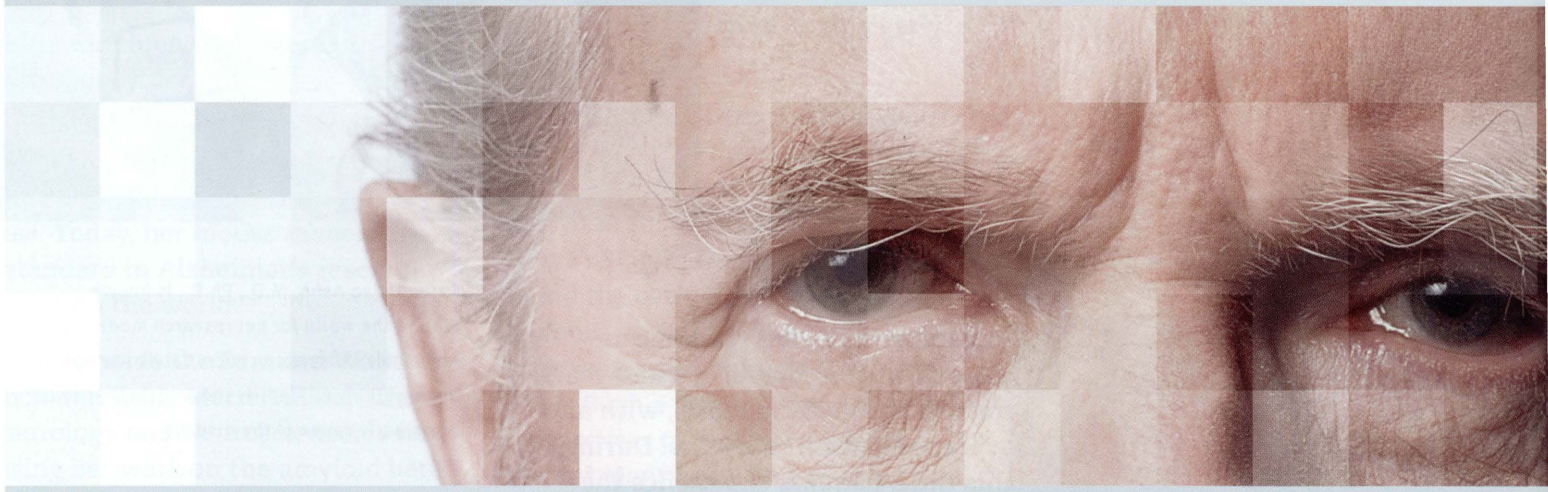
In a previous study (to be published in the March 2005 *American Journal of Psychiatry*), patients presenting more symptoms of disorganization showed reduced activity in the prefrontal cortex the very first time they were hospitalized. This study's results raise two important questions: Could activity in this region of the brain be increased through a nonpharmacological intervention? And if activity is increased, will it reduce disorganization symptoms?

To investigate this, MacDonald and his colleagues are using cognitive rehabilitation techniques first developed to help patients who had suffered from stroke. Schizophrenia patients in a pilot treatment study received a regimen of "mental push-ups" in what MacDonald describes as a "brain boot camp" in an individual setting. These patients worked with a personal computer and a program designed to increase the difficulty of the tasks as the patients' performance increased. Patients were then scanned using functional MRI exams before and after spending time with the computer program. The results from this group showed a reliable increase in functions associated with prefrontal cortex over the course of the training, while patients in the control group showed indifferent results. When the data from this study are fully analyzed, researchers will know whether the increase in performance is simply a "practice effect" or whether it physically changes prefrontal neurological activity. They will know whether "computer medicine" can improve symptoms by taking advantage of the underlying mechanisms of neuroplasticity.

This is just one of many examples of research at the University of Minnesota that is bringing light and understanding to unexplored areas of the brain – one more piece of the neurological puzzle that researchers are steadily assembling. MB

BY WOLFE MOLITOR

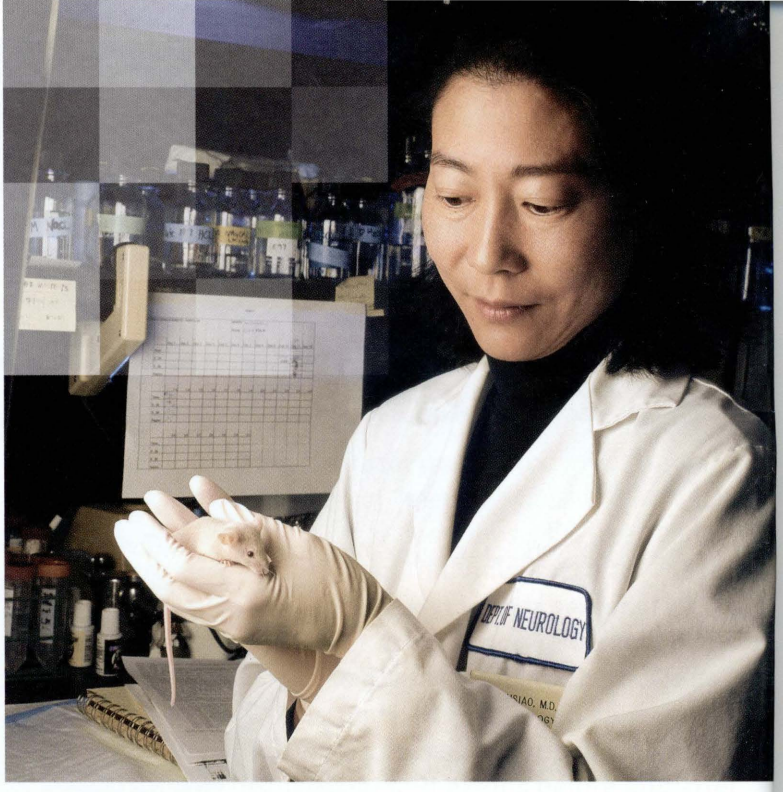
# The aging brain and Alzheimer's disease



Betty often wanders out of her home at night. Her daughter and primary caregiver, Sue, has to go look for her in the neighborhood and bring her home. Esther likes to take the bus downtown to do her banking and shopping, but once she couldn't remember how to get home. Fortunately, a kind stranger helped her find the right bus. Fred's wife, Ellen, provides round-the-clock care for her husband. She loves him dearly, but the exhausting care schedule wears her out. A social worker helps her find an adult day-care program that gives her respite three days a week.

These are just a few examples of the serious challenges that Alzheimer's patients and their families face on a daily basis. The most common of dementing disorders, Alzheimer's currently affects an estimated 4.5 million Americans. The Alzheimer's Association projects that by the year 2050, between 11 and 16 million Americans could have the disease unless a cure is found.

PHOTOS: TIM RUMMELHOFF




Karen Hsiao Ashe, M.D., Ph.D., is known around the world for her research modeling Alzheimer's disease in mice. Lately she has been working to identify the protein that could be an early cause of the disease.

**The most common of dementing disorders, Alzheimer's currently affects an estimated 4.5 million Americans. The Alzheimer's Association projects that by the year 2050, between 11 and 16 million could have the disease unless a cure is found.**

### The personal toll

Alzheimer's disease can have an unusually long course, up to 20 years from the time of diagnosis, with an average duration of 8 years. During this time, patients experience the gradual impairment of memory, thinking, and behavior. Eventually, 24-hour care is required, including assistance with daily activities such as eating, grooming, and using the toilet.

Families struggle with role reversal, with children assuming the parenting role. Maintaining the patient's dignity and individuality must be balanced with insuring their safety inside and outside the home. For many families, relinquishing the car keys is an especially painful turning point.

Medication mismanagement is an even greater issue. Patients often want to continue managing their multiple medications, and families may hesitate to step in and make sure all medications are being taken appropriately. Unfortunately, due to short-term memory problems, patients may forget that they've taken their medications and take them again—or forget to take them altogether. Since many Alzheimer's patients suffer from other serious conditions, such errors can be extremely dangerous.

### The economic impact

According to the Alzheimer's Association, the average lifetime cost of Alzheimer's care for an individual is $170,000. The total national direct and indirect costs of caring for individuals with Alzheimer's add up to at least $100 billion per year – an amount that is expected to increase as the baby-boomer generation ages.

Early diagnosis and treatment is key to managing and eventually preventing Alzheimer's disease. Basic science researchers at the University of Minnesota are hard at work investigating possible molecular causes of Alzheimer's, while clinical researchers are

**Ashe's recent findings suggest that plaques are not the problem after all. The revised theory is that there is a form of A beta protein yet to be discovered. "If we're right, then we will have found the early cause of Alzheimer's. It would be like finding that a bacterium causes tuberculosis."**

exploring the efficacy of known and approved medications as well as the accuracy of various diagnostic methods.

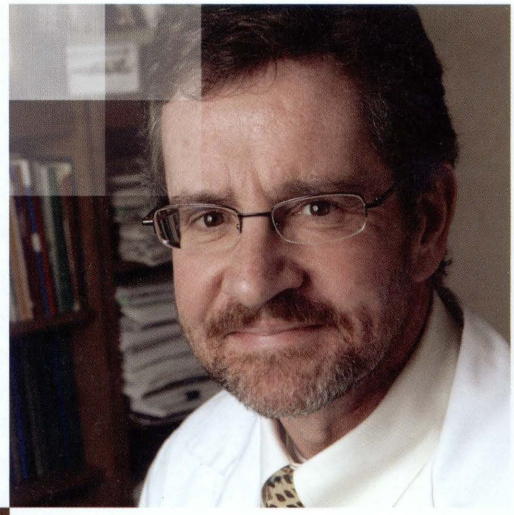
### Looking for clues to prevent early memory deficit

Karen Hsiao Ashe, M.D., Ph.D., made headlines in 1996 with the development of the Alzheimer's transgenic mouse. Today, her mouse models are the standard in Alzheimer's research labs around the world.

Ashe, who holds the Edmund Wallace Tulloch and Anne Marie Tulloch Chairs in Neurology and Neuroscience, is now focusing her work on the amyloid beta (A beta) protein found naturally in the brain. Abnormalities or mutations in this protein either increase the production of it to detrimental levels or decrease its ability to degrade naturally. It's unclear whether this excess buildup leads to or is a result of Alzheimer's.

Alzheimer's disease is characterized by plaques and tangles of different proteins in the brain, and also by brain atrophy. Scientists initially thought that the plaques were responsible for the memory deficits seen in both humans and in the mouse models. However, the mice only developed plaques and none of the neuron loss or atrophy seen in human Alzheimer's patients. The validity of the mouse model was questioned, but Ashe's subsequent experiments led to the conclusion that the mouse models resembled the latent or precursor form of Alzheimer's rather than the later stages, and therefore are still valuable in studying methods for preventing or even reversing early memory deficit.

Ashe's recent findings also suggest that the plaques are not the problem after all. The revised theory is that there is a form of A beta yet to be discovered. "If we're right, then we will have found the early cause of Alzheimer's. It would be like finding that a bacterium causes tuberculosis," explains Ashe. Such a finding would enable researchers to make huge strides toward identifying and treating this disease in its very earliest stages. "Ideally, you would want to intervene at the very earliest possible phase of illness—before the loss of neurons—to hopefully prevent all these devastating later changes."



Maurice Dysken, M.D. (left), and J. Riley McCarten, M.D. (above), are leading a clinical trial exploring different combinations of vitamin E and drugs for treating patients with mild to moderate Alzheimer's disease.

**We would like to implement a lot of what we do at the VA's Geriatric Research, Education and Clinical Center (GRECC) into a similar patient clinic at the University of Minnesota.**

–J. Riley McCarten, M.D.

### Studying the effectiveness of drugs and vitamin E

Psychiatry professor Maurice W. Dysken, M.D., is principal investigator for a new four-year, $8.1 million clinical trial to explore the efficacy of two drugs already approved for Alzheimer's: donepezil (also known by its brand name, Aricept) and memantine (also known as Namenda). By studying these drugs alone and in combination with vitamin E, Dysken and his collaborators hope to determine which combination, if any, is most effective in treating mild to moderate Alzheimer's. The trial, funded by the Department of Veterans Affairs Cooperative Studies Program, will be conducted at 10 VA sites across the country starting in the fall of 2005. Dysken's role as director of the Geriatric Research, Education and Clinical Center (GRECC) at the Minneapolis Veterans Affairs Medical Center makes him especially qualified to lead this important clinical trial.

J. Riley McCarten, M.D., assistant professor in the Department of Neurology and medical director of the GRECC, will be in charge of the study at the Minneapolis site. His primary ongoing responsibility is the GRECC Memory Loss Clinic where he is the staff neurologist. His own research interests include working with fellow researchers on a coordinated program using several different methodologies in the same patient—MEG (magnetoencephalography), fMRI (functional magnetic resonance imaging), PET (positron-emission tomography) scanning, and cerebrospinal fluid analysis—to identify not only a biomarker of disease but also a biomarker that changes in response to treatment.

Still, as the U.S. population ages, there's an increasing need for even more research—and the University of Minnesota is rising to the challenge. Under the direction of Dean Deborah Powell, the Medical School has made it a priority to recruit a nationally renowned physician-scientist in dementia research, with plans to add a second position in the near future. With the search committee now in place, the four neurosciences departments are building a stronger foundation for basic and clinical research devoted to Alzheimer's and other cognitive impairments.

### Providing comprehensive care in the community

Of course, research into the causes and treatments of Alzheimer's disease is only helpful if it leads to clinical trials that can effectively make the transition from laboratory science to real solutions for patients.

In Minnesota, the Geriatric Research, Education and Clinical Center at the Minneapolis VA Medical Center is providing that crucial link. The GRECC program was established in the mid-1970s as the VA's response to an aging veteran population. Each of the nation's 21 GRECCs is affiliated with a major university as part of its structure. For this reason, all Minneapolis GRECC researchers hold academic appointments in a department of the University of Minnesota.

"The GRECC Memory Loss Clinic is a great service for veterans, but there's nothing I know of that is comparable for the civilian population," says clinic director Dysken.

His colleague Riley McCarten agrees. "There is a real need for it in the community. We would like to implement a lot of what we do [at GRECC] into a similar patient clinic at the University of Minnesota."

Currently, no Twin Cities health facility offers such a clinic. Most nursing homes have an Alzheimer's unit of some kind, and there are some individual physicians in the area with clinical expertise in working with Alzheimer's patients, but there is no center of excellence dedicated to a comprehensive system of basic science and clinical research combined with ongoing patient care.

In response to this need, two University department heads have developed a plan to build a memory clinic in collaboration with University of Minnesota Physicians. Created by S. Charles Schulz, M.D., of the Department of Psychiatry and David Anderson, M.D., of the Department of Neurology, the proposal calls for a coordinated service to assess patients showing signs of cognitive impairment or dementia. Patients referred to the clinic would receive clinical exams, neuropsychological tests, and laboratory evaluations from a team of specialists including a neurologist, neuropsychologist, psychiatrist, and psychometrician.

"Establishing this clinic is an important first step," says Schulz. "Patients will have a place to go for a multidisciplinary assessment, plus a chance to participate in clinical trials. Meanwhile, the University's research initiatives will thrive by having patients who are candidates for clinical studies." MB

BY ANDREA J. PETERSON

PHOTO: TIM RUMMELHOFF

## Caring for one another

WAYNE CARON, Ph.D., L.M.F.T., began the first support group in the Twin Cities for Alzheimer's patients and their caregivers, and has been running weekly support groups since 1993. Through his work as director of the Family Caregiving Center in the Department of Family Social Science, Caron has come to believe that successful care of Alzheimer's patients lies in talking to them—working *with* them and not *on* them. "They are wise—older than we are, and they have a lot more life experience than we do," he observes. "We can and need to learn from them."

Through the years, Caron has seen an amazing and encouraging capacity for empathy and caring between Alzheimer's patients in his groups. He offers the following stories as examples:

"I'm often asked how long should a person be in a support group—implying that after a time the person doesn't benefit and their more severe symptoms can depress others. In a decade's experience with these groups, I find group members are highly tolerant and loyal to the members with more advanced symptoms—helping them along and making sure they feel included. They see their own future and treat the others as they hope they will be treated—with respect and caring.

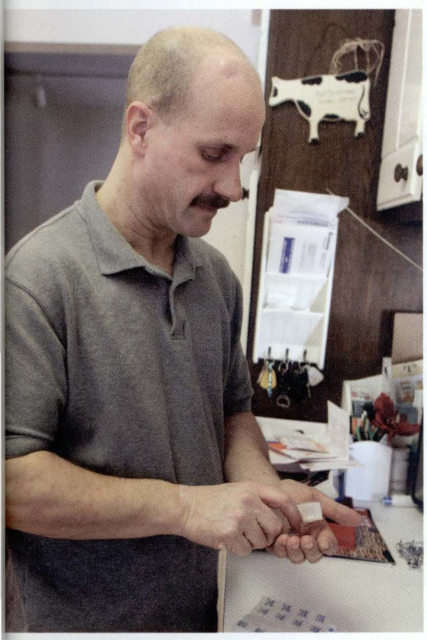
"One group member was a continual concern for me. He had very poor social skills and limited insight. And he was profoundly deaf—so he wasn't good at listening, but he was good at talking. He would constantly interrupt others and come back to the same stories again and again. I worried that he was ruining the group for others. Then he took ill and missed a month of group. Every week, someone would ask how he was doing and when he was coming back. He frustrated the other group members, but they cared about him.

"Our group members also watch out for each other outside the group. On a number of occasions, group members have attended adult day-care programs together or even moved into the same nursing homes. They seek each other out, somehow remembering that they have a connection. On one occasion, one of our members was extremely reluctant to attend an adult day program. He, in fact, was adamant that he would go only once and that was it. When he got to the program, another member of the group saw him and walked across the room to shake his hand. That was the end of the resistance."

*Support group meetings are held in the Department of Family Social Science on the University of Minnesota's St. Paul campus. For more information, contact Wayne Caron at wcaron@umn.edu or 612-625-1900.*

# Regaining control of Parkinson's disease

Three years ago, there wasn't a whole lot Andrew Stickney could do. Trapped in the advanced stages of Parkinson's disease, he spent his days at home in the Twin Cities suburb of Woodbury swinging back and forth between being "frozen up" and wiggling uncontrollably due to side effects from the medications he took to "thaw" the frozen state.



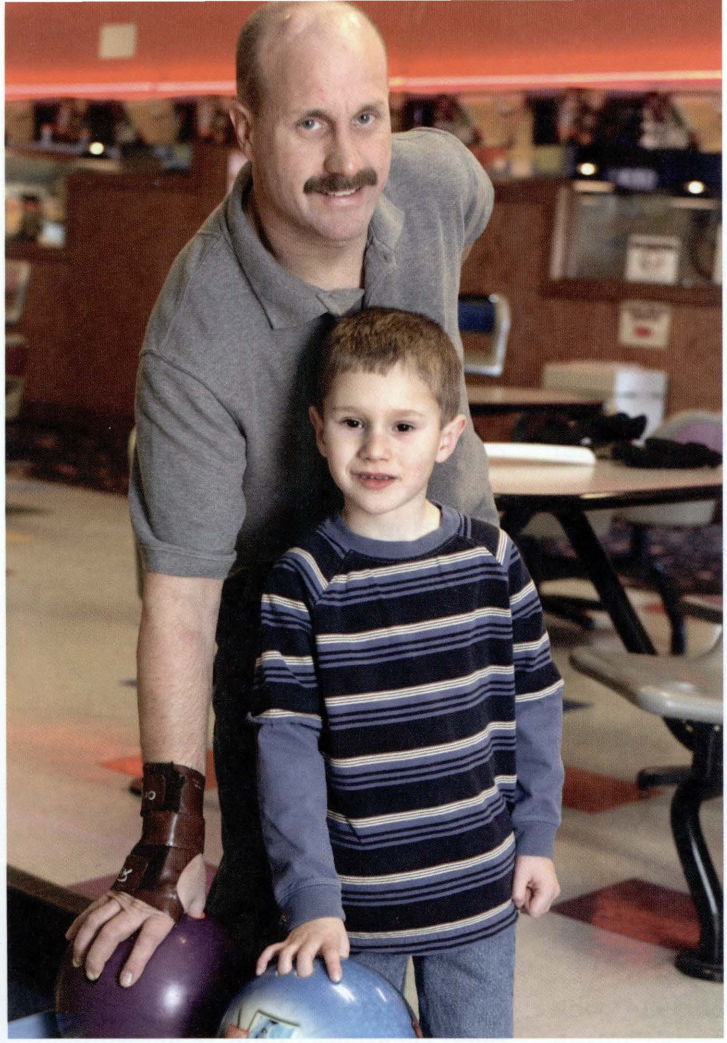
Andrew Stickney still takes about 20 pills a day to control his disease.

Out of 16 waking hours, he'd spend 3 to 6 of them with arms and legs that did what he asked them to. The rest of the time his body refused to respond to his brain's wishes: Sometimes he was slow, sometimes he was mobile, and sometimes his wiggling state left him out of control. He often didn't know what the next hour—or minute—would bring.

"In the frozen state I was in a lot of pain because my muscles were tense, sort of like a charley horse feels," he says. "I'd take medications to relieve that and then, as I'd transition, I'd be overstimulated, wiggly." Stickney knows the symptoms well; he's been experiencing them since 1991. "It hampers everything you do. I remember at times rolling on the floor, crying, asking God for a new body."

Then, in December 2001, University of Minnesota neurosurgeon Robert Maxwell, M.D., Ph.D., turned Stickney's life around. In a 12-and-half-hour procedure, Maxwell implanted two tiny electrodes, one on each side, into key locations deep inside Stickney's brain. After making sure the electrodes were in the exact right spot—in the middle of a tiny island of brain tissue known as the subthalamic nucleus—he then connected the electrodes via wire leads beneath the skin to two battery-operated devices implanted just below Stickney's collarbone. After the surgery, the devices were programmed to deliver steady pulses of electricity to implanted electrodes deep within Stickney's brain. By lessening (or silencing) the abnormal "noisy" brain activity that characterizes Parkinson's, the pulses tamed Stickney's unruly body.

You don't have to be a brain surgeon to see the difference the device has had on Stickney's life. Since receiving the implant, Stickney has been able to cut back on his medication and so reduce the negative side effects. He has had the energy and endurance to start a



PHOTOS: TIM RUMMELHOFF

Now that his symptoms are under control, Andrew Stickney is back to a full schedule, including bowling with his son, Ben.

**In the frozen state I was in a lot of pain because my muscles were tense, sort of like a charley horse feels. It hampers everything you do. I remember at times rolling on the floor, crying, asking God for a new body.**

–Andrew Stickney

business making racks for the thin-film coating industry. He also is able to volunteer at school and on field trips, and bowls in an adult-child league with his seven-year-old son, Ben.

"My life has gone from 20 to 40 percent of my day being good, productive time, to about 80 to 90 percent now," he says.

### Looking for better ways

Some 1.5 million Americans suffer from Parkinson's disease, a disorder in which the brain gradually loses its ability to make dopamine, a chemical that helps nerve cells tell muscles what to do. The consequences include tremors, stiffness, and difficulty moving. Early on, Parkinson's disease is often treated with medications that fill in for the missing dopamine. But over time the treatment loses its efficacy. In many cases it also causes uncontrolled movements called dyskinesias.

In the 1950s and '60s, researchers looking for better ways to control Parkinson's symptoms developed a treatment that involved creating lesions in the parts of the brain that control movement. The lesions were effective in some cases, but not all. They also caused adverse side effects and had the downside of being irreversible. Then, in the 1980s, French surgeons who were making lesions to control tremors noticed that

**What we're trying to do is perhaps turn back the clock five, six, seven years, and allow Parkinson's patients to be productive, to enjoy activities they're now deprived of. But this is a progressive illness. They're going to continue to progress. There's going to be a need for additional tools to manage, treat, and cure the disease.**

– Robert Maxwell, M.D., Ph.D.

stimulating certain parts of the brain with electrodes—part of the process of confirming the correct location for the incision—temporarily quelled Parkinson's symptoms. Why not, they thought, use deep brain stimulation rather than destruction to help Parkinson's patients regain control? The researchers began working with Medtronic, the Minnesota-based cardiac pacemaker manufacturer, to develop and refine a device that could do just that.

### The Minnesota connection

Maxwell, who headed the Department of Neurosurgery from 1995 to 2003, first implanted an experimental deep-brain-stimulation (DBS) device into one of his patients in the early 1990s. Several years later he and his colleague Timothy Ebner, M.D., Ph.D., began doing more of the surgeries as part of federally funded clinical trials of the Medtronic device.

"Once there was pretty solid evidence that it was effective, we gained authorization to do it in a research protocol in the latter part of the 1990s," he says, "and of course we found it to be quite effective."

In 1997, Medtronic's Activa Parkinson's Control System received FDA approval for treatment of essential tremor, a Parkinson's-like disorder. In 2002 it was approved for use in people with Parkinson's disease.

### Not for everyone

To date, Maxwell has implanted more than 200 of the deep-brain-stimulation devices. But he is quick to point out that as life-altering as it is for some, DBS is not for everyone.

"We select patients using a number of fairly refined criteria," he says. Before surgery, patients are assessed by Paul Tuite, M.D., head of the Movement Disorders Clinic, to determine whether they're a good candidate for the procedure.

Of the 15,000 Minnesotans currently diagnosed with Parkinson's disease, perhaps 5 to 10 percent could be seriously considered for the treatment, says Tuite. Conditions that would preclude implantation of the Activa device include the presence of significant cognitive difficulties, atypical Parkinsonism, prior strokes, or other significant medical problems. Some believe those over age 70 may not do as well as others with the surgery. In addition, prospective recipients need to be able to understand and cooperate

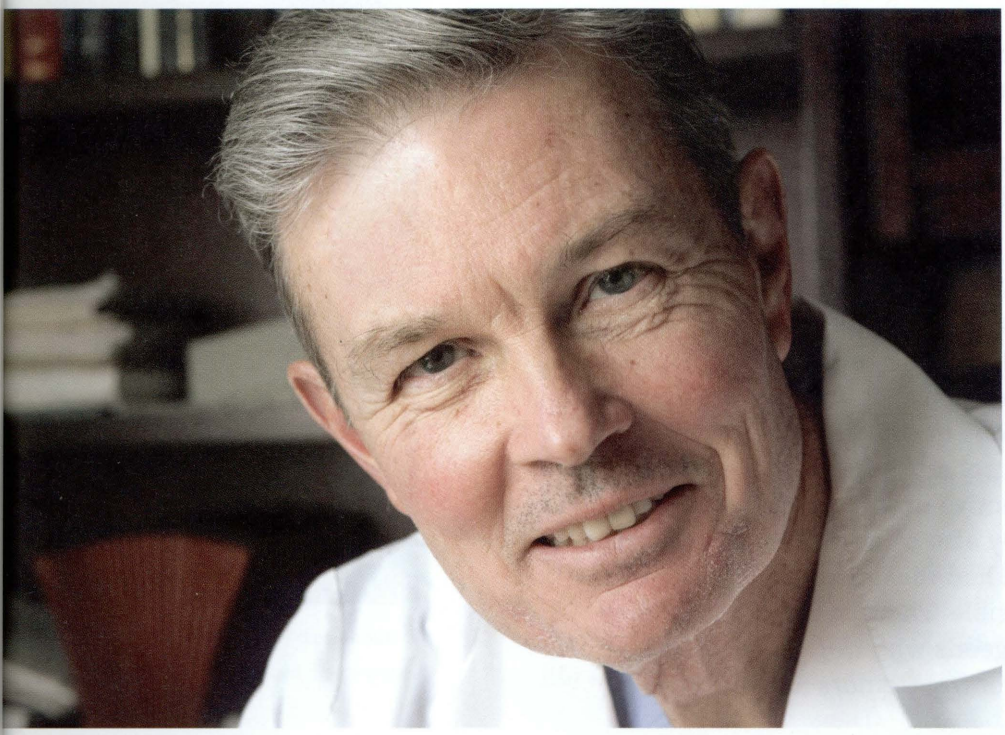


PHOTO: TIM RUMMELHOFF

Neurosurgeon Robert Maxwell, M.D., Ph.D., implanted the deep-brain-stimulation device that helped Andrew Stickney. Maxwell has improved the quality of life for more than 200 others with the same surgery.

with the therapy and have a good support system as they adjust to their new, somewhat bionic lives. They also receive a thorough rundown of potential negative outcomes, which can include infection, bleeding, behavioral changes, and weight gain.

"The majority of patients that have received surgery have obtained great benefits – less medication, more mobility, less involuntary wiggling," says Tuite. "But it's still a potentially risky proposition, as it is brain surgery with its inherent risks, and individuals will need to have their device managed after surgery."

Stickney did experience some problems with infection after his surgery. And he's in line for another surgery soon to replace the pulse generators implanted in his chest because the batteries are wearing out. But he has no second thoughts.

"I would do it all again in a heartbeat," he says.

Plenty of other people are following in his footsteps. Currently Maxwell and his team are implanting 30 to 40 devices each year. Other hospitals in Minnesota and around the country are beginning to offer the surgery, too.

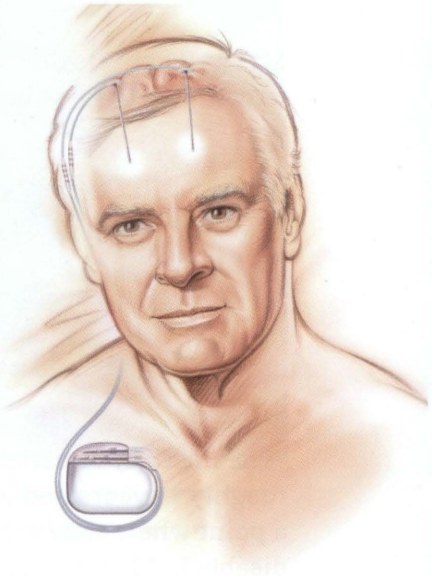
Maxwell says physicians are increasingly likely to recommend that their patients with Parkinson's look into DBS as a treatment option. "It's that old axiom, 'Neither be the first to try the new nor the last to lay aside the old,'" he says. "We're out of that phase of being the first to try the new and into not wanting to be the last to lay the old aside."

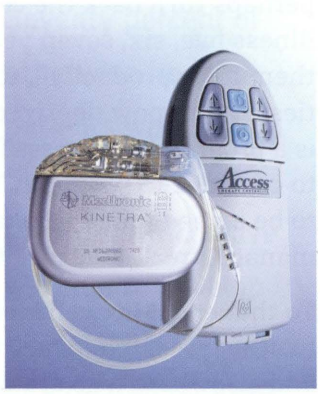
## Efforts to improve

As the surgeries continue, so do efforts to improve the device and the procedure used to implant it. A year ago, Medtronic switched from the dual controls to a dual-chamber, single-battery device, eliminating the need for two of the incisions originally required to get everything up and running. Research is also under way to find ways to minimize or eliminate the unwanted side effects.

Maxwell is leading the way to assess the use of MRI technology rather than the patient's motor response to guide electrode placement. Currently patients like Stickney are required to stay awake during the electrode-implanting surgery so that the surgical team can monitor symptoms to gauge when the electrodes are placed correctly. MRI-guided placement would allow the use of general anesthesia during the surgery, a huge benefit for patients whose Parkinson's makes it painful or impossible to lie awake on the operating table for the many hours the surgery currently requires.

"We are finding that the patients we need to do under general anesthesia using anatomical criteria by and large are doing quite well," says Maxwell. "If we find eventually that we can be just as effective doing it in a way that would be much quicker, that would be a really positive thing. It will not only reduce time and stress on the patient, but we should also be able to reduce the cost of the procedure and allow it to be done in more centers."






PRODUCT IMAGES COURTESY OF MEDTRONIC

When the neurostimulator is implanted under a patient's collarbone, Parkinson's-related tremors can be controlled with electrodes through two thin wires connected to the brain.

Maxwell expects demand for the device to continue to grow in the future.

"Parkinsonism is a disease that increases in frequency as we get older, and we have an aging population, so I think Parkinsonism is something we're going to see more and more of," he says. Still, he emphasizes that deep brain stimulation is a treatment, not a cure.

"The majority of patients have had it roughly 10 years and are now reaching a point where they are becoming very disabled. What we're trying to do is perhaps turn back the clock on their illness five, six, seven years, and allow them to be productive, to enjoy activities they're now deprived of. But this is a progressive illness. They're going to continue to progress. There's going to be a need for additional tools to manage, treat, and cure the disease."

To that end, Maxwell looks with hope to other researchers at the University and elsewhere who are doing basic research in stem cell biology and other areas that could lead to novel treatment options—and perhaps even a cure—for Parkinson's disease.

"For the immediate future, deep brain stimulation is going to be the most effective technology available for treating Parkinsonism once proven to be refractory to medical management," he says. "But if we can find a way to replace the tissue and cells and biochemical substrates the brain needs to function normally, that's going to be a major breakthrough." MB

BY MARY HOFF

# The sleep

## Exploring the connection b and neurodegenerative dis

FOR MARK MAHOWALD, M.D., and Carlos Schenck, M.D., working at the Minnesota Regional Sleep Disorders Center is no snooze.

The two have been researching sleep disorders together since 1982, and they've always had plenty to discover. Recently they've found that a fascinating sleep disorder in which people act out their dreams is strongly linked to Parkinson's disease.

When a patient came into their clinic in the mid-1980s complaining of "violent moving nightmares," the doctors watched him sleep and observed him kicking and punching in bed. The man had dreamed he was fighting off an attacker.

Schenck, a senior researcher at the sleep center and associate professor of psychiatry at the University, noticed that the patient's violent behavior was happening during periods of rapid eye movement sleep (REM), a stage in which a person's body normally is paralyzed but the mind shows an electrical activity pattern similar to being awake.

And suddenly, a subject that at first seemed a curiosity became "extraordinarily interesting," says Mahowald, director of the sleep center and a neurology professor at the University.

They may not have known it at the time, but the sleep disorder they discovered—called REM Sleep Behavior Disorder, or RBD—was an

PHOTO: CARLOS SCHENCK, M.D.

A sleeping patient throws a punch while dreaming he is fighting off an attacker. His was the first documented case of REM Sleep Behavior Disorder.

# link

## etween a sleep disorder eases

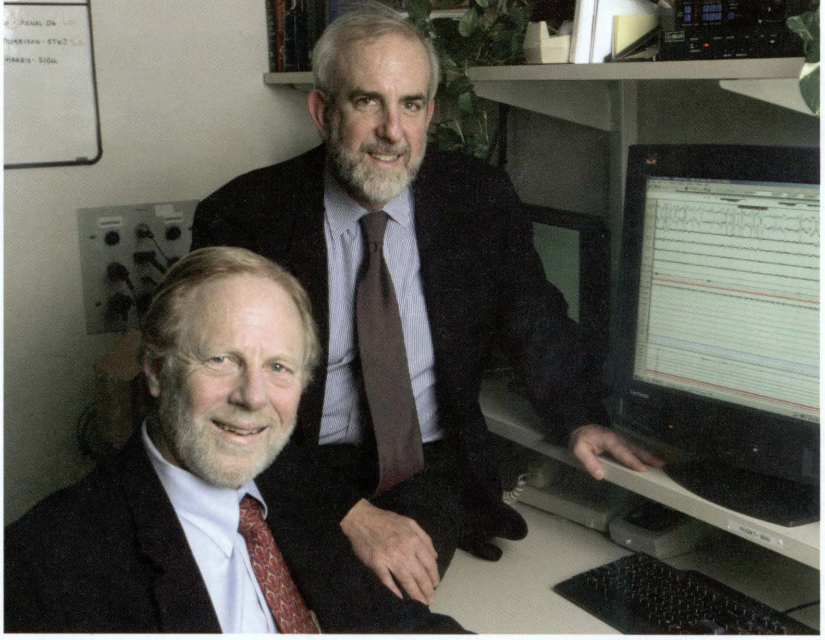


PHOTO: TIM RUMMELHOFF

Sleep researchers Mark Mahowald, M.D. (left), and Carlos Schenck, M.D., are studying a rare sleep disorder that has proven to be an early sign of Parkinson's disease.

early warning sign of a serious neurodegenerative disease for most patients.

During the 20 years they've been studying RBD, Mahowald and Schenck have found that 70 percent of otherwise healthy patients with the sleep disorder have gone on to develop Parkinson's disease or a related disease, usually within 10 to 15 years of RBD's onset.

Schenck and Mahowald documented the first human cases of RBD in a 1986 report that explained the basics of the disorder. While most people are paralyzed during the REM sleep cycle, people with RBD are not. So instead of lying still, people with RBD often act out their dreams, thrashing, yelling, running out of bed, and sometimes hurting others around them. They might get out of bed and move around, but the only sensations they feel are those occurring in their dreams.

It's a little like sleepwalking. Sleepwalkers, however, walk around in non-REM sleep and are hard to wake up, says Mahowald. When they do awaken, they're confused and disoriented.

People with RBD are immediately alert after being awakened and often can give detailed accounts of what they were dreaming. One patient remembered dreaming he was a running back heading for a touchdown. He had gotten out of bed and ran hard into his bedroom dresser. Another patient dreamed he was about to break a suffering deer's neck, but in reality he nearly broke his wife's neck.

RBD is a nonpsychiatric disorder that affects mostly older men. More than 90 percent of RBD patients are male, and the disorder usually becomes apparent after age 50, although some patients have been as young as 9. People with RBD may act out violent dreams when they're asleep, but most are good-natured when they're awake.

The underlying abnormality is not known. Antidepressants such as Prozac, Zoloft, and Effexor can induce or aggravate RBD in some people.

The connection between RBD and neurodegenerative diseases is equally cloudy. While 70 percent of people with the sleep disorder develop a Parkinsonian disease, only 25 percent of those with Parkinson's disease have RBD. An average of 13 years pass between development of the sleep problem and development of the Parkinsonian disease.

The good news for RBD patients is that the sleep disorder is easily diagnosed and easily treated. An anticonvulsant medication suppresses RBD behaviors in 90 percent of patients. But for the majority of RBD patients who will eventually develop Parkinson's, the bad news is that there's currently no drug to stop the progression of the disease.

There's still much to learn about the connection between the sleep disorder and neurodegenerative diseases. The early appearance of RBD in Parkinson's will be valuable when researchers develop medications that alter the disease's progression, Mahowald says. He believes that what researchers discover in the next 10 years with new technologies will be greater than everything they've learned up to this point. "It's going to blow the lid off what we know." MB

BY NICOLE CHRISTIANSEN

**Seventy percent of otherwise healthy patients with REM Sleep Behavior Disorder (RBD) have gone on to develop Parkinson's disease or a related disease, usually within 10 to 15 years of RBD's onset.**

# Minnesota marks 50-year partnership with Korean university

## Neal Gault honored with honorary doctorate

WHEN N. L. "NEAL" GAULT ARRIVED in Korea in 1959 to help foster the progress of medical education there, he couldn't believe what he saw. In the wake of the Korean War, the hospital at Seoul National University was treating patients without essential drugs and equipment, but it was surviving.

Gault was in Seoul as part of Operation Korea, a partnership between two countries—and two universities—separated by an ocean of differences. Last year marked 50 years since the start of that pioneering collaboration. In 1954, the U.S. government enlisted the University of Minnesota to help rebuild and develop the teaching and research programs in medicine, nursing, agriculture, veterinary medicine, engineering, and public administration at Seoul National University. What began in response to the ravages of war has matured into a mutually beneficial relationship that continues to this day.

In the 45 years since his first visit, Gault has invested a large part of his career in helping Korean medical students. In honor of that continuing commitment, Seoul National University presented Gault with an honorary doctorate in medicine this past September in Seoul.

The two universities also marked the 50-year milestone in Minneapolis with a joint stem cell symposium on November 15. That symposium featured lectures from researchers Shin Yong Moon and Woo Suk Hwang, who made headlines last year when they were the first to clone human embryos to produce embryonic stem cells. MB

N. L. "Neal" Gault, M.D., dean of the Medical School from 1972 to 1984, received an honorary doctorate in medicine from Seoul National University for his contributions to medical education there.

PHOTO: RICHARD ANDERSON

Louis Ling, M.D.

## High marks for graduate medical program

In December, the University of Minnesota's graduate medical education program received praise from an independent accrediting group, which cited the program's strong leadership, quality program directors and residents, and available academic and research opportunities.

These merits topped the list of strengths that helped the program gain a five-year favorable approval from the Institutional Review Committee of the Accreditation Council for Graduate Medical Education (ACGME). The committee, which conducted a site visit in the spring of 2004, also lauded the program for its mentoring groups, duty hour survey, and innovation in teaching and evaluating core competencies.

"We are proud to have our programs cited for innovation in teaching and evaluating the next generation of physicians," says Louis Ling, M.D., associate dean for graduate medical education.

ACGME is a private professional organization responsible for the accreditation of more than 7,900 residency education programs. MB

## Magazine names Steve Miles "Minnesotan of the Year"

A Medical School professor and alumnus has been recognized for being a proponent of human rights and a national player in political and health care reform.

Steve Miles, M.D., was named "Minnesotan of the Year" in *Minnesota Monthly*'s January issue. Miles is not only a professor of medicine and member of the Center for Bioethics at the University of Minnesota; he's also a graduate of the Medical School's class of 1976.

Miles was recognized for calling public attention to the failings of medical staff at the Abu Ghraib prison near Baghdad. He alleged that the medical staff didn't protect detainees' human rights or properly report deaths or injuries by beatings. Miles was also acknowledged for more than 20 years of significant achievements in his study of political reform and for his role in advocating for publicly subsidized health-care assistance programs.

"We are proud to recognize Dr. Miles for his many important contributions to Minnesota, as well as the world," writes Jeff Johnson, editor of *Minnesota Monthly*. "His tireless reform work has benefited many people across the globe."

This is the second year in a row that a U of M leader has been named "Minnesotan of the Year." In January 2004, University President Robert Bruininks received the honor. MB

## University professor leads clinic named best in treating cystic fibrosis

A recent article in the *New Yorker* magazine has revealed that the Minnesota Cystic Fibrosis Center is considered the country's most successful program in keeping patients healthy. The Cystic Fibrosis Foundation examined 117 such programs nationwide, and the clinic at Fairview-University Children's Hospital came out on top.

Much of the program's success is attributed to clinic founder and University of Minnesota pediatrics professor Warren Warwick, M.D., according to author Atul Gawande, M.D. Gawande writes that although the Minnesota Cystic Fibrosis Center uses the same drugs and treatment regimens as other clinics of its kind, Warwick's inventiveness and ability to motivate patients to keep up with their treatments helped nudge the program to the top.

The average life expectancy of cystic fibrosis patients nationwide was two years when Warwick started treating cystic fibrosis in the late 1950s. Today the average life expectancy nationwide is 33. At the Minnesota Cystic Fibrosis Center, it's almost 48. The clinic's oldest patient is 64 years old.

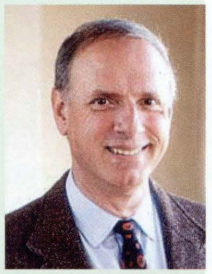
To ensure participation, the Cystic Fibrosis Foundation's study doesn't normally identify the facilities and their scores; only the clinic would learn of its own rating. This time the foundation released the names of the five highest-scoring facilities when a group of doctors in Cincinnati requested them to improve their own program. MB

*Gawande's article, "The Bell Curve," appeared in the December 6 issue of the* New Yorker.

## Two named to Institute of Medicine

Two University faculty members have been named to the Institute of Medicine of the National Academy of Sciences, one of the highest honors in the field of medicine.

**Apostolos Georgopoulos, M.D., Ph.D.,** is known for his work involving the motor cortex and brain mechanisms that contribute to cognitive function. He is professor of neuroscience and director of the Brain Sciences Center at the Minneapolis Veterans Affairs Medical Center.



Apostolos Georgopoulos, M.D., Ph.D. (top); Michael Osterholm, M.P.H., Ph.D.

**Michael Osterholm, M.P.H, Ph.D.,** is an internationally recognized expert in public health who's been at the forefront in addressing national issues related to public health preparedness, infectious disease, bioterrorism, and agricultural and food biosecurity. He is director of the University's Center for Infectious Disease Research and Policy (CIDRAP) and professor of public health.

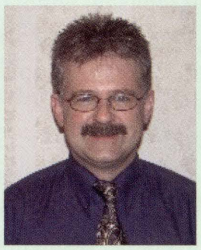
Georgopoulos and Osterholm are 2 of 65 new members who were chosen through a highly selective process. Membership in the Institute of Medicine is given to those who have contributed significantly to medical science, health care, and public health. MB

# New leaders, new energy in Pediatrics

ONE OF THE MEDICAL SCHOOL'S LARGEST departments, Pediatrics, is getting some fresh direction under the leadership of new head **John Schreiber, M.D., M.P.H.** Schreiber, who holds the Ruben-Bentson Chair in Pediatric Community Health, arrived on campus in August from Case Western Reserve School of Medicine in Cleveland. He earned his medical degree at Tulane University School of Medicine after completing a master's degree in public health and tropical medicine at Tulane.

John Schreiber, M.D.

Schreiber has a vision—and a passion—to achieve national recognition in the department's education, research, and patient care programs. He's now reinvigorating its research program while actively working to improve patient care. New clinical facilities are at the top of his agenda. "Minneapolis is a world-class city," he says, "and there needs to be a world-class facility to take care of children."

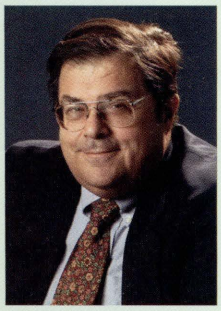


Mark Schleiss, M.D.

In January, the Pediatrics Department welcomed **Mark Schleiss, M.D.**, who was recruited from the University of Cincinnati to head the Pediatric Infectious Disease Division.

Schleiss, who holds the American Legion Chair in Pediatric Infectious Disease and Immunology, will be energizing research on a viral infection that leads to hearing loss in infants. He'll also have a role in strengthening the relationship among his colleagues in pediatric infectious diseases, pediatrics, medicine, microbiology, the Center for Immunology, and the School of Public Health. MB

## Cerra honored with lifetime achievement award



Frank Cerra, M.D., was honored on January 16 with a lifetime achievement award from the Society of Critical Care Medicine (SCCM). The SCCM gives this award annually to a member who has made major contributions to critical care medicine through advances in medical science, medical education, or medical care.

Cerra, the University's senior vice president for health sciences, has been a distinguished scientist, teacher, and leader in critical care research since joining the faculty in 1981. He was responsible for developing an integrated critical care service and for replacing an organ-based approach with a patient-based care system. It was one of the first programs of its kind in the nation. Cerra also holds six patents for critical-care innovations. MB

## Powell and Cerra tapped to lead at national level

Two influential national organizations devoted to academic medicine are looking to the University of Minnesota to fill some top leadership roles.

The Association of American Medical Colleges (AAMC) has found a new leader in Medical School Dean Deborah Powell, M.D. She was elected chair of the Council of Deans on November 30 and assumed leadership immediately.

In her new role, Powell is guiding the group in its mission to improve the nation's medical schools in terms of education, research, and patient care.

The Council of Deans is an association of medical school deans that identifies issues affecting academic medicine and develops strategies to help deans achieve their various missions. The AAMC represents all 125 accredited medical schools in the United States plus 17 accredited schools in Canada.

Frank Cerra, M.D., has been appointed chair-elect of another prominent organization, the Association of Academic Health Centers (AHC). Cerra is the University's senior vice president for health sciences and leader of its Academic Health Center.

AHC is a national, nonprofit organization that has served and represented academic health centers for more than 40 years. Currently, the group represents more than 100 institutions at major universities across the country. In his new role, Cerra will lead the 11-member board, which oversees the association's programs, strategies, and finances, starting in the fall of 2005. He currently serves as the group's associate chair for public health. MB

# Mentor program sparks meaningful connections

PHOTOS: TIM RUMMELHOFF

RIGHT Physician David Cline, '62, chats with first-year medical student Esther Kao.

BELOW First-year medical student Deborah Hatanpa visits with her mentor, physician Susan Roe.

THANKS TO A QUICK RESPONSE from alumni and community physicians, all Medical School students who signed up for the Connections mentoring program this year were quickly placed with mentors.

This year 96 students signed up to receive advice and guidance from practicing physicians throughout their years in medical school. Of the 96 mentors matched with students, 61 were Medical School alumni—M.D.'s, residents, fellows, or Ph.D.'s.

To give the students and their mentors a chance to meet, the Minnesota Medical Foundation held a kick-off breakfast for the Connections program on November 19 at the McNamara Alumni Center. Nearly 80 medical students and mentors attended.

Ted Thompson, M.D., director of clinical education for the Medical School, is a major supporter of the mentoring program. Students have told him that spending time with their mentors has helped shape their careers and has helped them get valuable experience in clinics. "It's been a very, very positive program, and students truly enjoy that opportunity," says Thompson.

In partnership with the Hennepin and Ramsey Medical Societies, all Twin Cities–area physicians are invited to participate. If you are interested in serving as a mentor for a medical student next fall, please contact Emily Heagle, director of alumni relations, at MAS@mmf.umn.edu, 612-624-9161, or 1-800-922-1663. MB

## Surprise! 1911 time capsule unearthed in Jackson Hall

Frank Cerra, M.D., started the new year with a look back—*way* back. On January 5, the University's senior vice president for health sciences carefully pried open a time capsule dating back to 1911. The dark metal box had been discovered about two months earlier by workers renovating Jackson Hall.

With U of M medical historian Jennifer Gunn at his side, Cerra lifted out several items, including local newspapers, a picture-book of the University, catalogs from its colleges, a book on medical teaching, and several Masonic books.

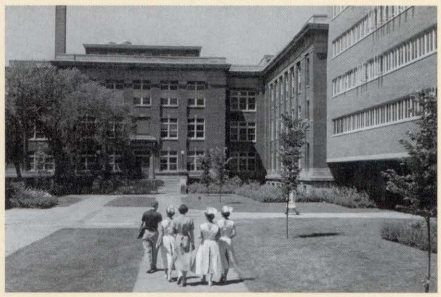


PHOTO: UNIVERSITY OF MINNESOTA ARCHIVES

Jackson Hall, circa 1955

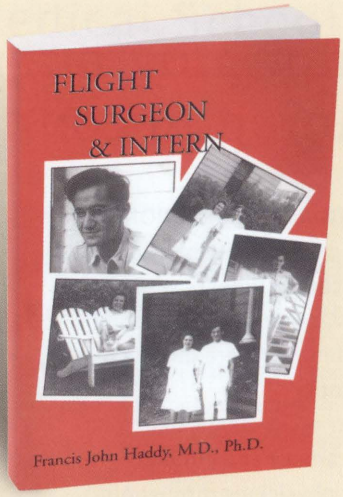
But the items of most interest were the rolled-up sketches by architect Cass Gilbert, the same man who designed Minnesota's state capitol.

Much of Gilbert's vision for the campus went unfulfilled. The renderings include overhead views of Northrop Mall and a proposed medical quadrant that would have included two L-shaped buildings north of two amphitheaters leading to the Mississippi River.

The time capsule was dated September 5, 1911, the same day the University's first hospital, Elliot Memorial, was dedicated. Jackson Hall was finished the following year.

Much of the time capsule's contents are now in the University Archives collection. MB

# Alumnus publishes book about military medicine, love




COURTESY OF NOBLE HOUSE

FRANCIS JOHN HADDY, M.D., Ph.D., never planned to write a book. But after half a century of looking at a stack of love letters from the post-World War II era, he decided to do something with them.

Haddy recently published *Flight Surgeon and Intern*, a 278-page story about the time he spent away from his new bride practicing medicine with the U.S. Army in Panama. The book includes daily narratives about life at the Rio Hato Airbase and how he thought everything he experienced would have been better if his wife were only there.

Haddy and his wife, Theresa Brey Haddy, M.D., are both graduates of the University of Minnesota Medical School. In fact, a classmate introduced them to each other in a rather unromantic setting: over a cadaver in their gross anatomy class. "She somehow figured that Terry and I belonged together, and she was right," he says.

The two had been married just 14 months when Francis was sent to Panama. He had finished medical school with a loan from the federal government, and he was to serve two years of active service as a medical officer to pay it back. While Francis traveled to the jungle, Terry stayed behind to finish her rotating internship at Minneapolis General Hospital.

Fifty years later, when Francis was ready to retire, he combined the love letters he and his wife exchanged with a little history and started to write *Flight Surgeon and Intern*. He wanted to record his experiences for his seven grandchildren, and he believes his classmates and colleagues will also enjoy reading the book and relating to his stories.

Francis Haddy has had plenty of practice writing scientific articles and book chapters—he has published more than 250 of them—but this is his first book.

After working at universities across the country, the Haddys have retired to Rochester, Minnesota. MB

Flight Surgeon and Intern *is available at local bookstores and through major Internet booksellers.*

## Save the date!

### MINNESOTA MEDICAL FOUNDATION GOLF CLASSIC

Monday, August 8, 2005
Midland Hills Country Club, St. Paul

Plan to join us for the 15th annual Golf Classic at Midland Hills Country Club. Money raised at the Golf Classic supports the University of Minnesota's medical education programs. Thanks to sponsors and participants, about $615,000 has been contributed to medical programs at the University since the first Golf Classic in 1991. MB

## PREVIOUS AWARD WINNER

HAROLD S. DIEHL AWARD

1962 Owen H. Wangensteen, '21
1963 Donald J. Cowling
Charles G. Sheppard, '35
1964 Vernon D. E. Smith, '30
1965 Karl W. Anderson, '23
1966 J. Arthur Myers, '20
1967 Theodore R. Fritsche, '30
1968 Walter H. Halloran, '15
Anderson C. Hilding, '18
Carl H. Holmstrom, '29
1969 Karl R. Lundeberg, '25
1970 Robert N. Barr, '30
LeRoy J. Larson, '20
1971 William C. Bernstein, '27
J. C. Grant, '42
1972 J. Richards Aurelius, '22
Barbara M. Puumala, '59
Marie Bepko Puumala
Reino Puumala
Ricard R. Puumala, '59

# It's nomination time for the 2005 Alumni Awards

IF YOU KNOW a graduate of the Medical School who deserves recognition, the Medical Alumni Society would like to know. Nominations are now being accepted for three awards: the Harold S. Diehl, the Distinguished Alumni, and the Early Distinguished Career awards. The awards will be presented May 20 at the annual alumni recognition banquet.

**The Harold S. Diehl Award** is presented to those who have made outstanding professional contributions throughout their careers. It's named in honor of the Medical School's fifth dean, Harold Sheely Diehl, M.D.

Criteria used in the selection process are as follows:

- ☐ Graduate of the University of Minnesota Medical School*
- ☐ Not currently engaged in an academic capacity*
- ☐ Outstanding contributions to the Medical School, the University, its alumni, and the community
- ☐ Significant experience in the medical service field or a related field

** preferred but not required*

The Society expanded its award program last year to recognize a greater number of deserving alumni and faculty members. This year will mark the second time for the Distinguished Alumni Award, which has replaced the Alumni Recognition Award, and the second time for the Early Distinguished Career Award.

**The Distinguished Alumni Award** recognizes Medical School alumni who have made outstanding contributions to their local, regional, or national community through medical practice, teaching, research, or other humanitarian activities. Nominees should be graduates of the University of Minnesota Medical School.

**The Early Distinguished Career Award** is given to a physician for exceptional accomplishments within 15 years of graduation from medical school.

Nominees should:

- ☐ Be academically affiliated with the University of Minnesota Medical School, either directly or as an affiliate educator for the Medical School
- ☐ Have made exceptional contributions to medicine or the Minnesota medical community or have exhibited exceptional and outstanding service to the University of Minnesota Medical School

Nominations for all three awards require a letter of nomination, supporting letters of recommendation, and a curriculum vitae. Nominations should be received by March 14.

Send materials to:

Medical Alumni Society
Awards Committee
McNamara Alumni Center
200 Oak Street SE, Suite 300
Minneapolis, MN 55455-2030

| | |
|---|---|
| 1973 | Phillip Halenbeck<br>Olga Hansen Litzenberg, '15 |
| 1974 | Ann Arnold<br>Roger A. MacDonald, '46<br>Carl O. Rice, '25<br>R. S. Ylvisaker, '26 |
| 1975 | Reuben Berman, '32<br>Bror F. Pearson, '31<br>Lawrence Richdorf, '20 |
| 1976 | Milton M. Hurwitz, '39<br>Leonard Lang, '28<br>Russell O. Sather, '32 |
| 1977 | Ruth E. Boynton, '20<br>Virgil J. P. Lundquist, '42 |
| 1978 | Lester H. Bendix, '28<br>Herman E. "Tiny" Drill, '29 |
| 1979 | Miland E. Knapp, '29<br>Harold E. Wilmot, '23 |
| 1980 | Helen L. Knudsen, '43<br>Donald E. Stewart, '37 |
| 1981 | Eva Jane (Ostergren) Larson, '38<br>Carl Ragnar Wall, '28 |
| 1982 | Stuart Lane Arey, '31<br>Kristofer Hagen, '42 |
| 1983 | John J. Eustermann<br>John J. Regan Sr., '43 |
| 1984 | Arnold S. Anderson, '43<br>John W. Anderson, '51 |
| 1985 | Kenneth W. Covey, '43<br>Frank E. Johnson, '43 |
| 1986 | A. Boyd Thomes, '42 |
| 1987 | Marcy L. Ditmanson, '54<br>Malcolm M. Fifield, '50 |
| 1988 | Chester A. Anderson, '44<br>Robert B. Howard, '44<br>Arnold J. Kremen, '37 |
| 1989 | Howard L. Horns, '43<br>Austin M. McCarthy, '42 |
| 1990 | M. Elizabeth "Peggy" Craig, '45<br>John P. Stapp, '43 |
| 1991 | Dorothy Bernstein<br>Irving C. Bernstein, '42 |
| 1992 | Frederic J. Kottke, '45<br>William A. O'Brien Jr., '46 |
| 1993 | John I. Coe, '45<br>Howard B. Burchell |
| 1994 | Tague Clement Chisholm<br>N. L. "Neal" Gault Jr., '50 |
| 1995 | Stanton A. Hirsh, '45<br>Melvin Sigel, '56 |
| 1996 | Stanley Goldberg, '56<br>Severin H. Koop Jr., '55 |
| 1997 | Joyce L. Funke, '50<br>Thomas A. Stolee, '58 |
| 1998 | Jesse E. Edwards<br>John B. Sanford, '48 |
| 1999 | B. J. Kennedy, '45<br>C. Walton Lillehei, '41<br>Ben P. Owens, '47 |
| 2000 | H. Mead Cavert, '50<br>Richard M. Magraw, '43 |
| 2001 | Arthur C. Aufderheide, '46<br>Mildred S. Hanson, '51 |
| 2002 | Henry Buchwald<br>William H. Knobloch |
| 2003 | Malcolm A. McCannel<br>Alfred F. Michael<br>John E. "Jack" Verby Jr. |
| 2004 | James G. Boulger<br>Robert L. Goodale Jr.<br>Naip Tuna |

ALUMNI RECOGNITION AWARD

| | |
|---|---|
| 1998 | June M. LaValleur, '87 |
| 1999 | Richard L. Stennes, '69 |
| 2000 | Paul S. Sanders, '70<br>Valerie K. Ulstad, '82 |
| 2001 | Charles I. Benjamin, '65 |
| 2002 | James H. House, '63<br>Audrey M. Nelson, '65 |
| 2003 | Michael A. Maddaus, '82<br>C. Gail Summers, '79 |

DISTINGUISHED ALUMNI AWARD

| | |
|---|---|
| 2004 | Michael B. Belzer, '74<br>Robert J. Desnick, '71 |

EARLY DISTINGUISHED CAREER AWARD

| | |
|---|---|
| 2004 | Gregory A. Plotnikoff, '89 |

## Mark your calendars for Reunion Weekend

If you graduated from the University of Minnesota Medical School in the class of 1945, 1950, 1955, 1965, 1970, 1975, 1980, or 1995, you're invited to this year's Reunion Weekend. Planned for May 20 and 21, this is a wonderful opportunity to reconnect with classmates and enjoy a host of other events, including:

- ☐ Alumni Day at the Medical School with tours, forums, and presentations by prominent faculty
- ☐ Stimulating CME opportunities
- ☐ Alumni recognition banquet
- ☐ Private class dinners at the McNamara Alumni Center

Alumni from all Medical School classes are welcome to attend Alumni Day and the alumni recognition banquet on Friday, May 20. Private dinners for the celebrating classes are Saturday, May 21.

If you are a member of a celebrating reunion class, you should have received a reunion questionnaire to be used in creating a class memory book. You also may fill out your questionnaire online at www.mmf.umn.edu/alumni. You can expect reunion and registration materials to arrive in mid-April.

Let us know now what you want to see at the 2005 reunion by taking the Medical Alumni Society reunion poll. Go to www.mmf.umn.edu/reunions for details. MB

**QUESTIONS** Call Emily Heagle at 612-624-9161, Sue Clark at 612-626-0619, or the alumni office at 1-800-922-1663. E-mail inquiries may be sent to MAS@mmf.umn.edu.

## Remembering Ancel Keys

THE UNIVERSITY of Minnesota has lost a prominent public health leader who had a great impact on the Medical School and the world.

Ancel Keys, Ph.D., the scientist who invented the K ration and pioneered studies linking high-fat diets to heart disease, died of natural causes November 20 at the age of 100.

Keys was a professor of physiology at the University from 1936 to 1972. In 1940 he founded the Laboratory of Physiological Hygiene, which was built under the stands of Memorial Stadium. His lab paved the way for the School of Public Health's Division of Epidemiology, which quickly became a research and training center in the new field.


Keys worked with the army during World War II to develop rations for soldiers to carry in combat. They were marked with the letter K, for Keys.

After conducting a groundbreaking study on the eating habits of Minnesota businessmen in the 1950s, Keys linked fatty diets and cholesterol to heart disease. He actively promoted the Mediterranean diet, heavy on fruits and vegetables and light on fats and meats. With his wife's help, Keys wrote a best-selling book on his research, called *Eat Well and Stay Well*. He appeared on the cover of *Time* magazine in 1961.

Keys is survived by his wife, Margaret, two children, eight grandchildren, and six great-grandchildren. MB

# In Memoriam

**ROBERT B. BREITENBUCHER, M.D.,** Class of 1946, Minneapolis, died October 3 at age 82. He served in the army during the Korean War. He practiced internal medicine in Minneapolis and was a clinical instructor at the University of Minnesota. He specialized in infectious diseases until he switched to geriatric care in the late 1970s and became director of the extended care program at Hennepin County Medical Center in 1977. He is survived by his wife, Lorraine, and seven children.

**S. PAUL EHRLICH, M.D.,** Class of 1957, Delray Beach, Florida, died January 6 at age 72. He served as acting surgeon general from 1973 to 1977 under Presidents Nixon, Ford, and Carter and as U.S. representative to the World Health Organization. He was part of the Public Health Service for 25 years, receiving the group's Outstanding Service Medal, Distinguished Service Medal, and Meritorious Service Medal. He was also deputy director of the Pan American Health Organization. He is survived by his wife, Geraldine, and three children.

**CARL D. EKLUND, M.D.,** Class of 1949, Duluth, Minnesota, died September 4 at age 87. He had his own practice and was on staff at the three Duluth hospitals. He served as the St. Louis County coroner for a period of time. He is survived by his wife, Evalyn, and three children.

**LOUIS L. FLYNN Jr., M.D.,** Class of 1944, St. Paul, died September 13 at age 84. He served in the army in World War II and returned to practice psychiatry in St. Paul. He was preceded in death by wives Cathy and Rita. He is survived by his third wife, Mary Clare, 11 children, and 15 stepchildren.

**ORLEY W. FOSTER, M.D.,** Class of 1943, Boca Raton, Florida, died January 11, 2004, at age 90. He was a retired surgeon. He was preceded in death by his wife, Nellie. He is survived by two children.

**WARREN F. HOFFMAN, M.D.,** Class of 1962, Marina del Rey, California, died September 5 at age 67. He practiced general and vascular surgery for 37 years in California. He is survived by his wife, Carole, and two children.

**CHARLES F. KELLY, M.D.,** Class of 1951, Edina, Minnesota, died August 26 at age 82. He served in the army during World War II. He cofounded Emergency Physicians Professional Association and was on staff at several hospitals before retiring in 1988. He was preceded in death by two sons. He is survived by his wife, Kathleen, and five children.

**JAY L. KEVERN, M.D.,** Class of 1944, Henning, Minnesota, died August 28 at age 88. He served in the military in World War II. He practiced in Henning and established the Coronary Care Unit at Tri-County Hospital in Wadena. He is survived by his wife, Alice, and four children.

**PAUL J. KUSHNER, M.D.,** Class of 1948, Laguna Niguel, California, died August 3, 2003 at age 81. He served in the army during World War II and in Korea after medical school. He practiced anesthesiology for 40 years in New York and California. He is survived by three children.

**LOWELL L. KVAM, M.D.,** Class of 1959, Punta Gorda, Florida, died October 19 at age 71. He practiced pathology in St. Paul and became director of pathology at St. Joseph's and St. John's Hospitals. He was preceded in death by a son. He is survived by his wife, Carolyn, and a son.

**RICHARD B. LANGER, M.D.,** Class of 1964, Molokai, Hawaii, died September 11 at age 65. He served in the military in Vietnam. He was a family physician in Molokai, Hawaii, for over 30 years. He was preceded in death by his wife, Ruth. He is survived by a son.

**RICHARD O. LEAVENWORTH Jr., M.D.,** Class of 1950, Lake Minnetonka, Minnesota, died October 31 at age 80. He practiced ophthalmology at Park Nicollet Medical Center for 31 years. He is survived by his wife, Anne, and three children.

**ALEXANDER D. LOWE, M.D.,** Class of 1956, South St. Paul, died September 6 at age 75. He had his own practice in South St. Paul for almost 40 years. He is survived by his wife, Marlys, and six children.

**CHARLES C. MERCHANT, M.D.,** Class of 1946, Lakeland, Florida, died March 10 at age 79. He built and operated a hospital in Tezpur, India for 11 years, until 1960. For most of his career he was a general surgeon in Lakeland, FL. He is survived by his wife, Mayburn, and six children.

**ROBERT L. MERRICK, M.D.,** Class of 1943, North Oaks, Minnesota, died October 16 at age 89. He practiced neurosurgery in St. Paul for 30 years. He is survived by his wife, Charlotte Merrick, M.D., Class of 1943, and two children.

**EMERSON L. MEYER, M.D.,** Class of 1938, Healdsburg, California, died October 22 at age 94. He served in the army during World War II. He practiced medicine in Healdsburg until his retirement in 1972. He is survived by his wife, Addie Marie, and two children.

**STEVEN J. MILLER, M.D.,** Class of 1985, Edina, Minnesota, died August 30 at age 46. He practiced radiology at Abbott Northwestern Hospital in Minneapolis and was director of the radiology program at Regina Hospital in Hastings, Minnesota. He is survived by his wife, Nancy, and six children.

**MELVIN G. OPPEN, M.D.,** Class of 1950, Minnetonka, Minnesota, died September 12 at age 79. He served in the air force. He practiced family medicine at the Minnetonka Clinic for 25 years. He is survived by his wife, Phyllis, and three children.

**BROR F. PEARSON, M.D.**, Class of 1931, Mercer Island, Washington, died August 24 at age 98. He practiced family medicine in Shakopee, Minnesota, for 42 years. He served as a civilian member of a navy medical team during the Vietnam War. Dr. Pearson helped start a leprosarium in Zambia, and worked with the Catholic Medical Mission Board in Latin America and Africa. He was a volunteer physician at Sage Memorial Hospital in Ganado, Arizona. In 1975, the Medical Alumni Society awarded Dr. Pearson the Harold S. Diehl Award. B. F. Pearson Elementary School in Shakopee, Minnesota is named for him. He was preceded in death by his first wife, Elizabeth, and his second wife, Dora Pearson, M.D. He is survived by four children.

**JAMES H. PULFORD, M.D.**, Class of 1943, Salinas, California, died September 28 at age 86. He served in the army in World War II. He practiced urology in Salinas, California, for 36 years and was chief of staff and medical director of Salinas Valley Memorial Hospital. He was preceded in death by a son. He is survived by his wife, Edith, and three children.

**THOMAS K. RUCKER, M.D.**, Class of 1956, Minneapolis, died October 25 at age 74. He is survived by his wife, Ann, and two children.

**JOHN J. SATORY, M.D.**, Class of 1938, La Crosse, Wisconsin, died March 25 at age 94. He served in the army during World War II. He practiced surgery in La Crosse beginning in 1946. He founded the Grandview Clinic in 1948 and served as director, chief of staff, and chief surgeon. He was preceded in death by his first wife, Mina. He is survived by his second wife, Irene, and 10 children and stepchildren.

**HOWARD A. SHAW, M.D.**, Class of 1940, Inver Grove Heights, Minnesota, died October 17 at age 91. He served in the air force during World War II. He practiced ophthalmology for 35 years. He was a clinical professor in the Department of Ophthalmology and received its Distinguished Service Award in 1977. He was chief of ophthalmology at Hennepin County Medical Center for over a decade. He was preceded in death by his first wife, Mary Ann, and his second wife, Dorothy. He is survived by two children and two stepchildren.

**BERNARD E. STATLAND, M.D., Ph.D., J.D.**, Class of 1966, Rockville, Maryland, died October 19 at age 62. Most recently, he was a lawyer specializing in health law and food and drug law. He had previously worked as a clinical laboratory director and in academic positions at major university medical centers. He also had been CEO and medical director of the Consolidated Laboratory Network for the North Shore-Long Island Jewish Health Care System; medical director at Roche Diagnostics; CEO and president of the National Reference Laboratory at the National Health Laboratories; chair of pathology and laboratory medicine at Clarian Health System in Indianapolis; and director of the office of device evaluation in the FDA's Center for Devices and Radiological Health. He is survived by his wife, Alexandra, and two children.

**LEONARD A. TITRUD, M.D., Ph.D.**, Class of 1935, Minneapolis, died October 18 at age 93. He served in the army during World War II and remained in the army reserve until 1966. He practiced medicine in Minneapolis until 1985 and served on the staffs of several Twin Cities hospitals. He was a clinical professor of neurological surgery and taught for over 23 years. He was preceded in death by his wife, Geraldine. He is survived by four children.

**ROBERT B. TUDOR, M.D.**, Class of 1937, Bismarck, North Dakota, died May 22 at age 91. He practiced pediatrics in Bismarck. He is survived by his wife, June, and three children.

**GERALD J. VOSIKA, M.D.**, Class of 1967, Moorhead, Minnesota, died October 27 at age 62. He was professor of hematology at the University of North Dakota and head of the Oncology Department at the Veterans Hospital. He was preceded in death by four children. He is survived by his wife, Karen, and three children.

Through [French's] ceaseless efforts, the treatment of patients with brain tumors and stroke was greatly improved, a generation of neurosurgeons was trained, and the University of Minnesota's status as a world-class academic health center was assured.

– Stephen Haines, M.D.
Head, Department of Neurosurgery

# Neurosurgery pioneer Lyle French helped forge tradition of excellence

Lyle A. French, M.D., Class of 1939, a pioneer of neurosurgery and the University of Minnesota's first vice president for health sciences, died unexpectedly October 19. He was 89.

French saw neurosurgery at the University through many changes in his 42 years as a student, professor, chief of medical staff, and administrator. He trained under William Peyton, M.D., the first director of the neurosurgical division of the Department of Surgery.

After 12 years of teaching and Peyton's retirement, French was appointed director of the division in 1960. He was the first clinical scientist to document the value of dexamethasone for treating cerebral edema, and his team made other significant advances in research and clinical activities.

By 1968, neurosurgery at the Medical School had expanded, and the University established neurosurgery as its own department. French was its first leader. He inspired many young neurosurgeons to pursue academic careers and trained 11 eventual neurosurgical department chairs.

A couple of years after neurosurgery became a department, the University responded to a growing demand for teamwork among health professionals and grouped the health sciences together. French became the University's first vice president for health sciences and led the newly organized grouping of the Medical School, School of Public Health, School of Nursing, College of Pharmacy, School of Dentistry, and College of Veterinary Medicine.

In the years following French's promotion, the Department of Neurosurgery kept advancing. The team established a division of pediatric neurosurgery and collaborated with other departments to start a spine center. It also developed programs for epilepsy, neuro-oncology, skull base surgery, and spinal surgery.

Today the department provides a wide range of services and emphasizes treating patients with brain tumors, epilepsy, movement disorders, cerebrovascular disease, spine disorders, and pediatric brain disorders. The journal *Surgical Neurology* consistently ranks it among the 10 best programs in the country for neurosurgical training, and *U.S. News & World Report* ranks it one of the nation's top 20 neurosurgery programs.

Stephen J. Haines, M.D., is the current head of the Department of Neurosurgery and holder of the first Lyle A. French Chair in Neurosurgery. "The University of Minnesota and the world of neurosurgery have lost one of the greatest leaders, innovators, and educators of our time," says Haines. "Through his ceaseless efforts, the treatment of patients with brain tumors and stroke was greatly improved, a generation of neurosurgeons was trained, and the University of Minnesota's status as a world-class academic health center was assured."

French is survived by his wife Gene, three children, and several grandchildren. MB

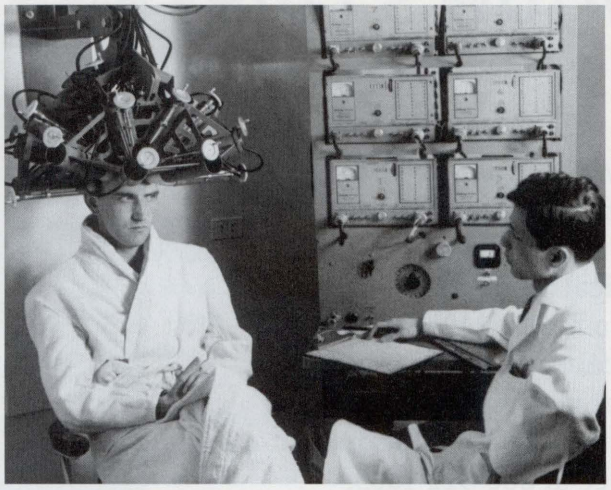


PHOTO: UNIVERSITY OF MINNESOTA ARCHIVES

Shelley Chou, M.D., examines a patient wearing an early 1950s version of positron-emission tomography equipment. More commonly known as the PET scan, this technology has changed a great deal in the last 50 years.

# Foundation board elects new leadership and three new trustees

At its annual meeting on October 25, the Minnesota Medical Foundation elected four current board members to new positions of leadership. Beth Erickson, previously the board vice chair and chair of the planning committee, was named board chair; John M. Murphy Jr., former treasurer and chair of the finance and audit committee ascended to the position of board vice chair; Paul Citron retained his position as board secretary; and George E. Maas was elected treasurer and chair of the finance and audit committee.

The board also welcomed three new trustees—Catherine L. Agee; Joel L. Boyd, M.D.; and Don J. Hodapp—each elected to serve a four-year term.

The board is responsible for providing overall guidance for the Foundation as it pursues its mission of supporting research and education at the University of Minnesota Medical School, School of Public Health, Cancer Center, and other related centers and programs. For more information, see the roster on the following page or go to www.mmf.umn.edu.

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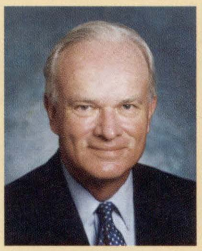

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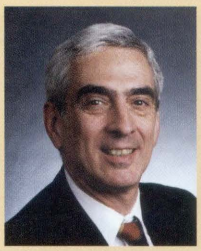
VICE CHAIR
*Managing Partner, Somerset Asset Management LLC*



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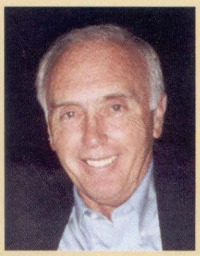
*Vice President, Science and Technology, Medtronic, Inc.*



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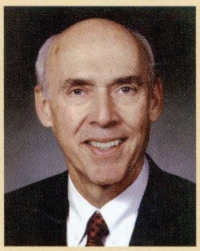
*Orthopaedic surgeon and team physician, Minnesota Wild and Lynx*



Don J. Hodapp
*Retired executive, Hormel Foods Corp.*

# Minnesota Medical Foundation

The Minnesota Medical Foundation is a nonprofit organization that provides support for health-related research and education at the University of Minnesota Medical School and School of Public Health.

For more information about the Minnesota Medical Foundation or to update your address, please contact us at:

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McNamara Alumni Center
University of Minnesota
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612-625-1440
www.mmf.umn.edu

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